[Annex No.21 Form]

Application Form for the Re-examination of Pharmaceuticals	Processed within 150 days

Application no.		Application date		Issue date	

Applicant	Business license (Report) no.			
	Name of Manufacturing (business) site	Allergan Korea Ltd.		
	Location of Manufacturing (business) site	14F, East Building, GT Tower, Seochodaero 411, Seocho-gu, Seoul		
	Representative			
Manufacturer	Name of manufacturer	Allergan Pharmaceuticals Ireland	Country of manufacture	Ireland
	Location	Allergan Pharmaceuticals Ireland, Castlebar Road, Westport County Mayo, Ireland		
Product on re-examination		Botox Inj.(Clostridium Botulinum Toxin Type A)	Re-examination Period	31 Aug 2012 - 30 Aug 2016 (4 Years)
License no.			Date of Approval	16 Apr 2008

Result of study

Surveillance period and number of subjects

Period: 31 Aug 2012 - 30 Aug 2016

	Neurogenic Detrusor Overactivity	Overactive Bladder	Sum
No. of subjects whose CRF was retrieved	173	564	739*
No. of subjects included in safety evaluation	161	525	686
No. of subjects included in effectiveness evaluation	134	478	612

* A total number of 739 subjects whose CRFs were retrieved includes 2 subjects who were excluded in P4 study due to screening failure with unknown indications.

Overview of study results and analysis	Refer to re-examination report
Production (import) performance (shipments)	Refer to section "E. Delivery Performance" of re-examination report

The undersigned applies for the re-examination of the above pharmaceutical product under Article 32 of the Pharmaceutical Affairs Act and Article 23, Paragraph 1 of the Regulations on Safety of Pharmaceuticals, etc.

30 November 2016

To the Minister of the Ministry of Food and Drug Safety

Attachments	Fees
1. Safety and effectiveness data from results of domestic PMS 2. Data related to safety such as the occurrence of adverse events in domestic and foreign reports other than 1 3. Data reported regarding safety such as domestic and foreign literatures and academic information 4. Data on selling in domestic and foreign countries and approval status in foreign countries	Amount stated in the notification by MFDS Minister

Post-marketing Surveillance Re-examination Report on Botox® Inj. (Neurogenic Detrusor Overactivity and Overactive Bladder)

(Botox Inj., Clostridium Botulinum Toxin Type A)

Re-examination Period: 31 Aug 2012 ~ 30 Aug 2016

Allergan Korea Ltd.

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A. Neurogenic Detrusor Overactivity

Ⅰ. General Matters of Investigation (Neurogenic Detrusor Overactivity)

1. General Matters of Investigation (Neurogenic Detrusor Overactivity)

1.1 Re-examination period (Neurogenic Detrusor Overactivity)

31 Aug 2012 ~ 30 Aug 2016

1.2 Number of subjects (Neurogenic Detrusor Overactivity)

During the re-examination period, case report forms (CRFs) were collected from a total of 173 subjects. Among the subjects, 161 subjects were included in the safety evaluation, except 5 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), and 1 subject who violate the dosage (ie, subject received an unapproved dosage). Among the safety population, 134 subjects were included in the effectiveness evaluation, except 27 subjects whose record ICIQ Score at baseline or follow-up on the CRF are not completed.

Number of subjects whose CRFs were retrieved	173
Number of subjects included in safety evaluation	161
Number of subjects included in effectiveness evaluation	134

Number of sites	From 31 Aug 2012 to 30 Aug 2016, CRFs were collected from 173 subjects by 22 investigators in 21 hospitals.
Method of investigation	This PMS was done in a manner that subjects who received Botox Inj. following the signed date were asked to successively participate in the PMS, up to the requested number of subjects, and it was pooled with post-marketing clinical tiral (Phase 4) data for analysis.
CRF format	Appendix 2
Point to be investigated with priority	There was no specific focus in this surveillance since no specific issues had been identified in clinical study results during the development phase as well as in post-marketing experiences in other countries. During this re-examination period, very rarely occurring adverse events (AEs) and unexpected AEs of which causal relationship to the study drug had not been established

	were to be monitored and investigated with particular interest.

1.3 PMS management chart (Neurogenic Detrusor Overactivity)

Site									

Site									

* CRFs of subjects in the sites were collected through post-marketing clinical trial (Phase 4).
****** Contracted number of cases includes both Neurogenic Detrusor Overactivity and Overactive Bladder.

Ⅱ. Overview of PMS Results (Neurogenic Detrusor Overactivity)

2. Overview of PMS Results (Neurogenic Detrusor Overactivity)

2.1 Overview and purpose of PMS (Neurogenic Detrusor Overactivity)

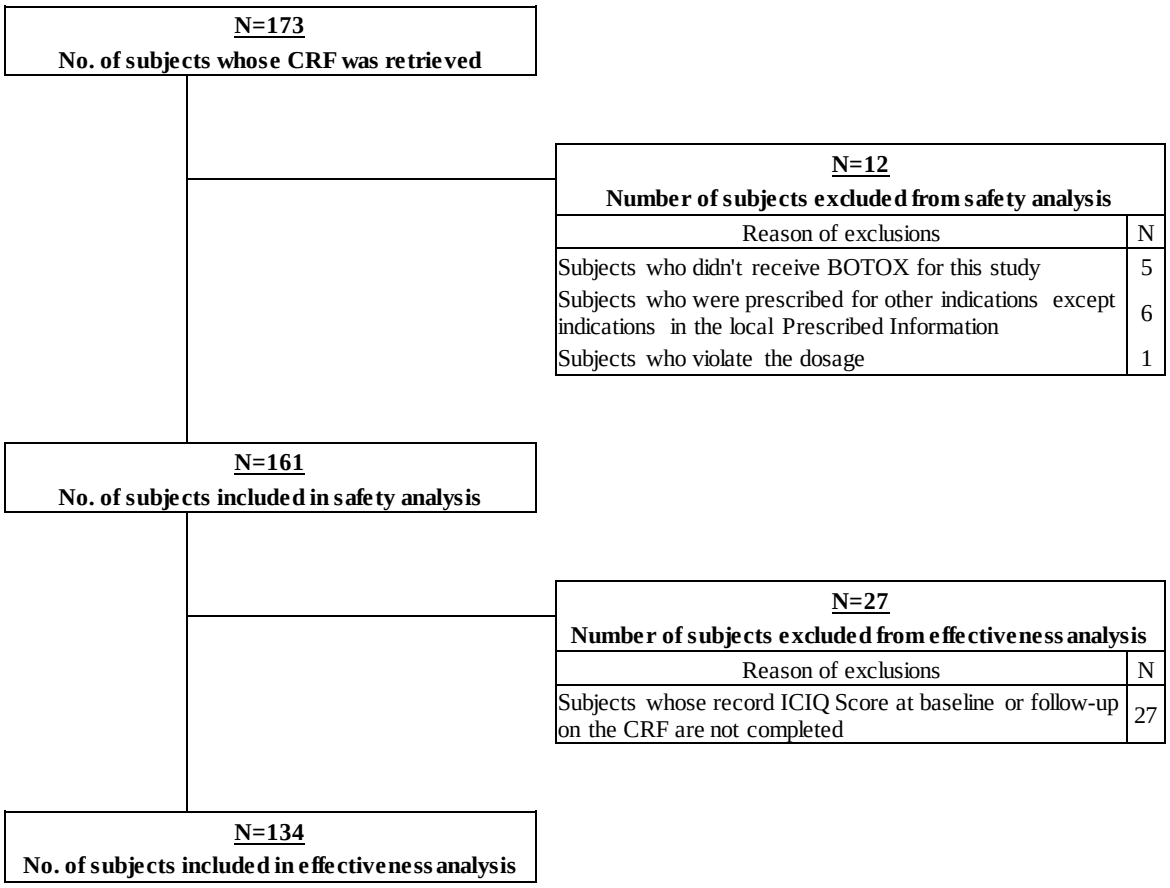
This PMS was conducted to examine whether AEs and SAEs occurred, frequency of AEs and the variations, and factors likely to influence the safety and effectiveness under the post-marketing uses of BOTOX in subjects of 'Treatment of urinary incontinence caused by Neurogenic Detrusor Overactivity (e.g. spinal cord injury, multiple sclerosis) in adults aged 18 years or over who have an inadequate response to or are intolerant of an anticholinergic therapy (hereafter 'Neurogenic Detrusor Overactivity') who received Botox Inj. (hereafter the 'study drug').

This PMS investigated subjects' fundamental demographic data, follow-up duration, past treatment history, medical history, special population, information of study drug administration, use of clean intermittent catheterization, safety, and effectiveness. This PMS was planned to investigate all types of AEs, which were incurred during the investigation period including AEs whose causal relationship to BOTOX Inj. has not been established yet and unexpected AEs/ADRs. The purpose of this study was to evaluate the safety and effectiveness of BOTOX for the treatment of NDO through active surveillance under routine clinical practice after the launch of BOTOX in Korea.□

2.2 Analysis set of PMS (Neurogenic Detrusor Overactivity)

During this PMS, CRFs were collected from 173 subjects. Among the subjects, 161 subjects were included in the safety evaluation, except 5 subjects who didn’t receive Botox for this study due to consent withdrawal or other reasons, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), and 1 subject who violate the dosage (ie, subject received an unapproved dosage). Among the safety population, 134 subjects were included in the effectiveness evaluation, except 27 subjects whose ICIQ Score at baseline or follow-up on the CRF are not completed (Figure 1).

Figure 1. Analysis set of PMS (Neurogenic Detrusor Overactivity)



2.3 Fundamental demographic data of subjects (Neurogenic Detrusor Overactivity)

2.3.1 All subjects

Of 173 subjects with CRFs collected, the mean age was 51.35±14.47 years, ranged from 18 to 86 years of age. The largest subject age group was '< 50 years' in 40.46% (70/173 subjects), followed by '≥ 50 years to < 60 years ' in 28.32% (49/173 subjects), '≥ 60 years to < 70 years ' in 20.23% (35/173 subjects), and '≥ 70 years' in 10.98% (19/173 subjects) (Table 1).

In all subjects, 'Male' accounted for 73.99% (128/173 subjects) and 'Female' accounted for 26.01% (45/173 subjects) (Table 1).

In all subjects, the mean height was 167.63±8.58 cm, ranged from 140.00 to 185.00 cm (Table 1).

In all subjects, the mean body weight was 64.75±10.21 kg, ranged from 39.00 to 90.00 kg (Table 1).

When classifying all subjects by treatment setting, 'Outpatient' was 70.52% (122/173 subjects) and 'Inpatient' was 29.48% (51/173 subjects) (Table 1).

The mean duration after diagnosis in all subjects was 11.16±10.86 years and the most common underlying neurologic condition (multiple counting allowed) was 'Spinal Cord Injury' in 92.49% (160/173 subjects), followed by 'Other' in 4.62% (8/173 subjects) and 'Multiple Sclerosis' in 3.47% (6/173 subjects). Underlying conditions belonging to 'Other' included 'Cerebral infarction' and 'stroke' (Table 1).

Among female subjects, there was no pregnant subject (Table 1).

Table 1. Demographic data in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Age	mean±std (years)	51.35± 14.47
	median	54.00
	min ~ max	18.00~ 86.00
	< 50 years	70(40.46)
	≥ 50 years to < 60 years	49(28.32)
	≥ 60 years to < 70 years	35(20.23)
	≥ 70 years	19(10.98)
	Total	173(100.00)
Sex	Male	128(73.99)
	Female	45(26.01)
	Total	173(100.00)
Height	n	172
	mean±std (cm)	167.63± 8.58
	median	170.00
	min ~ max	140.00~ 185.00
Weight	n	173
	mean±std (kg)	64.75± 10.21
	median	65.00
	min ~ max	39.00~ 90.00
Treatment Setting	Outpatient	122(70.52)
	Inpatient	51(29.48)
	Total	173(100.00)
Currently pregnant	Yes	0(0.00)
	No	173(100.00)
	Total	173(100.00)
Duration since NDO diagnosis	n	173
	mean±std (years)	11.16± 10.86
	median	7.00
	min ~ max	0.00~ 73.00
Underlying neurologic condition§ * for patients with NDO Overlapped¶	Multiple Sclerosis	6(3.47)
	Spinal Cord Injury	160(92.49)
	Other	8(4.62)
	Total	173(100.00)

The denominator is number of total subjects.

¶ The same subject may appear in different categories.

§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).

Unkown: 1 (Height)

2.3.2. Safety population

Of 161 subjects in the safety population, the mean age was 51.41±14.22 years, ranged from 18 to 86 years of age. The largest subject age group was '< 50 years' in 39.13% (63/161 subjects), followed by '≥ 50 years to < 60 years' in 29.81% (48/161 subjects), '≥ 60 years to < 70 years' in 21.12% (34/161 subjects), and '≥ 70 years' in 9.94% (16/161 subjects) (Table 2).

In the safety population, 'Male' accounted for 77.02% (124/161 subjects) and 'Female' accounted for 22.98% (37/161 subjects) (Table 2).

In the safety population, the mean height was 168.09±8.29 cm, ranged from 140.00 to 185.00 cm (Table 2).

In the safety population, the mean body weight was 64.77±10.01 kg, ranged from 39.00 to 90.00 kg (Table 2).

When classifying safety population by treatment setting, 'Outpatient' was 72.05% (116/161 subjects) and 'Inpatient' was 27.95% (45/161 subjects) (Table 2).

The mean duration after diagnosis in the safety population was 11.32±10.91 years and the most common underlying neurologic condition (multiple counting allowed) was 'Spinal Cord Injury' in 96.89% (156/161 subjects), followed by 'Multiple Sclerosis' in 3.11% (5/161 subjects) and 'Others' in 0.62% (1/161 subjects) (Table 2).

Among female subjects, there was no pregnant subject (Table 2).

Table 2. Demographic data in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Age	mean±std (years)	51.41± 14.22
	median	54.00
	min ~ max	18.00~ 86.00
	< 50 years	63(39.13)
	≥ 50 years to < 60 years	48(29.81)
	≥ 60 years to < 70 years	34(21.12)
	≥ 70 years	16(9.94)
	Total	161(100.00)
Sex	Male	124(77.02)
	Female	37(22.98)
	Total	161(100.00)
Height	n	160
	mean±std (cm)	168.09± 8.29
	median	170.00
	min ~ max	140.00~ 185.00
Weight	n	161
	mean±std (kg)	64.77± 10.01
	median	65.00
	min ~ max	39.00~ 90.00
Treatment Setting	Outpatient	116(72.05)
	Inpatient	45(27.95)

		Total n(%)
	Total	161(100.00)
Currently pregnant	Yes	0(0.00)
* for female	No	37(100.00)
	Total	37(100.00)
Duration since NDO diagnosis	n	161
	mean±std (years)	11.32± 10.91
	median	7.00
	min ~ max	0.00~ 73.00
Underlying neurologic condition§	Multiple Sclerosis	5(3.11)
* for patients with NDO	Spinal Cord Injury	156(96.89)
Overlapped¶	Other	1(0.62)
	Total	161(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).
Unkown: 1 (Height)

12 subjects were excluded in the safety evaluation for the following reasons: 5 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), and 1 subject who violate the dosage (ie, subject received an unapproved dosage).

2.4 Follow-up duration (Neurogenic Detrusor Overactivity)

2.4.1 All subjects

During the PMS period, the mean follow-up duration in all subjects was 51.40±26.12 days (Table 3).

Table 3. Follow-up duration in all subjects (Neurogenic Detrusor Overactivity)

	Total (N=173)
n	168
mean±std (days)	51.40± 26.12
median	42.00
min ~ max	27.00~ 183.00

Length of follow-up = Date of follow-up - Date of initial visit + 1
Missing: 5

2.4.2. Safety population

During the PMS period, the mean follow-up duration in the safety population was 51.32±26.26 days (Table 4).

Table 4. Follow-up duration in the safety population (Neurogenic Detrusor Overactivity)

	Total (N=161)
n	161
mean±std (days)	51.32± 26.26
median	42.00
min ~ max	27.00~ 183.00

Length of follow-up = Date of follow-up - Date of initial visit + 1

2.5 Past treatment history (Neurogenic Detrusor Overactivity)

2.5.1 All subjects

In all subjects, 98.84% (170/172 subjects) had received anticholinergic therapy, 1.16% (2/172 subjects) had sacral neuromodulation therapy, and 7.56% (13/172 subjects) had used the study drug or other botulinum toxin (Table 5).

Table 5. Past treatment history in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Previous Anticholinergic Therapy	Yes	170(98.84)
	No	2(1.16)
	Total	172(100.00)
Previous Use of Sacral Neuromodulation Therapy	Yes	2(1.16)
	No	170(98.84)
	Total	172(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	13(7.56)
	None	159(92.44)
	Total	172(100.00)

The denominator is number of total subjects.
Missing: 1

2.5.2. Safety population

In the safety population, 99.38% (160/161 subjects) had received anticholinergic therapy, 0.62% (1/161 subjects) had sacral neuromodulation therapy, and 7.45% (12/161 subjects) had used the study drug or other botulinum toxin (Table 6).

Table 6. Past treatment history in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Previous Anticholinergic Therapy	Yes	160(99.38)
	No	1(0.62)
	Total	161(100.00)

		Total n(%)
Previous Use of Sacral Neuromodulation Therapy	Yes	1(0.62)
	No	160(99.38)
	Total	161(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	12(7.45)
	None	149(92.55)
	Total	161(100.00)

The denominator is number of total subjects.

2.6 Medical history (Neurogenic Detrusor Overactivity)

2.6.1. All subjects

In all subjects, 75.00% (129/172 subjects) had medical history including surgeries and complications of underlying diseases (Table 7).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 40.31% (52/129 subjects), followed by 'Diseases of the nervous system' in 32.56% (42/129 subjects) and 'Factors influencing health status and contact with health services' in 26.36% (34/129 subjects) (Table 7).

In total, 5.20% (9/173 subjects) of subjects had allergy history (Table 7).

When analyzing the type of allergy history, 'Factors influencing health status and contact with health services' acoounted for 77.78% (7/9 subjects), followed by 'Injury, poisoning and certain other consequences of external causes' in 22.22% (2/9 subjects); the allergens included 'carbamazepine', 'ceftriaxone', and 'citopcin' (Table 7).

Table 7. Medical history in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	129(75.00)
	None	43(25.00)
	Total	172(100.00)
	Details for Medical History by dictionary (Overlapped¶)	
	Diseases of the circulatory system	52(40.31)
	Factors influencing health status and contact with health services	34(26.36)
	Endocrine, nutritional and metabolic diseases	32(24.81)
	Diseases of the genitourinary system	29(22.48)
	Diseases of the digestive system	33(25.58)
	Diseases of the musculoskeletal system and connective tissue	20(15.50)
	Neoplasms	12(9.30)
	Mental and behavioural disorders	15(11.63)
	Diseases of the nervous system	42(32.56)
	Diseases of the respiratory system	10(7.75)
	Diseases of the eye and adnexa	5(3.88)
	Injury, poisoning and certain other consequences of external causes	12(9.30)
	Certain infectious and parasitic diseases	3(2.33)

		Total n(%)
	Diseases of the skin and subcutaneous tissue	11(8.53)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2(1.55)
	Congenital malformations, deformations and chromosomal abnormalities	1(0.78)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	17(13.18)
History of Allergies	Yes	9(5.20)
	None	164(94.80)
	Total	173(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	7(77.78)
	Injury, poisoning and certain other consequences of external causes	2(22.22)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Missing: 1 (Medical History, Including Surgeries and Complications of Underlying Diseases)

2.6.2. Safety population

In the safety population, 73.91% (119/161 subjects) had medical history including surgeries and complications of underlying diseases (Table 8).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 37.82% (45/119 subjects), followed by 'Diseases of the nervous system' in 32.77% (39/119 subjects) and 'Diseases of the digestive system' in 26.89% (32/119 subjects) (Table 8).

In total, 5.59% (9/161 subjects) of subjects had allergy history (Table 8).

When analyzing the factors causing allergy, 'Factors influencing health status and contact with health services' accounted for 77.78% (7/9 subjects), followed by 'Injury, poisoning and certain other consequences of external causes' in 22.22% (2/9 subjects) (Table 8).

Table 8. Medical history in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	119(73.91)
	None	42(26.09)
	Total	161(100.00)
	Details for Medical History by dictionary (Overlapped¶)	
	Diseases of the circulatory system	45(37.82)
	Factors influencing health status and contact with health services	29(24.37)
	Endocrine, nutritional and metabolic diseases	29(24.37)
	Diseases of the genitourinary system	26(21.85)
	Diseases of the digestive system	32(26.89)
	Diseases of the musculoskeletal system and connective tissue	16(13.45)
	Neoplasms	10(8.40)
	Mental and behavioural disorders	13(10.92)

		Total n(%)
	Diseases of the nervous system	39(32.77)
	Diseases of the respiratory system	9(7.56)
	Diseases of the eye and adnexa	2(1.68)
	Injury, poisoning and certain other consequences of external causes	12(10.08)
	Certain infectious and parasitic diseases	3(2.52)
	Diseases of the skin and subcutaneous tissue	11(9.24)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2(1.68)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	14(11.76)
History of Allergies	Yes	9(5.59)
	None	152(94.41)
	Total	161(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	7(77.78)
	Injury, poisoning and certain other consequences of external causes	2(22.22)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10

2.7 Concomitant medications (Neurogenic Detrusor Overactivity)

2.7.1. All subjects

Subjects who received concomitant medications accounted for 98.26% (169/172 subjects) (Table 9).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 86.98% (147/169 subjects), followed by 'Central Nervous System' in 72.78% (123/169 subjects) and 'Gastrointestinal & Hepatobiliary System' in 66.27% (112/169 subjects) (Table 9).

Table 9. Concomitant medications in all subjects (Neurogenic Detrusor Overactivity)

	Total n(%)
Yes	169(98.26)
No	3(1.74)
Total	172(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	147(86.98)
Anaesthetics - Local & General	147(86.98)
Central Nervous System	123(72.78)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	40(23.67)
Analgesics (Non-Opioid) & Antipyretics	55(32.54)
Analgesics (Opioid)	30(17.75)
Hypnotics & Sedatives	14(8.28)
Antidepressants	35(20.71)
Drugs For Neuropathic Pain	44(26.04)

	Total n(%)
Anxiolytics	18(10.65)
Anticonvulsants	27(15.98)
Nootropics & Neurotonics	2(1.18)
Neurodegenerative Disease Drugs	3(1.78)
Antiparkinsonian Drugs	2(1.18)
Antipsychotics	3(1.78)
Antivertigo Drugs	1(0.59)
Gastrointestinal & Hepatobiliary System	112(66.27)
Antacids, Antireflux Agents & Antiulcerants	67(39.64)
GIT Regulators, Antiflatulents & Anti-inflammatories	50(29.59)
Digestives	14(8.28)
Laxatives, Purgatives	42(24.85)
Antiemetics	13(7.69)
Antispasmodics	11(6.51)
Antidiarrheals	1(0.59)
Cholagogues, Cholelitholytics & Hepatic Protectors	3(1.78)
Cardiovascular & Hematopoietic System	39(23.08)
Dyslipidaemic Agents	11(6.51)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	11(6.51)
Calcium Antagonists	10(5.92)
Angiotensin II Antagonists	7(4.14)
Other Antihypertensives	9(5.33)
Beta-Blockers	3(1.78)
Peripheral Vasodilators & Cerebral Activators	3(1.78)
Diuretics	1(0.59)
Other Cardiovascular Drugs	1(0.59)
Vasoconstrictors	4(2.37)
Phlebitis & Varicose Preparations	1(0.59)
Antidiuretics	2(1.18)
Musculo-Skeletal System	55(32.54)
Muscle Relaxants	52(30.77)
Neuromuscular Disorder Drugs	7(4.14)
Other Drugs Acting on the Musculo-Skeletal System	1(0.59)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	1(0.59)
Hyperuricemia & Gout Preparations	1(0.59)
Endocrine & Metabolic System	18(10.65)
Antidiabetic Agents	12(7.10)
Other Agents Affecting Metabolism	3(1.78)
Agents Affecting Bone Metabolism	3(1.78)
Intravenous & Other Sterile Solutions	18(10.65)
Intravenous & other sterile solutions	18(10.65)
Genito-Urinary System	24(14.20)
Drugs for Bladder & Prostate Disorders	23(13.61)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	2(1.18)
Respiratory System	16(9.47)
Antiasthmatic & COPD Preparations	9(5.33)
Cough & Cold Preparations	13(7.69)
Nasal Decongestant & Other Nasal Preparations	2(1.18)
Oncology	6(3.55)
Supportive Care Therapy	6(3.55)
Vitamins & Minerals	18(10.65)
Calcium / with Vitamins	13(7.69)

	Total n(%)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	2(1.18)
Vitamin B-complex / with C	3(1.78)
Vitamins &/or Minerals	1(0.59)
Vitamin C	1(0.59)
Vitamins & Minerals (Geriatric)	1(0.59)
Anti-infectives (systemic)	11(6.51)
Cephalosporins	6(3.55)
Quinolones	4(2.37)
Antivirals	1(0.59)
Antiamoebics	1(0.59)
Antibacterial Combinations	1(0.59)
Other Antibiotics	1(0.59)
Allergy & Immune System	4(2.37)
Antihistamines & Antiallergics	1(0.59)
Immunosuppressants	3(1.78)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	7(4.14)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	7(4.14)
Hormones	5(2.96)
Corticosteroid Hormones	3(1.78)
Oestrogens & Progesterones & Related Synthetic Drugs	1(0.59)
Other Drugs Affecting Hormonal Regulation	1(0.59)
Nutrition	11(6.51)
Parenteral Nutritional Products	9(5.33)
Electrolytes	6(3.55)
Appetite Enhancers	1(0.59)
Supplements & Adjuvant Therapy	1(0.59)
Eye	3(1.78)
Ophthalmic Lubricants	2(1.18)
Eye Anti-infectives & Antiseptics	1(0.59)
Dermatologicals	2(1.18)
Topical Corticosteroids	1(0.59)
Topical Antifungals & Antiparasites	1(0.59)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS
Missing: 1

2.7.2. Safety population

In the safety population, subjects who received concomitant medications accounted for 98.14% (158/161 subjects) (Table 10).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 88.61% (140/158 subjects), followed by 'Central Nervous System' in 71.52% (113/158 subjects) and 'Gastrointestinal & Hepatobiliary System' in 66.46% (105/158 subjects) (Table 10).

Table 10. Concomitant medications in the safety population (Neurogenic Detrusor Overactivity)

	Total n(%)
Yes	158(98.14)
No	3(1.86)
Total	161(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	140(88.61)
Anaesthetics - Local & General	140(88.61)
Central Nervous System	113(71.52)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	35(22.15)
Analgesics (Non-Opioid) & Antipyretics	53(33.54)
Analgesics (Opioid)	28(17.72)
Hypnotics & Sedatives	12(7.59)
Antidepressants	31(19.62)
Drugs For Neuropathic Pain	43(27.22)
Anxiolytics	17(10.76)
Anticonvulsants	24(15.19)
Neurodegenerative Disease Drugs	1(0.63)
Antiparkinsonian Drugs	2(1.27)
Antipsychotics	2(1.27)
Antivertigo Drugs	1(0.63)
Gastrointestinal & Hepatobiliary System	105(66.46)
Antacids, Antireflux Agents & Antiulcerants	62(39.24)
GIT Regulators, Antiflatulents & Anti-inflammatories	50(31.65)
Digestives	12(7.59)
Laxatives, Purgatives	41(25.95)
Antiemetics	12(7.59)
Antispasmodics	9(5.70)
Antidiarrheals	1(0.63)
Cholagogues, Cholelitholytics & Hepatic Protectors	2(1.27)
Cardiovascular & Hematopoietic System	32(20.25)
Dyslipidaemic Agents	7(4.43)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	7(4.43)
Calcium Antagonists	8(5.06)
Angiotensin II Antagonists	3(1.90)
Other Antihypertensives	7(4.43)
Beta-Blockers	2(1.27)
Peripheral Vasodilators & Cerebral Activators	2(1.27)
Other Cardiovascular Drugs	1(0.63)
Vasoconstrictors	4(2.53)
Phlebitis & Varicose Preparations	1(0.63)
Antidiuretics	2(1.27)
Musculo-Skeletal System	50(31.65)
Muscle Relaxants	48(30.38)
Neuromuscular Disorder Drugs	6(3.80)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	1(0.63)
Hyperuricemia & Gout Preparations	1(0.63)
Endocrine & Metabolic System	15(9.49)
Antidiabetic Agents	10(6.33)
Other Agents Affecting Metabolism	2(1.27)
Agents Affecting Bone Metabolism	3(1.90)
Intravenous & Other Sterile Solutions	16(10.13)
Intravenous & other sterile solutions	16(10.13)

	Total n(%)
Genito-Urinary System	22(13.92)
Drugs for Bladder & Prostate Disorders	21(13.29)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	2(1.27)
Respiratory System	15(9.49)
Antiasthmatic & COPD Preparations	9(5.70)
Cough & Cold Preparations	12(7.59)
Nasal Decongestant & Other Nasal Preparations	2(1.27)
Oncology	4(2.53)
Supportive Care Therapy	4(2.53)
Vitamins & Minerals	15(9.49)
Calcium / with Vitamins	11(6.96)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	2(1.27)
Vitamin B-complex / with C	2(1.27)
Vitamins &/or Minerals	1(0.63)
Vitamin C	1(0.63)
Vitamins & Minerals (Geriatric)	1(0.63)
Anti-infectives (systemic)	10(6.33)
Cephalosporins	5(3.16)
Quinolones	4(2.53)
Antivirals	1(0.63)
Antibacterial Combinations	1(0.63)
Other Antibiotics	1(0.63)
Allergy & Immune System	3(1.90)
Antihistamines & Antiallergics	1(0.63)
Immunosuppressants	2(1.27)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	5(3.16)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	5(3.16)
Hormones	3(1.90)
Corticosteroid Hormones	2(1.27)
Other Drugs Affecting Hormonal Regulation	1(0.63)
Nutrition	10(6.33)
Parenteral Nutritional Products	8(5.06)
Electrolytes	6(3.80)
Appetite Enhancers	1(0.63)
Supplements & Adjuvant Therapy	1(0.63)
Eye	3(1.90)
Ophthalmic Lubricants	2(1.27)
Eye Anti-infectives & Antiseptics	1(0.63)
Dermatologicals	2(1.27)
Topical Corticosteroids	1(0.63)
Topical Antifungals & Antiparasites	1(0.63)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS

2.8 Special population (Neurogenic Detrusor Overactivity)

2.8.1. All subjects

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 18.50% (32/173 subjects) were included in elderly group (Table 11).

In total, 1.73% (3/173 subjects) had renal impairment and the renal impairment included 'chronic kidney disease' and 'Chronic kidney disease, stage 4' (Table 11).

In total, 1.73% (3/173 subjects) had hepatic impairment and the hepatic impairment was 'fatty liver', 'HBV Liver cirrhosis', and 'hepatitis B' (Table 11).

Table 11. Special population in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Elderly	below 65 years	141(81.50)
	65 or/and over	32(18.50)
	Total	173(100.00)
Renal impairment	Yes	3(1.73)
	No	170(98.27)
	Total	173(100.00)
Hepatic impairment	Yes	3(1.73)
	No	170(98.27)
	Total	173(100.00)

The denominator is number of total subjects.

2.8.2. Safety population

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 17.39% (28/161 subjects) in the safety population were included in elderly group. Subjects with renal impairment and hepatic impairment accounted for 1.86% (3/161 subjects) each (Table 12).

Table 12. Special population in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Elderly	below 65 years	133(82.61)
	65 or/and over	28(17.39)
	Total	161(100.00)
Renal impairment	Yes	3(1.86)
	No	158(98.14)
	Total	161(100.00)
Hepatic impairment	Yes	3(1.86)
	No	158(98.14)
	Total	161(100.00)

The denominator is number of total subjects.

2.9 Information of study drug administration (Neurogenic Detrusor Overactivity)

2.9.1. All subjects

When analyzing the number of injection sites of study drug in all subjects, 30 sites accounted for 98.21% (165/168 subjects), followed by others in 1.19% (2/168 subjects) and 20 sites in 0.60% (1/168 subjects) (Table 13).

When analyzing the total units injected, 200 U accounted for 99.40% (167/168 subjects) and 100 U acoounted for 0.60% (1/168 subjects) (Table 13).

When investigating anesthesia upon the study drug administration, 'Local' accounted for 70.83% (119/168 subjects), 'General' 19.05% (32/168 subjects), and 'None' 10.12% (17/168 subjects) (Table 13).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 97.06% (165/170 subjects) (Table 13).

Table 13. Information of the study drug administration in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Number of Injection Sites	20	1(0.60)
	30	165(98.21)
	Other	2(1.19)
	Total	168(100.00)
Total Units Injected	100	1(0.60)
	200	167(99.40)
	Total	168(100.00)
Anesthesia	None	17(10.12)
	Local	119(70.83)
	General	32(19.05)
	Total	168(100.00)
Prophylactic Antibiotic Use	Yes	165(97.06)
	No	5(2.94)
	Total	170(100.00)

The denominator is number of total subjects.
Missing: 5 (Number of Injection Sites), 5 (Total Units Injected), 5 (Anesthesia), 3 (Prophylactic Antibiotic Use)

2.9.2. Safety population

When analyzing the number of injection sites of study drug and total units injected in the safety population, all subjects received total 200 U in 30 sites (Table 14).

When investigating anesthesia upon the study drug administration, 'Local' accounted for 71.43% (115/161 subjects), 'General' 18.01% (29/161 subjects), and 'None' 10.56% (17/161 subjects) (Table 14).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 96.89% (156/161 subjects) (Table 14).

Table 14. Information of the study drug administration in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Number of Injection Sites	20	0(0.00)
	30	161(100.00)
	Total	161(100.00)
Total Units Injected	100	0(0.00)
	200	161(100.00)
	Total	161(100.00)
Anesthesia	None	17(10.56)
	Local	115(71.43)
	General	29(18.01)
	Total	161(100.00)
Prophylactic Antibiotic Use	Yes	156(96.89)
	No	5(3.11)
	Total	161(100.00)

The denominator is number of total subjects.

2.10 Clean intermittent catheterization (Neurogenic Detrusor Overactivity)

2.10.1. All subjects

In all subjects, 84.39% (146/173 subjects) received clean intermittent catheterization before the study drug administration and 15.61% (27/173 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean post-void residual (PVR) urine volume prior to BOTOX treatment was 71.08±87.99 mL (Table 15).

Among the subjects not performing clean intermittent catheterization before the study drug administration, 37.04% (10/27 subjects) received catheterization after the study drug administration including 14.81% (4/27 subjects) who initiated catheterization due to urinary retention and 25.93% (7/27 subjects) who initiated catheterization due to other reason (Table 15).

Table 15. Clean intermittent catheterization in all subjects (Neurogenic Detrusor Overactivity)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	146(84.39)
	No	27(15.61)
	Total	173(100.00)
Post-Void Residual Urine Volume(before BOTOX)*	n	25
* In subjects not performing CIC before BOTOX	mean±std (mL)	71.08± 87.99
	median	50.00

		Total n(%)
	min ~ max	0.00~426.00
Initiation of CIC after BOTOX injection§ § In subjects not performing CIC before BOTOX	Yes	10(37.04)
	initiated CIC due to “Urinary Retention”	4(14.81)
	initiated CIC due to “Other Reason”	7(25.93)
	No	17(62.96)
	Total	27(100.00)

The denominator is number of total subjects.
Missing: 3(Catheterization after BOTOX injection)
Unknown: 2(Post-Void Residual Urine Volume(before BOTOX))
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

2.10.2. Safety population

In the safety population, 87.58% (141/161 subjects) received clean intermittent catheterization before the study drug administration and 12.42% (20/161 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean PVR urine volume prior to BOTOX treatment was 81.22±98.01 mL (Table 16).

Among the subjects not performing clean intermittent catheterization before the study drug administration, 40.00% (8/20 subjects) received catheterization after the study drug administration including 15.00% (3/20 subjects) who initiated catheterization due to urinary retention and 25.00% (5/20 subjects) who initiated catheterization due to other reason (Table 16).

Table 16. Clean intermittent catheterization in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	141(87.58)
	No	20(12.42)
	Total	161(100.00)
Post-Void Residual Urine Volume(before BOTOX)* * In subjects not performing CIC before BOTOX	n	18
	mean±std (mL)	81.22± 98.01
	median	57.50
	min ~ max	0.00~426.00
Initiation of CIC after BOTOX injection§	Yes	8(40.00)

§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	3(15.00)
	initiated CIC due to "Other Reason"	5(25.00)
	No	12(60.00)
	Total	20(100.00)

The denominator is number of total subjects.
Unknown: 2(Post-Void Residual Urine Volume(before BOTOX))

Ⅲ. Results of PMS
(Neurogenic Detrusor Overactivity)

3. Results of PMS (Neurogenic Detrusor Overactivity)

3.1 Incidence of Adverse Events (Neurogenic Detrusor Overactivity)

Source: Post-marketing Surveillance
Events to be reported: All AEs occurring to subjects during the entire surveillance period were to be included in the report, regardless of their causal relationship to the study drug.

It was specified that any AEs, which occurred during the PMS period, should be reported by the physician (investigator) to Allergan Korea Ltd. irrespective of their causal relationship to the study drug, and of these, any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to a series of procedure as soon as they are reported.

In this report, classification of AEs was presented in accordance with the WHO-ART 092 classification criteria.

During the PMS period, 27 AEs occurred in 19 out of 161 subjects in the safety population, which indicated that incidence of AEs was 11.80% (Table 17).

Table 17. Incidence of AEs (Neurogenic Detrusor Overactivity)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)
Total	19(11.80)	(6.82, 16.78)	27	161(100.00)

† The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects of safety analysis sets) * 100%
‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.

3.1.1 Serious AEs/ADRs

It was specified that any SAEs, which occurred during the PMS period, should be reported irrespective of their causal relationship to the study drug, and any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to the procedure as soon as they are reported.

During the PMS period, 2 SAEs of 'HAEMATURIA' under "Urinary system disorders" occurred in 1 subject of all 168 subjects (0.60%) except those who didn't receive the study drug. They were not SADRs which cannot rule out the relationship to the study drug (Table 18).

The subject who was occurred 2 SAEs of 'HAEMATURIA' was prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), so that excluded from the safety population. Therefore, no SAE was reported in the safety population.

Individual SAEs are presented in the table below (Table 19).

Table 18. SAEs onset status in all subjects except those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.60)	(0.00, 1.76)	2	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.60)	(0.00, 1.76)	2	0(0.00)	(0.00, 0.00)	0
Total	1(0.60)	(0.00, 1.76)	2	0(0.00)	(0.00, 0.00)	0

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of SAE' = (No. subjects of SAE / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
The percentage of 'Incidence rate of SADR' = (No. subjects of SADR / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
95% Confidence Interval for SAE/SADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)
Dictionary: WHO-ART 092

Table 19. Details of SAEs incurred in all subjectsexcept those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-09	2015-11-11	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-20	2015-11-25	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

3.1.2 Unexpected AEs/ADRs

During the PMS period, a total of 9 unexpected AEs were reported in 8 of all 168 subjects (4.76%) who receive the study drug (Table 20).

Examining the unexpected AEs by SOC, the highest incidence was found in 'Body as a whole - general disorders' and 'Central & peripheral nervous system disorders' each in 1.19% (2/168 subjects), followed by 'Gastro-intestinal system disorders', 'Metabolic and nutritional disorders', 'Reproductive disorders, male', 'Psychiatric disorders', and 'Respiratory system disorders' each in 0.60% (1/168 subjects). Examining the unexpected AEs by PT, 'HEADACHE' occurred in 1.19% (2/168 subjects), followed by 'DYSPEPSIA', 'PELVIC PAIN', and 'PAIN IN LIMB' each in 0.60% (1/168 subjects) (Table 20).

Among them, 1 event of 'TESTIS DISORDER' was an unexpected ADR which cannot rule out the relationship to the study drug (Table 20).

Individual unexpected AEs are presented in the table below (Table 21).

Table 20. Unexpected AEs onset status in all subjects except those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Gastro-intestinal system disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
TESTIS DISORDER	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
Psychiatric disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
합 계	8(4.76)	(1.54, 7.98)	9	1(0.60)	(0.00, 1.76)	1

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)
Dictionary: WHO-ART 092

Table 21. Details of unexpected AEs in all subjects except those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]-	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

During the PMS period, a total of 9 unexpected AEs were reported from 8 subjects (4.97%) in the safety population (Table 22).

Examining the unexpected AEs by SOC, the highest incidence was found in 'Body as a whole - general disorders' and 'Central & peripheral nervous system disorders' each in 1.24% (2/161 subjects), followed by 'Gastro-intestinal system disorders', 'Metabolic and nutritional disorders', 'Reproductive disorders, male', 'Psychiatric disorders', and 'Respiratory system disorders' each in 0.62% (1/161 subjects). Examining the unexpected AEs by PT, 'HEADACHE' occurred in 1.24% (2/161 subjects), followed by 'DYSPEPSIA', 'PELVIC PAIN', and 'PAIN IN LIMB' each in 0.62% (1/161 subjects) (Table 22).

Among them, 1 event of 'TESTIS DISORDER' was an unexpected ADR which cannot rule out the relationship to the study drug (Table 22).

Individual unexpected AEs are presented in the table below (Table 23).

Table 22. Unexpected AEs onset status in the safety population (Neurogenic Detrusor Overactivity)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Gastro-intestinal system disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Reproductive disorders, male	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
TESTIS DISORDER	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
Psychiatric disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Total	8(4.97)	(1.61, 8.33)	9	1(0.62)	(0.00, 1.83)	1

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE / No. subjects of safety analysis sets) * 100%
The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 23. Details of unexpected AEs in the safety population (Neurogenic Detrusor Overactivity)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes

During the PMS period, no unexpected AE was reported in the subjects excluded from the safety population.

3.1.3 AEs/ADRs

During the PMS period, a total of 30 AEs were reported in 21 of all 168 subjects (12.50%) who received the study drug (Table 24).

Examining the AEs by SOC, the highest incidence was found in 'Urinary system disorders' in 3.57% (6/168 subjects), followed by 'Gastro-intestinal system disorders' and 'Resistance mechanism disorders' each in 2.98% (5/168 subjects), and 'Body as a whole - general disorders', 'Central & peripheral nervous system disorders', and 'Musculo-skeletal system disorders' each in 1.19% (2/168 subjects). Examining the AEs by PT, 'URINARY TRACT INFECTION' occurred in 2.98% (5/168 subjects), followed by 'URINARY RETENTION', 'DYSURIA', 'HEADACHE', and 'MYALGIA' each in 1.19% (2/168 subjects), and 'HAEMATURIA', 'PYURIA', and 'DIFFICULTY IN MICTURITION' each in 0.60% (1/168 subjects) (Table 24).

Among them, 11 events occurred in 10 subjects (5.95%) were ADRs which cannot rule out the relationship to the study drug.

Examining the ADRs by SOC, the highest incidence was found in 'Urinary system disorders' in 2.38% (4/168 subjects), followed by 'Resistance mechanism disorders' and 'Musculo-skeletal system disorders' each in 1.19% (2/168 subjects), and 'Gastro-intestinal system disorders' and 'Reproductive disorders, male' each in 0.60% (1/168 subjects). Examining the ADRs by PT, 'URINARY RETENTION', 'DYSURIA', 'URINARY TRACT INFECTION', and 'MYALGIA' occurred in 1.19% (2/168 subjects) each, followed by 'DIFFICULTY IN MICTURITION', 'CONSTIPATION', and 'TESTIS DISORDER' each in 0.60% (1/168 subjects) (Table 24).

Individual AEs are presented in the table below (Table 25).

Table 24. AEs onset status in all subjects except those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	6(3.57)	(0.77, 6.38)	8	4(2.38)	(0.08, 4.69)	5
URINARY RETENTION	2(1.19)	(0.00, 2.83)	2	2(1.19)	(0.00, 2.83)	2
DYSURIA	2(1.19)	(0.00, 2.83)	2	2(1.19)	(0.00, 2.83)	2
HAEMATURIA	1(0.60)	(0.00, 1.76)	2	0(0.00)	(0.00, 0.00)	0
PYURIA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
Gastro-intestinal system disorders	5(2.98)	(0.41, 5.55)	5	1(0.60)	(0.00, 1.76)	1
NAUSEA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
DYSPEPSIA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	5(2.98)	(0.41, 5.55)	5	2(1.19)	(0.00, 2.83)	2
URINARY TRACT INFECTION	5(2.98)	(0.41, 5.55)	5	2(1.19)	(0.00, 2.83)	2
Body as a whole - general disorders	2(1.19)	(0.00, 2.83)	3	0(0.00)	(0.00, 0.00)	0

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
FEVER	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(1.19)	(0.00, 2.83)	3	0(0.00)	(0.00, 0.00)	0
DIZZINESS	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.19)	(0.00, 2.83)	2	2(1.19)	(0.00, 2.83)	2
MYALGIA	2(1.19)	(0.00, 2.83)	2	2(1.19)	(0.00, 2.83)	2
Metabolic and nutritional disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
TESTIS DISORDER	1(0.60)	(0.00, 1.76)	1	1(0.60)	(0.00, 1.76)	1
Psychiatric disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.60)	(0.00, 1.76)	1	0(0.00)	(0.00, 0.00)	0
Total	21(12.50)	(7.50, 17.50)	30	10(5.95)	(2.37, 9.53)	11

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)
Dictionary: WHO-ART 092

Table 25. Details of AEs incurred in all subjects except those who didn't receive the study drug (Neurogenic Detrusor Overactivity)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes	Unexpected AE
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	CONSTIPATION	2015-12-21	2015-12-25	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Expected AE
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	DIFFICULTY IN MICTURITION	2015-01-29	2015-01-29	Mild	Not applicable	Resolved without sequelae	Certain	Unassessable/unclassifiable	No	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	DYSURIA	2015-03-03	2015-03-03	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unassessable/unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2014-04-07		Moderate	None	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2014-06-08	2014-06-08	Mild	Not applicable	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-10-01	2015-10-04	Moderate	Not applicable	Resolved without sequelae	Unassessable /unclassifiable	Unassessable/unclassifiable	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-02-25	2015-02-25	Mild	Not applicable	Resolved without sequelae	Possible	Possible	No	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-09	2015-11-11	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-20	2015-11-25	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-25	2016-06-01	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-03-21	2016-03-28	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2015-12-21	2015-12-23	Mild	None	Resolved without sequelae	Probable/likely	Unlikely	No	Expected AE
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	PYURIA	2016-01-05	2016-01-10	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Gastro-intestinal system disorders	MOUTH DRY	2016-02-02	2016-04-26	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]-	Gastro-intestinal system disorders	ABDOMINAL DISCOMFORT	2016-01-11	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2016-03-10	2016-04-27	Mild	None	Resolved without sequelae	Possible	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-31	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Possible	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

During the PMS period, a total of 27 AEs were reported from 19 subjects (11.80%) in the safety population (Table 26).

Examining the AEs by SOC, the highest incidence was found in 'Gastro-intestinal system disorders' and 'Resistance mechanism disorders' in 3.11% (5/161 subjects) each, followed by 'Urinary system disorders' in 2.48% (4/161 subjects) and 'Body as a whole - general disorders', 'Central & peripheral nervous system disorders', and 'Musculo-skeletal system disorders' each in 1.24% (2/161 subjects). Examining the AEs by PT, 'URINARY TRACT INFECTION' occurred in 3.11% (5/161 subjects), followed by 'DYSURIA', 'HEADACHE', and 'MYALGIA' each in 1.24% (2/161 subjects), and 'URINARY RETENTION', 'PYURIA', and 'DIFFICULTY IN MICTURITION' each in 0.62% (1/161 subjects) (Table 26).

Among them, 10 events occurred in 9 subjects (5.59%) were ADRs which cannot rule out the relationship to the study drug.

Examining the ADRs by SOC, the highest incidence was found in 'Urinary system disorders' in 1.86% (3/161 subjects), followed by 'Resistance mechanism disorders' and 'Musculo-skeletal system disorders' each in 1.24% (2/161 subjects) and 'Gastro-intestinal system disorders' and 'Reproductive disorders, male' each in 0.62% (1/161 subjects). Examining the ADRs by PT, 'DYSURIA', 'URINARY TRACT INFECTION', and 'MYALGIA' occurred in 1.24% (2/161 subjects) each, followed by 'URINARY RETENTION', 'DIFFICULTY IN MICTURITION', 'CONSTIPATION', and 'TESTIS DISORDER' each in 0.62% (1/161 subjects) (Table 26).

Individual AEs are presented in the table below (Table 27).

Table 26. AEs onset status in the safety population (Neurogenic Detrusor Overactivity)

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	4(2.48)	(0.08, 4.89)	5	3(1.86)	(0.00, 3.95)	4
URINARY RETENTION	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
DYSURIA	2(1.24)	(0.00, 2.95)	2	2(1.24)	(0.00, 2.95)	2
PYURIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
Gastro-intestinal system disorders	5(3.11)	(0.43, 5.79)	5	1(0.62)	(0.00, 1.83)	1
NAUSEA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
DYSPEPSIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	5(3.11)	(0.43, 5.79)	5	2(1.24)	(0.00, 2.95)	2
URINARY TRACT INFECTION	5(3.11)	(0.43, 5.79)	5	2(1.24)	(0.00, 2.95)	2
Body as a whole - general disorders	2(1.24)	(0.00, 2.95)	3	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(1.24)	(0.00, 2.95)	3	0(0.00)	(0.00, 0.00)	0
DIZZINESS	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.24)	(0.00, 2.95)	2	2(1.24)	(0.00, 2.95)	2
MYALGIA	2(1.24)	(0.00, 2.95)	2	2(1.24)	(0.00, 2.95)	2
Metabolic and nutritional disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
TESTIS DISORDER	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1
Psychiatric disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Total	19(11.80)	(6.82, 16.78)	27	9(5.59)	(2.04, 9.14)	10

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects of safety analysis sets) * 100%
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 27. Details of AEs incurred in the safety population (Neurogenic Detrusor Overactivity)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes	Unexpected AE
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	CONSTIPATION	2015-12-21	2015-12-25	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Expected AE
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	DIFFICULTY IN MICTURITION	2015-01-29	2015-01-29	Mild	Not applicable	Resolved without sequelae	Certain	Unassessable/ unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2015-03-03	2015-03-03	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unassessable/ unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2014-04-07		Moderate	None	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2014-06-08	2014-06-08	Mild	Not applicable	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-10-01	2015-10-04	Moderate	Not applicable	Resolved without sequelae	Unassessable /unclassifiable	Unassessable/ unclassifiable	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-25	2016-06-01	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-03-21	2016-03-28	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2015-12-21	2015-12-23	Mild	None	Resolved without sequelae	Probable/likely	Unlikely	No	Expected AE
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	PYURIA	2016-01-05	2016-01-10	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	MOUTH DRY	2016-02-02	2016-04-26	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ABDOMINAL DISCOMFORT	2016-01-11	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2016-03-10	2016-04-27	Mild	None	Resolved without sequelae	Possible	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-31	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Possible	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE

3.1.4 Classification of AEs/ADRs by severity

A. Severity of AEs

When classifying and evaluating the severity of AEs reported in all 168 subjects ,, 'Mild' occurred in 8.93% (15/168 subjects), 'Moderate' in 4.17% (7/168 subjects) and none were severe (Table 28).

Table 28. Severity of AEs in all subjects except those who didn't receive the study drug by AE type (Neurogenic Detrusor Overactivity)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	3(1.79)	(0.00, 3.80)	4	3(1.79)	(0.00, 3.79)	4	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	2	0(0.00)	(0.00, 0.00)	0
PYURIA	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	4(2.38)	(0.08, 4.68)	4	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
NAUSEA	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Resistance mechanism disorders	4(2.38)	(0.08, 4.68)	4	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	4(2.38)	(0.08, 4.68)	4	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	2(1.19)	(0.00, 2.83)	3	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	2	0(0.00)	(0.00, 0.00)	0
DIZZINESS	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	0(0.00)	(0.00, 0.00)	0	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Total	15(8.93)	(4.62, 13.24)	19	7(4.17)	(1.15, 7.19)	11	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%

95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

Dictionary: WHO-ART 092

When classifying and evaluating the severity of AEs reported in the safety population into three of 'Mild', 'Moderate', and 'Severe', 'Mild' occurred in 8.70% (14/161 subjects), 'Moderate' in 3.73% (6/161 subjects) and none were severe (Table 29).

Table 29. Severity of AEs in the safety population by AE type (Neurogenic Detrusor Overactivity)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	2(1.24)	(0.00, 2.95)	3	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	4(2.48)	(0.08, 4.88)	4	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
NAUSEA	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
DYSPEPSIA	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	4(2.48)	(0.08, 4.88)	4	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	4(2.48)	(0.08, 4.88)	4	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	2(1.24)	(0.00, 2.95)	3	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	2	0(0.00)	(0.00, 0.00)	0
DIZZINESS	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Total	14(8.70)	(4.35, 13.05)	18	6(3.73)	(0.80, 6.66)	9	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

B. Severity of ADRs

When classifying and evaluating the severity of ADRs reported in all 168 subjects except those who didn't receive the study drug, , 'Mild' occurred in 4.17% (7/168 subjects), 'Moderate' in 1.79% (3/168 subjects), and none were severe (Table 30).

Table 30. Severity of ADRs in all subjects except those who didn't receive the study drug by ADR type (Neurogenic Detrusor Overactivity)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	2(1.19)	(0.00, 2.83)	3	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
URINARY TRACT INFECTION	1(0.60)	(0.00, 1.77)	1	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(1.19)	(0.00, 2.83)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.60)	(0.00, 1.77)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	7(4.17)	(1.15, 7.19)	8	3(1.79)	(0.00, 3.79)	3	0(0.00)	(0.00, 0.00)	0

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR / No. subjects who enrolled this study and received BOTOX and received BOTOX) * 100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)
Dictionary: WHO-ART 092

When classifying and evaluating the severity of ADRs reported in the safety population, 'Mild' occurred in 3.73% (6/161 subjects), 'Moderate' in 1.86% (3/161 subjects) and none were severe (Table 31).

Table 31. Severity of ADRs in the safety population by ADR type (Neurogenic Detrusor Overactivity)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.62)	(0.00, 1.83)	2	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	0(0.00)	(0.00, 0.00)	0	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	1(0.62)	(0.00, 1.83)	1	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(1.24)	(0.00, 2.95)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.62)	(0.00, 1.83)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	6(3.73)	(0.80, 6.66)	7	3(1.86)	(0.00, 3.95)	3	0(0.00)	(0.00, 0.00)	0

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

3.1.5 Classification of AEs in the safety population

The 27 AEs reported in the safety population were analyzed in detail.

When classifying and evaluating the expectedness of AEs into two of 'Expected AE' and 'Unexpected AE', 'Expected AE' accounted for 66.67% (18/27 events) and 'Unexpected AE' accounted for 33.33% (9/27 events) (Table 32).

When classifying and evaluating the seriousness of AEs into two of 'Serious' and 'Non-serious', all AEs were 'Non-serious' (Table 32).

When classifying and evaluating the severity of AEs into three of 'Mild', 'Moderate', and 'Severe', 'Mild' occurred in 66.67% (18/27 events) and 'Moderate' in 33.33% (9/27 events) (Table 32).

When classifying and evaluating the outcome of AEs incurred into four of 'Ongoing', 'Resolved without sequelae' 'Resolved with sequelae', and 'Death', 'Resolved without sequelae' was reported in 92.59% (25/27 events) and 'Ongoing' in 7.41% (2/27 events) (Table 32).

When classifying and evaluating the causal relationship of AEs to the study drug into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and 'Unassessable/Unclassifiable', 'Unlikely' was reported in 62.96% (17/27 events), 'Possible' and 'Conditional/Unclassified' was reported in 11.11% (3/27 events) each, and 'Certain' was reported in 7.41% (2/27 events) (Table 32).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and 'Unassessable/Unclassifiable', 'Unlikely' was 77.78% (21/27 events), and 'Possible' and 'Unassessable/Unclassifiable' was 11.11% (3/27 events) each (Table 32).

When classifying and evaluating the change in the study drug administration after AEs into four of 'None', 'Regimen changed', 'Discontinued', and 'Not applicable', 'None' was 55.56% (15/27 cases) and 'Not applicable' was 44.44% (12/27 cases) (Table 32).

When classifying and evaluating use of AE treatment into two of 'Yes' and 'No', 'Yes' accounted for 55.56% (15/27 events) and 'No' accounted for 44.44% (12/27 events) (Table 32).

Table 32. Classification of AEs in the safety population (Neurogenic Detrusor Overactivity)

		Total n(%)
Expected	Expected AE	18(66.67)
	Unexpected AE	9(33.33)
Seriousness	Serious	0(0.00)
	Non-serious	27(100.00)
Severity	Mild	18(66.67)
	Moderate	9(33.33)
	Severe	0(0.00)
Current Status	Ongoing	2(7.41)
	Resolved without sequelae	25(92.59)

		Total n(%)
	Resolved with sequelae	0(0.00)
	Death	0(0.00)
Causal Relationship	Certain	2(7.41)
	Probable/Likely	1(3.70)
	Possible	3(11.11)
	Unlikely	17(62.96)
	Conditional/Unclassified	3(11.11)
	Unassessable/Unclassifiable	1(3.70)
BOTOX Injection procedure	Certain	0(0.00)
	Probable/Likely	0(0.00)
	Possible	3(11.11)
	Unlikely	21(77.78)
	Conditional/Unclassified	0(0.00)
	Unassessable/Unclassifiable	3(11.11)
Change in BOTOX treatment after AE	None	15(55.56)
	Regimen changed	0(0.00)
	Discontinued	0(0.00)
	Not applicable	12(44.44)
Treatment received	Yes	15(55.56)
	No	12(44.44)
Total		27(100.00)

The denominator is number of total AE counts.

A. Expectedness

Incidence of AEs based on the expectedness is presented by AE type in the table below (Table 33).

Table 33. AEs onset status based on the expectedness by AE type (Neurogenic Detrusor Overactivity)

	Expected AE n(%)	Unexpected AE n(%)	Total n(%)
Urinary system disorders	5(100.00)	0(0.00)	5(18.52)
URINARY RETENTION	1(100.00)	0(0.00)	1(3.70)
DYSURIA	2(100.00)	0(0.00)	2(7.41)
PYURIA	1(100.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	1(3.70)
Gastro-intestinal system disorders	4(80.00)	1(20.00)	5(18.52)
NAUSEA	1(100.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	1(3.70)
CONSTIPATION	1(100.00)	0(0.00)	1(3.70)
DYSPEPSIA	0(0.00)	1(100.00)	1(3.70)
MOUTH DRY	1(100.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	5(100.00)	0(0.00)	5(18.52)
URINARY TRACT INFECTION	5(100.00)	0(0.00)	5(18.52)
Body as a whole - general disorders	1(33.33)	2(66.67)	3(11.11)
FEVER	1(100.00)	0(0.00)	1(3.70)
PELVIC PAIN	0(0.00)	1(100.00)	1(3.70)

	Expected AE n(%)	Unexpected AE n(%)	Total n(%)
PAIN IN LIMB	0(0.00)	1(100.00)	1(3.70)
Central & peripheral nervous system disorders	1(33.33)	2(66.67)	3(11.11)
DIZZINESS	1(100.00)	0(0.00)	1(3.70)
HEADACHE	0(0.00)	2(100.00)	2(7.41)
Musculo-skeletal system disorders	2(100.00)	0(0.00)	2(7.41)
MYALGIA	2(100.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	1(100.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	1(100.00)	1(3.70)
Reproductive disorders, male	0(0.00)	1(100.00)	1(3.70)
TESTIS DISORDER	0(0.00)	1(100.00)	1(3.70)
Psychiatric disorders	0(0.00)	1(100.00)	1(3.70)
INSOMNIA	0(0.00)	1(100.00)	1(3.70)
Respiratory system disorders	0(0.00)	1(100.00)	1(3.70)
THROAT PAIN	0(0.00)	1(100.00)	1(3.70)
Total	18(66.67)	9(33.33)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

B. Seriousness

Incidence of AEs based on the seriousness is presented by AE type in the table below (Table 34).

Table 34. AEs onset status based on the seriousness by AE type (Neurogenic Detrusor Overactivity)

	Serious n(%)	Non-serious n(%)	Total n(%)
Urinary system disorders	0(0.00)	5(100.00)	5(18.52)
URINARY RETENTION	0(0.00)	1(100.00)	1(3.70)
DYSURIA	0(0.00)	2(100.00)	2(7.41)
PYURIA	0(0.00)	1(100.00)	1(3.70)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	1(3.70)
Gastro-intestinal system disorders	0(0.00)	5(100.00)	5(18.52)
NAUSEA	0(0.00)	1(100.00)	1(3.70)
ABDOMINAL DISCOMFORT	0(0.00)	1(100.00)	1(3.70)
CONSTIPATION	0(0.00)	1(100.00)	1(3.70)
DYSPEPSIA	0(0.00)	1(100.00)	1(3.70)
MOUTH DRY	0(0.00)	1(100.00)	1(3.70)
Resistance mechanism disorders	0(0.00)	5(100.00)	5(18.52)
URINARY TRACT INFECTION	0(0.00)	5(100.00)	5(18.52)
Body as a whole - general disorders	0(0.00)	3(100.00)	3(11.11)
FEVER	0(0.00)	1(100.00)	1(3.70)
PELVIC PAIN	0(0.00)	1(100.00)	1(3.70)
PAIN IN LIMB	0(0.00)	1(100.00)	1(3.70)
Central & peripheral nervous system disorders	0(0.00)	3(100.00)	3(11.11)
DIZZINESS	0(0.00)	1(100.00)	1(3.70)
HEADACHE	0(0.00)	2(100.00)	2(7.41)
Musculo-skeletal system disorders	0(0.00)	2(100.00)	2(7.41)

	Serious n(%)	Non-serious n(%)	Total n(%)
MYALGIA	0(0.00)	2(100.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	1(100.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	1(100.00)	1(3.70)
Reproductive disorders, male	0(0.00)	1(100.00)	1(3.70)
TESTIS DISORDER	0(0.00)	1(100.00)	1(3.70)
Psychiatric disorders	0(0.00)	1(100.00)	1(3.70)
INSOMNIA	0(0.00)	1(100.00)	1(3.70)
Respiratory system disorders	0(0.00)	1(100.00)	1(3.70)
THROAT PAIN	0(0.00)	1(100.00)	1(3.70)
Total	0(0.00)	27(100.00)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

C. Severity of AEs

Incidence of AEs based on the severity is presented in the table below (Table 35).

Table 35. AEs onset status based on the Severity by AE type (Neurogenic Detrusor Overactivity)

	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)
Urinary system disorders	3(60.00)	2(40.00)	0(0.00)	5(18.52)
URINARY RETENTION	0(0.00)	1(100.00)	0(0.00)	1(3.70)
DYSURIA	1(50.00)	1(50.00)	0(0.00)	2(7.41)
PYURIA	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Gastro-intestinal system disorders	4(80.00)	1(20.00)	0(0.00)	5(18.52)
NAUSEA	0(0.00)	1(100.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	1(3.70)
CONSTIPATION	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DYSPEPSIA	1(100.00)	0(0.00)	0(0.00)	1(3.70)
MOUTH DRY	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	4(80.00)	1(20.00)	0(0.00)	5(18.52)
URINARY TRACT INFECTION	4(80.00)	1(20.00)	0(0.00)	5(18.52)
Body as a whole - general disorders	3(100.00)	0(0.00)	0(0.00)	3(11.11)
FEVER	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PELVIC PAIN	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PAIN IN LIMB	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	1(33.33)	2(66.67)	0(0.00)	3(11.11)
DIZZINESS	0(0.00)	1(100.00)	0(0.00)	1(3.70)
HEADACHE	1(50.00)	1(50.00)	0(0.00)	2(7.41)
Musculo-skeletal system disorders	2(100.00)	0(0.00)	0(0.00)	2(7.41)
MYALGIA	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	1(100.00)	0(0.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	1(100.00)	0(0.00)	1(3.70)
Reproductive disorders, male	1(100.00)	0(0.00)	0(0.00)	1(3.70)
TESTIS DISORDER	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Psychiatric disorders	0(0.00)	1(100.00)	0(0.00)	1(3.70)

INSOMNIA	0(0.00)	1(100.00)	0(0.00)	1(3.70)
Respiratory system disorders	0(0.00)	1(100.00)	0(0.00)	1(3.70)
THROAT PAIN	0(0.00)	1(100.00)	0(0.00)	1(3.70)
Total	18(66.67)	9(33.33)	0(0.00)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

D. Outcome of AEs

Incidence of AEs based on the outcome is presented by AE type in the table below (Table 36).

Table 36. Outcome of AEs by AE type (Neurogenic Detrusor Overactivity)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
Urinary system disorders	1(20.00)	4(80.00)	0(0.00)	0(0.00)	5(18.52)
URINARY RETENTION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DYSURIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(7.41)
PYURIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Gastro-intestinal system disorders	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(18.52)
NAUSEA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
CONSTIPATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DYSPEPSIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
MOUTH DRY	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(18.52)
URINARY TRACT INFECTION	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(18.52)
Body as a whole - general disorders	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
FEVER	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PELVIC PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PAIN IN LIMB	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
DIZZINESS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
HEADACHE	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Musculo-skeletal system disorders	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
MYALGIA	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
DIABETES MELLITUS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Reproductive disorders, male	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
TESTIS DISORDER	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Psychiatric disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
INSOMNIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Respiratory system disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
THROAT PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Total	2(7.41)	25(92.59)	0(0.00)	0(0.00)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

E. Relationship to the study drug

Incidence of AEs based on the relationship to the study drug is presented by AE type in the table below (Table 37).

Table 37. AEs onset status based on the relationship to the study drug by AE type (Neurogenic Detrusor Overactivity)

	Certain n(%)	Probable/ Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessable/ Unclassifiable n(%)	Total n(%)
Urinary system disorders	2(40.00)	0(0.00)	1(20.00)	1(20.00)	1(20.00)	0(0.00)	5(18.52)
URINARY RETENTION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
DYSURIA	0(0.00)	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	2(7.41)
PYURIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	0(0.00)	4(80.00)	1(20.00)	0(0.00)	5(18.52)
NAUSEA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(3.70)
DYSPEPSIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
MOUTH DRY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	0(0.00)	0(0.00)	1(20.00)	3(60.00)	0(0.00)	1(20.00)	5(18.52)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	1(20.00)	3(60.00)	0(0.00)	1(20.00)	5(18.52)
Body as a whole - general disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
FEVER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PAIN IN LIMB	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
HEADACHE	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Musculo-skeletal system disorders	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	0(0.00)	2(7.41)
MYALGIA	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Reproductive disorders, male	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(3.70)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(3.70)
Psychiatric disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
INSOMNIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Respiratory system disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
THROAT PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Total	2(7.41)	1(3.70)	3(11.11)	17(62.96)	3(11.11)	1(3.70)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

F. Relationship to the study drug administration procedure

Incidence of AEs based on the relationship to the study drug administration procedure is presented by AE type in the table below (Table 38).

Table 38. AEs onset status based on the relationship to the study drug administration procedure by AE type (Neurogenic Detrusor Overactivity)

	Certain n(%)	Probable/ Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessable/ Unclassifiable n(%)	Total n(%)
Urinary system disorders	0(0.00)	0(0.00)	1(20.00)	2(40.00)	0(0.00)	2(40.00)	5(18.52)
URINARY RETENTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DYSURIA	0(0.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(7.41)
PYURIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(18.52)
NAUSEA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DYSPEPSIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
MOUTH DRY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	0(0.00)	0(0.00)	1(20.00)	3(60.00)	0(0.00)	1(20.00)	5(18.52)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	1(20.00)	3(60.00)	0(0.00)	1(20.00)	5(18.52)
Body as a whole - general disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
FEVER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
PAIN IN LIMB	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(11.11)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
HEADACHE	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Musculo-skeletal system disorders	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
MYALGIA	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Reproductive disorders, male	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Psychiatric disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
INSOMNIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(3.70)
Respiratory system disorders	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
THROAT PAIN	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Total	0(0.00)	0(0.00)	3(11.11)	21(77.78)	0(0.00)	3(11.11)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

G. Change in the study drug administration after AE

Incidence of AEs based on change in the study drug administration after AE is presented by AE type in the table below (Table 39).

Table 39. AEs onset status based on the actions taken to the study drug by AE type (Neurogenic Detrusor Overactivity)

	None n(%)	Regimen changed n(%)	Discontinued n(%)	Not applicable n(%)	Total n(%)
Urinary system disorders	3(60.00)	0(0.00)	0(0.00)	2(40.00)	5(18.52)
URINARY RETENTION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
DYSURIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(7.41)

	None n(%)	Regimen changed n(%)	Discontinued n(%)	Not applicable n(%)	Total n(%)
PYURIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
Gastro-intestinal system disorders	4(80.00)	0(0.00)	0(0.00)	1(20.00)	5(18.52)
NAUSEA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
DYSPEPSIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
MOUTH DRY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Resistance mechanism disorders	1(20.00)	0(0.00)	0(0.00)	4(80.00)	5(18.52)
URINARY TRACT INFECTION	1(20.00)	0(0.00)	0(0.00)	4(80.00)	5(18.52)
Body as a whole - general disorders	1(33.33)	0(0.00)	0(0.00)	2(66.67)	3(11.11)
FEVER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
PAIN IN LIMB	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	3(100.00)	0(0.00)	0(0.00)	0(0.00)	3(11.11)
DIZZINESS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
HEADACHE	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(7.41)
Musculo-skeletal system disorders	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(7.41)
MYALGIA	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(7.41)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
Reproductive disorders, male	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
Psychiatric disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
INSOMNIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(3.70)
Respiratory system disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
THROAT PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(3.70)
Total	15(55.56)	0(0.00)	0(0.00)	12(44.44)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

H. AE treatment

Incidence of AEs based on the use of AE treatment is presented by AE type in the table below (Table 40).

Table 40. AEs onset status based on the use of AEs treatment by AE type (Neurogenic Detrusor Overactivity)

	Yes n(%)	No n(%)	Total n(%)
Urinary system disorders	2(40.00)	3(60.00)	5(18.52)
URINARY RETENTION	0(0.00)	1(100.00)	1(3.70)
DYSURIA	1(50.00)	1(50.00)	2(7.41)
PYURIA	1(100.00)	0(0.00)	1(3.70)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	1(3.70)
Gastro-intestinal system disorders	3(60.00)	2(40.00)	5(18.52)
NAUSEA	1(100.00)	0(0.00)	1(3.70)

	Yes n(%)	No n(%)	Total n(%)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	1(3.70)
CONSTIPATION	1(100.00)	0(0.00)	1(3.70)
DYSPEPSIA	0(0.00)	1(100.00)	1(3.70)
MOUTH DRY	0(0.00)	1(100.00)	1(3.70)
Resistance mechanism disorders	4(80.00)	1(20.00)	5(18.52)
URINARY TRACT INFECTION	4(80.00)	1(20.00)	5(18.52)
Body as a whole - general disorders	1(33.33)	2(66.67)	3(11.11)
FEVER	0(0.00)	1(100.00)	1(3.70)
PELVIC PAIN	0(0.00)	1(100.00)	1(3.70)
PAIN IN LIMB	1(100.00)	0(0.00)	1(3.70)
Central & peripheral nervous system disorders	1(33.33)	2(66.67)	3(11.11)
DIZZINESS	0(0.00)	1(100.00)	1(3.70)
HEADACHE	1(50.00)	1(50.00)	2(7.41)
Musculo-skeletal system disorders	0(0.00)	2(100.00)	2(7.41)
MYALGIA	0(0.00)	2(100.00)	2(7.41)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	1(3.70)
DIABETES MELLITUS	1(100.00)	0(0.00)	1(3.70)
Reproductive disorders, male	1(100.00)	0(0.00)	1(3.70)
TESTIS DISORDER	1(100.00)	0(0.00)	1(3.70)
Psychiatric disorders	1(100.00)	0(0.00)	1(3.70)
INSOMNIA	1(100.00)	0(0.00)	1(3.70)
Respiratory system disorders	1(100.00)	0(0.00)	1(3.70)
THROAT PAIN	1(100.00)	0(0.00)	1(3.70)
Total	15(55.56)	12(44.44)	27(100.00)

The denominator is number of total AE counts.
Dictionary: WHO-ART 092

3.1.6 Adverse events by factors

The 27 AEs reported in the safety population were analyzed by factor.

A. Background factors

When analyzing AE incidence by age group, it was 15.87% (10/63 subjects, 15 events) in '< 50 years', 10.42% (5/48 subjects, 7 events) in '≥ 50 years to < 60 years', 8.82% (3/34 subjects, 3 events) in '≥ 60 years to < 70 years', and 6.25% (1/16 subjects, 2 events) in '≥ 70 years'. Difference in AE incidences between the groups was not statistically significant (p=0.7282) (Table 41).

When analyzing AE incidence by sex, incidence of AEs was 10.48% (13/124 subjects, 16 events) in 'Male' and 16.22% (6/37 subjects, 11 events) in 'Female', and difference in AE incidences between the groups was not statistically significant (p=0.3852) (Table 41).

When analyzing AE incidence by treatment setting, incidence of AEs was 8.62% (10/116 subjects, 14 events) in 'Outpatient' and 20.00% (9/45 subjects, 13 events) in 'Inpatient', and difference in AE incidences between the groups was statistically significant (p=0.0446) (Table 41).

When analyzing AE incidence by underlying neurologic conditions, AE incidence in 'Multiple Sclerosis' was 20.00% (1/5 subjects, 1 event), followed by 'Spinal Cord Injury' in 11.54% (18/156 subjects, 26 events), and no AE was reported in subjects with 'Other' conditions (Table 41).

Among female subjects, there was no pregnant subject (Table 41).

Table 41. AEs onset status by background factor (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Age	< 50 years	10(15.87)	(6.85, 24.90)	15	63(39.13)	0.7282 Fisher's Exact test
	≥ 50 years to < 60 years	5(10.42)	(1.77, 19.06)	7	48(29.81)	
	≥ 60 years to < 70 years	3(8.82)	(0.00, 18.36)	3	34(21.12)	
	≥ 70 years	1(6.25)	(0.00, 18.11)	2	16(9.94)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Sex	Male	13(10.48)	(5.09, 15.88)	16	124(77.02)	0.3852 Fisher's Exact test
	Female	6(16.22)	(4.34, 28.09)	11	37(22.98)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Treatment Setting	Outpatient	10(8.62)	(3.51, 13.73)	14	116(72.05)	0.0446 Chi square test
	Inpatient	9(20.00)	(8.31, 31.69)	13	45(27.95)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Currently pregnant * for female	Yes	0(0.00)	(0.00, 0.00)	0	0(0.00)	NA
	No	6(3.73)	(0.80, 6.65)	11	161(0.00)	
	Total	6(16.22)	(4.34, 28.09)	11	37(100.00)	
Underlying neurologic condition§ * for patients with NDO Overlapped¶	Multiple Sclerosis	1(20.00)	(0.00, 55.06)	1	5(3.11)	
	Spinal Cord Injury	18(11.54)	(6.52, 16.55)	26	156(96.89)	
	Other	0(0.00)	(0.00, 0.00)	0	1(0.62)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).

B. Past treatment history

When analyzing AE incidence by previous anticholinergic therapy, it was 11.88% (19/160 subjects, 27 events) in subjects who had received anticholinergic therapy, and no AE was reported in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 42).

When analyzing AE incidence by previous use of sacral neuromodulation therapy, no AE was reported in subjects who had received sacral neuromodulation therapy, and 11.88% (19/160 subjects, 27 events) in subject who had not. Difference in AE incidences between the groups

was not statistically significant (p=1.0000) (Table 42).

When analyzing AE incidence by past treatment history with the study drug or other botulinum toxin, it was 16.67% (2/12 subjects, 2 events) in subjects who had used the study drug or other botolinum toxin and 11.41% (17/149 subjects, 25 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.6360) (Table 42).

Table 42. AEs onset status by past treatment history (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Previous Anticholinergic Therapy	Yes	19(11.88)	(6.86, 16.89)	27	160(99.38)	1.0000
	No	0(0.00)	(0.00, 0.00)	0	1(0.62)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Previous Use of Sacral Neuromodulation Therapy	Yes	0(0.00)	(0.00, 0.00)	0	1(0.62)	1.0000
	No	19(11.88)	(6.86, 16.89)	27	160(99.38)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	2(16.67)	(0.00, 37.75)	2	12(7.45)	0.6360
	None	17(11.41)	(6.30, 16.51)	25	149(92.55)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

C. Medical history

When analyzing AE incidence by medical history including surgeries and complications of underlying diseases, it was 15.13% (18/119 subjects, 26 events) in subjects with medical history and 2.38% (1/42 subjects, 1 event) in subjects without medical history. The difference in AE incidences between the groups was statistically significant (p=0.0268) (Table 43).

When analyzing AE incidence by the type of medical history (multiple counting allowed), it was 66.67% (2/3 subjects, 2 events) in 'Certain infectious and parasitic diseases', followed by 'Diseases of the musculoskeletal system and connective tissue' in 37.50% (6/16 subjects, 6 events) and 'Diseases of the skin and subcutaneous tissue' in 27.27% (3/11 subjects, 3 events) (Table 43).

When analyzing AE incidence by allergy history, it was 33.33% (3/9 subjects, 3 events) in subjects with allergy history and 10.53% (16/152 subjects, 24 events) in subject without allergy history. Difference in AE incidences between the groups was not statistically significant (p=0.0743) (Table 43).

Table 43. AEs onset status by medical history (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	18(15.13)	(8.69, 21.56)	26	119(73.91)	0.0268
	None	1(2.38)	(0.00, 6.99)	1	42(26.09)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
	Details for Medical History by dictionary (Overlapped¶)					
	Diseases of the circulatory system	2(4.44)	(0.00, 10.47)	2	45(37.82)	
	Factors influencing health status and contact with health services	4(13.79)	(1.24, 26.34)	5	29(24.37)	
	Endocrine, nutritional and metabolic diseases	4(13.79)	(1.24, 26.34)	8	29(24.37)	
	Diseases of the genitourinary system	6(23.08)	(6.88, 39.27)	7	26(21.85)	
	Diseases of the digestive system	7(21.88)	(7.55, 36.20)	8	32(26.89)	
	Diseases of the musculoskeletal system and connective tissue	6(37.50)	(13.78, 61.22)	6	16(13.45)	
	Neoplasms	0(0.00)	(0.00, 0.00)	0	10(8.40)	
	Mental and behavioural disorders	3(23.08)	(0.17, 45.98)	3	13(10.92)	
	Diseases of the nervous system	8(20.51)	(7.84, 33.19)	14	39(32.77)	
	Diseases of the respiratory system	2(22.22)	(0.00, 49.38)	4	9(7.56)	
	Diseases of the eye and adnexa	0(0.00)	(0.00, 0.00)	0	2(1.68)	
	Injury, poisoning and certain other consequences of external causes	3(25.00)	(0.50, 49.50)	4	12(10.08)	
	Certain infectious and parasitic diseases	2(66.67)	(13.32, 100.00)	2	3(2.52)	
	Diseases of the skin and subcutaneous tissue	3(27.27)	(0.95, 53.59)	3	11(9.24)	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	0(0.00)	(0.00, 0.00)	0	2(1.68)	
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	3(21.43)	(0.00, 42.92)	3	14(11.76)	
History of Allergies	Yes	3(33.33)	(2.53, 64.13)	3	9(5.59)	0.0743
	None	16(10.53)	(5.65, 15.41)	24	152(94.41)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
	Details for History of Allergies by dictionary					
	Factors influencing health status and contact with health services	2(28.57)	(0.00, 62.04)	2	7(77.78)	
	Injury, poisoning and certain other consequences of external causes	1(50.00)	(0.00, 100.00)	1	2(22.22)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

Dictionary: KCD 7 and ICD 10

D. Concomitant medications

When analyzing AE incidence by use of concomitant medications, it was 12.03% (19/158 subjects, 27 events) in subjects with concomitant medications, and no AE was reported in subjects without concomitant medications. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 44).

When analyzing AE incidence by concomitant medications (multiple counting allowed), it was 60.00% (6/10 subjects, 6 events) in 'Anti-infectives (systemic)', followed by 'Dermatologicals'

in 50.00% (1/2 subjects, 1 event) and 'Allergy & Immune System' and 'Eye' each in 33.33% (1/3 subjects, 1 event) (Table 44).

Table 44. AEs onset status by concomitant medications (Neurogenic Detrusor Overactivity)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Yes	19(12.03)	(6.95, 17.10)	27	158(98.14)	1.0000
No	0(0.00)	(0.00, 0.00)	0	3(1.86)	Fisher's Exact test
Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Details for Concomitant Medication by dictionary (Overlapped¶)					
Anaesthetics- Local & General	15(10.71)	(5.59, 15.84)	22	140(88.61)	
Anaesthetics - Local & General	15(10.71)	(5.59, 15.84)	22	140(88.61)	
Central Nervous System	15(13.27)	(7.02, 19.53)	23	113(71.52)	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	6(17.14)	(4.66, 29.63)	13	35(22.15)	
Analgesics (Non-Opioid) & Antipyretics	9(16.98)	(6.87, 27.09)	14	53(33.54)	
Analgesics (Opioid)	5(17.86)	(3.67, 32.04)	9	28(17.72)	
Hypnotics & Sedatives	0(0.00)	(0.00, 0.00)	0	12(7.59)	
Antidepressants	7(22.58)	(7.86, 37.30)	12	31(19.62)	
Drugs For Neuropathic Pain	2(4.65)	(0.00, 10.95)	2	43(27.22)	
Anxiolytics	2(11.76)	(0.00, 27.08)	6	17(10.76)	
Anticonvulsants	3(12.50)	(0.00, 25.73)	3	24(15.19)	
Neurodegenerative Disease Drugs	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Antiparkinsonian Drugs	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Antipsychotics	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Antivertigo Drugs	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Gastrointestinal & Hepatobiliary System	16(15.24)	(8.36, 22.11)	23	105(66.46)	
Antacids, Antireflux Agents & Antiulcerants	9(14.52)	(5.75, 23.28)	9	62(39.24)	
GIT Regulators, Antiflatulents & Anti-inflammatories	7(14.00)	(4.38, 23.62)	14	50(31.65)	
Digestives	1(8.33)	(0.00, 23.97)	1	12(7.59)	
Laxatives, Purgatives	9(21.95)	(9.28, 34.62)	15	41(25.95)	
Antiemetics	4(33.33)	(6.66, 60.01)	4	12(7.59)	
Antispasmodics	2(22.22)	(0.00, 49.38)	4	9(5.70)	
Antidiarrheals	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Cholagogues, Cholelitholytics & Hepatic Protectors	1(50.00)	(0.00, 100.00)	1	2(1.27)	
Cardiovascular & Hematopoietic System	6(18.75)	(5.23, 32.27)	7	32(20.25)	
Dyslipidaemic Agents	1(14.29)	(0.00, 40.21)	1	7(4.43)	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	2(28.57)	(0.00, 62.04)	3	7(4.43)	
Calcium Antagonists	0(0.00)	(0.00, 0.00)	0	8(5.06)	
Angiotensin II Antagonists	0(0.00)	(0.00, 0.00)	0	3(1.90)	
Other Antihypertensives	0(0.00)	(0.00, 0.00)	0	7(4.43)	
Beta-Blockers	1(50.00)	(0.00, 100.00)	1	2(1.27)	
Peripheral Vasodilators & Cerebral Activators	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Other Cardiovascular Drugs	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Vasoconstrictors	1(25.00)	(0.00, 67.44)	1	4(2.53)	
Phlebitis & Varicose Preparations	1(100.00)	(100.00, 100.00)	1	1(0.63)	
Antidiuretics	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Musculo-Skeletal System	4(8.00)	(0.48, 15.52)	5	50(31.65)	
Muscle Relaxants	4(8.33)	(0.51, 16.15)	5	48(30.38)	
Neuromuscular Disorder Drugs	1(16.67)	(0.00, 46.49)	1	6(3.80)	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	0(0.00)	(0.00, 0.00)	0	1(0.63)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Hyperuricemia & Gout Preparations	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Endocrine & Metabolic System	2(13.33)	(0.00, 30.54)	3	15(9.49)	
Antidiabetic Agents	2(20.00)	(0.00, 44.79)	3	10(6.33)	
Other Agents Affecting Metabolism	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Agents Affecting Bone Metabolism	0(0.00)	(0.00, 0.00)	0	3(1.90)	
Intravenous & Other Sterile Solutions	4(25.00)	(3.78, 46.22)	8	16(10.13)	
Intravenous & other sterile solutions	4(25.00)	(3.78, 46.22)	8	16(10.13)	
Genito-Urinary System	4(18.18)	(2.06, 34.30)	9	22(13.92)	
Drugs for Bladder & Prostate Disorders	4(19.05)	(2.25, 35.84)	9	21(13.29)	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	1(50.00)	(0.00, 100.00)	1	2(1.27)	
Respiratory System	4(26.67)	(4.29, 49.05)	6	15(9.49)	
Antiasthmatic & COPD Preparations	3(33.33)	(2.53, 64.13)	3	9(5.70)	
Cough & Cold Preparations	3(25.00)	(0.50, 49.50)	3	12(7.59)	
Nasal Decongestant & Other Nasal Preparations	1(50.00)	(0.00, 100.00)	3	2(1.27)	
Oncology	1(25.00)	(0.00, 67.44)	1	4(2.53)	
Supportive Care Therapy	1(25.00)	(0.00, 67.44)	1	4(2.53)	
Vitamins & Minerals	4(26.67)	(4.29, 49.05)	5	15(9.49)	
Calcium / with Vitamins	4(36.36)	(7.94, 64.79)	5	11(6.96)	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	1(50.00)	(0.00, 100.00)	2	2(1.27)	
Vitamin B-complex / with C	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Vitamins &/or Minerals	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Vitamin C	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Vitamins & Minerals (Geriatric)	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Anti-infectives (systemic)	6(60.00)	(29.64, 90.36)	6	10(6.33)	
Cephalosporins	5(100.00)	(100.00, 100.00)	5	5(3.16)	
Quinolones	2(50.00)	(1.00, 99.00)	2	4(2.53)	
Antivirals	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Antibacterial Combinations	1(100.00)	(100.00, 100.00)	1	1(0.63)	
Other Antibiotics	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Allergy & Immune System	1(33.33)	(0.00, 86.68)	1	3(1.90)	
Antihistamines & Antiallergics	1(100.00)	(100.00, 100.00)	1	1(0.63)	
Immunosuppressants	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	1(20.00)	(0.00, 55.06)	1	5(3.16)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	1(20.00)	(0.00, 55.06)	1	5(3.16)	
Hormones	0(0.00)	(0.00, 0.00)	0	3(1.90)	
Corticosteroid Hormones	0(0.00)	(0.00, 0.00)	0	2(1.27)	
Other Drugs Affecting Hormonal Regulation	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Nutrition	2(20.00)	(0.00, 44.79)	6	10(6.33)	
Parenteral Nutritional Products	2(25.00)	(0.00, 55.01)	6	8(5.06)	
Electrolytes	1(16.67)	(0.00, 46.49)	1	6(3.80)	
Appetite Enhancers	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Supplements & Adjuvant Therapy	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Eye	1(33.33)	(0.00, 86.68)	1	3(1.90)	
Ophthalmic Lubricants	1(50.00)	(0.00, 100.00)	1	2(1.27)	
Eye Anti-infectives & Antiseptics	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Dermatologicals	1(50.00)	(0.00, 100.00)	1	2(1.27)	
Topical Corticosteroids	0(0.00)	(0.00, 0.00)	0	1(0.63)	
Topical Antifungals & Antiparasites	1(100.00)	(100.00, 100.00)	1	1(0.63)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*

‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.
* The p-value is about that relation between Category and Incidence rate of AEs.
¶ The same subject may appear in different categories.
Dictionary: KIMS

E. Special population

When classifying and analyzing AE incidence in elderly group who was '65 or/and over', it was 10.71% (3/28 subjects, 4 events) in subjects of '65 or/and over' and 12.03% (16/133 subjects, 23 events) in subjects of 'below 65 years'. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 45).

When analyzing AE incidence by renal impairment, no AE was reported in subjects with renal impairment, and it was 12.03% (19/158 subjects, 27 events) in subject without renal impairment. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 45).

When analyzing AE incidence by hepatic impairment, no AE was reported in subjects with hepatic impairment, and it was 12.03% (19/158 subjects, 27 events) in subject without renal impairment. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 45).

Table 45. AEs onset status in special subjects (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Elderly	below 65 years	16(12.03)	(6.50, 17.56)	23	133(82.61)	1.0000
	65 or/and over	3(10.71)	(0.00, 22.17)	4	28(17.39)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Renal impairment	Yes	0(0.00)	(0.00, 0.00)	0	3(1.86)	1.0000
	No	19(12.03)	(6.95, 17.10)	27	158(98.14)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Hepatic impairment	Yes	0(0.00)	(0.00, 0.00)	0	3(1.86)	1.0000
	No	19(12.03)	(6.95, 17.10)	27	158(98.14)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%
‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.
* The p-value is about that relation between Category and Incidence rate of AEs.

F. Information of the study drug administration

When analyzing AE incidence by the number of injection sites of study drug and total units injected, all subjects received total 200 U of the study drug in 30 sites and thus the AE incidence

was the same as that in the safety population (Table 46).

When analyzing AE incidence by use of anesthesia at the study drug administration, it was 17.65% (3/17 subjects, 3 events) in 'None', followed by 'General' in 13.79% (4/29 subjects, 5 events) and 'Local' in 10.43% (12/115 subjects, 19 events). Difference in AE incidences among the groups was not statistically significant (p=0.5748) (Table 46).

When analyzing AE incidence by use of prophylactic antibiotics before, during, and after the study drug administration, it was 12.18% (19/156 subjects, 27 events) in subjects with antibiotics, and no AE was reported in subjects without antibiotics. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 46).

Table 46. AEs onset status based on the information of study drug administration (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Number of Injection Sites	20	0(0.00)	(0.00, 0.00)	0	0(0.00)	NA
	30	19(11.80)	(6.82, 16.78)	27	161(100.00)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Total Units Injected	100	0(0.00)	(0.00, 0.00)	0	0(0.00)	NA
	200	19(11.80)	(6.82, 16.78)	27	161(100.00)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Anesthesia	None	3(17.65)	(0.00, 35.77)	3	17(10.56)	0.5748 Fisher's Exact test
	Local	12(10.43)	(4.85, 16.02)	19	115(71.43)	
	General	4(13.79)	(1.24, 26.34)	5	29(18.01)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Prophylactic Antibiotic Use	Yes	19(12.18)	(7.05, 17.31)	27	156(96.89)	1.0000 Fisher's Exact test
	No	0(0.00)	(0.00, 0.00)	0	5(3.11)	
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

G. Clean intermittent catheterization

When analyzing AE incidence by use of clean intermittent catheterization before the study drug administration, it was 11.35% (16/141 subjects, 23 events) in subjects with clean intermittent catheterization and 15.00% (3/20 subjects, 4 events) in subjects without clean intermittent catheterization, and difference in AE incidences between the groups was not statistically significant (p=0.7092) (Table 47).

When analyzing AE incidence by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, it was 25.00% (2/8 subjects, 3 events) in subjects with urinary catheterization and 8.33% (1/12 subjects, 1 event) in subjects without urinary catheterization, and difference in

AE incidences between the groups was not statistically significant (p=0.5368). Among the subjects with urinary catheterization, AE incidence was 66.67% (2/3 subjects, 3 events) in subjects who initiated catheterization due to urinary retention and no AE was reported in subjects who initiated catheterization due to other reason (Table 47).

Table 47. AEs onset status by clean intermittent catheterization (Neurogenic Detrusor Overactivity)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Routine Urinary Catheterization(before BOTOX)	Yes	16(11.35)	(6.11, 16.58)	23	141(87.58)	0.7092
	No	3(15.00)	(0.00, 30.65)	4	20(12.42)	Fisher's Exact test
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Initiation of CIC after BOTOX injection§	Yes	2(25.00)	(0.00, 55.01)	3	8(40.00)	0.5368**
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	2(66.67)	(13.32, 100.00)	3	3(15.00)	Fisher's Exact test
	initiated CIC due to "Other Reason"	0(0.00)	(0.00, 0.00)	0	5(25.00)	
	No	1(8.33)	(0.00, 23.97)	1	12(60.00)	
	Total	3(15.00)	(0.00, 30.65)	4	20(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event incidence rate
95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and incidence rate of AEs

**The p-value is about that relation between Yes/No and incidence rate of AEs.

H. Factors that may affect safety

Regarding the safety in this PMS, incidence of AEs was investigated by age, sex, treatment setting, pregnancy status, underlying neurological conditions, past treatment history, medical history, concomitant medications, information of study drug administration, and clean intermittent catheterization as well as in special population such as the elderly and subjects with renal or hepatic impairment.

The analysis results showed statistically significant difference in AE incidence by 2 factors: treatment setting (p=0.0446) and presence of medical history including surgeries and complications of underlying diseases (p=0.0268).

When analyzing AE incidence by treatment setting, incidence of AEs was 8.62% (10/116 subjects, 14 events) in 'Outpatient' and 20.00% (9/45 subjects, 13 events) in 'Inpatient', and

difference in AE incidences between the groups was statistically significant (p=0.0446). It seemed that underlying condition of subjects requiring hospitalization may have affected these results, but it was considered difficult to determine clinical significance solely with the data.

When analyzing AE incidence by medical history including surgeries and complications of underlying diseases, it was 15.13% (18/119 subjects, 26 events) in subjects with medical history and 2.38% (1/42 subjects, 1 event) in subjects without medical history. The difference in AE incidences between the groups was statistically significant (p=0.0268). These results are not surprising as generally, patients with other medical histories or comorbidities may have more reports of AEs as they are a "sicker" population than those without medical histories. It seemed that the above reason may have affected the results, but it was considered difficult to determine clinical significance solely with the data.

3.1.7 Other AEs

No distant spread of toxin was identified.

3.2 Effectiveness data (Neurogenic Detrusor Overactivity)

3.2.1 Effectiveness evaluation

Effectiveness evaluation was conducted by the subject using incontinence questionnaire (ICIQ-SF) before the study drug administration and 1 ~ 4 month(s) after the study drug administration. Evaluation should be carried out based on the change in total score before and after the study drug administration. A decrease in score indicates an improvement in symptoms.

When comparing and analyzing changes in the ICIQ score in 134 subjects of the effectiveness population, the mean score decreased by 6.84±5.53 from 14.34±4.97 before the study drug administration to 7.51±5.83 after the study drug administration. The mean change in ICIQ from baseline was statistically significant (p<0.0001) (Table 48).

Table 48. Change in ICIQ score (Neurogenic Detrusor Overactivity)

	n	mean± std	median	min~ max
before BOTOX injection	134	14.34± 4.97	15.00	0.00~ 21.00
after BOTOX injection	134	7.51± 5.83	7.00	0.00~ 21.00
after BOTOX injection - before BOTOX injection	134	-6.84± 5.53	-7.00	-21.00~ 10.00
p-value(paired t-test)		<0.0001		

When analyzing changes in ICIQ scores in the effectiveness population by range, it was '< 5' in 64.93% (87/134 subjects), '≥ -5 to < 0' in 17.91% (24/134 subjects), '≥ 0 to < 5' in 15.67% (21/134 subjects), and '≥ 5' in 1.49% (2/134 subjects) (Table 49).

Table 49. Change in ICIQ score by range (Neurogenic Detrusor Overactivity)

	Total n(%)
< -5	87(64.93)
≥ -5 to < 0	24(17.91)
≥ 0 to < 5	21(15.67)
≥ 5	2(1.49)
Total	134(100.00)

The denominator is number of total subjects.

The mean time to ICIQ assessment completion from baseline was 47.49±23.84 days (Table 50).

Table 50. Time to ICIQ assessment completion (Neurogenic Detrusor Overactivity)

	Total (N=134)
n	134
mean±std (days)	47.49± 23.84
median	40.50
min ~ max	27.00~ 183.00

Duration between baseline and follow-up ICIQ completion = Date of after BOTOX treatment - Date of before BOTOX treatment + 1

When investigating the degree of urine leaks before/after the study drug administration by multiple counting, 'Never-urine does not leak' accounted for 7.52% (10/133 subjects) before the study drug administration, but it accounted for 59.85% (79/132 subjects) after the study drug administration (Table 51).

'Leaks before you can get to the toilet' accounted for 21.05% (28/133 subjects) before the study drug administration, but it accounted for 8.33% (11/132 subjects) after the study drug administration (Table 51).

'Leaks when you cough or sneeze' accounted for 6.77% (9/133 subjects) before the study drug administration, but it accounted for 6.06% (8/132 subjects) after the study drug administration (Table 51). Note that 'Leaks when you cough or sneeze' is a symptom of stress incontinence, which is not indicated for BOTOX.

'Leaks when you are asleep' accounted for 21.80% (29/133 subjects) before the study drug administration, but it accounted for 7.58% (10/132 subjects) after the study drug administration (Table 51).

'Leaks when are physically active/exercising' accounted for 19.55% (26/133 subjects) before the study drug administration, but it accounted for 12.12% (16/132 subjects) after the study drug administration (Table 51). Note that 'Leaks when are physically active/exercising' is a symptom of stress incontinence, which is not indicated for BOTOX.

'Leaks when you have finished urinating and are dressed' accounted for 5.26% (7/133 subjects) before the study drug administration, but it accounted for 1.52% (2/132 subjects) after the study drug administration (Table 51).

'Leaks for no obvious reason' accounted for 61.65% (82/133 subjects) before the study drug administration, but it accounted for 14.39% (19/132 subjects) after the study drug administration (Table 51).

'Leaks all the time' accounted for 11.28% (15/133 subjects) before the study drug administration, but it accounted for 6.06% (8/132 subjects) after the study drug administration (Table 51).

Table 51. Degree of urine leaks before/after the study drug administration (Neurogenic Detrusor Overactivity)

Overlapped¶	Before BOTOX n(%)	After BOTOX n(%)
Never-urine does not leak	10(7.52)	79(59.85)
Leaks before you can get to the toilet	28(21.05)	11(8.33)
Leaks when you cough or sneeze	9(6.77)	8(6.06)
Leaks when you are asleep	29(21.80)	10(7.58)
Leaks when are physically active/exercising	26(19.55)	16(12.12)
Leaks when you have finished urinating and are dressed	7(5.26)	2(1.52)
Leaks for no obvious reason	82(61.65)	19(14.39)
Leaks all the time	15(11.28)	8(6.06)
Total	133(100.00)	132(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
Missing: 1 (Before BOTOX), 2 (After BOTOX)

3.2.2 Effectiveness evaluation by factor

A. Background factors

When analyzing ICIQ score change before/after the study drug administration by age, the mean decrease of 6.70±5.78 was found in subjects '< 50 years' and it was statistically significant (p<0.0001). The mean decrease of 6.87±5.46 was found in '≥ 50 years to < 60 years', which was statistically significant (p<0.0001). The mean decrease of 5.20±4.76 was found in '≥ 60 years to < 70 years', which was statistically significant (p<0.0001). The mean decrease of 10.00±5.14 was found in '≥ 70 years', which was statistically significant (p<0.0001). Difference in ICIQ score changes among the groups was not statistically significant (p=0.0662) (Table 52).

When analyzing ICIQ score change before/after the study drug administration by sex, the mean decrease of 6.60±4.73 was found in 'Male' subjects and it was statistically significant (p<0.0001). The mean decrease of 7.55±7.52 was found in 'Female' subjects, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.5025) (Table 52).

When analyzing ICIQ score change before/after the study drug administration by treatment setting, the mean decrease of 6.53±4.71 was found in 'Outpatient' subjects and it was

statistically significant (p<0.0001). The mean decrease of 7.54±7.07 was found in 'Inpatient', which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.4066) (Table 52).

When analyzing ICIQ score change before/after the study drug administration by underlying neurologic conditions, the mean decrease of 7.80±6.26 was found in 'Multiple Sclerosis' subjects and it was statistically significant (p=0.0495). The mean decrease of 6.80±5.53 was found in 'Spinal Cord Injury' subjects, which was statistically significant (p<0.0001). Decrease of 10.00 was found in 'Other' subjects (Table 52).

Among female subjects, there was no pregnant subject (Table 52).

Table 52. Effectiveness evaluation by background factor (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Age	< 50 years	56	-6.70± 5.78	-7.00	-21.00~ 3.00	<0.0001	0.0662
	≥ 50 years to < 60 years	38	-6.87± 5.46	-7.00	-18.00~ 9.00	<0.0001	
	≥ 60 years to < 70 years	25	-5.20± 4.76	-7.00	-14.00~ 10.00	<0.0001	
	≥ 70 years	15	-10.00± 5.14	-8.00	-21.00~ -1.00	<0.0001	
Sex	Male	101	-6.60± 4.73	-7.00	-21.00~ 9.00	<0.0001	0.5025
	Female	33	-7.55± 7.52	-8.00	-21.00~ 10.00	<0.0001	
Treatment Setting	Outpatient	93	-6.53± 4.71	-7.00	-18.00~ 9.00	<0.0001	0.4066
	Inpatient	41	-7.54± 7.07	-7.00	-21.00~ 10.00	<0.0001	
Currently pregnant	Yes	0					NA
* for female	No	33	-7.55± 7.52	-8.00	-21.00~ 10.00	<0.0001	
Underlying neurologic condition§	Multiple Sclerosis	5	-7.80± 6.26	-6.00	-16.00~ 0.00	0.0495	NA
* for patients with NDO	Spinal Cord Injury	129	-6.80± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Overlapped¶	Other	1	-10.00	-10.00	-10.00~ -10.00		

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).

B. Past treatment history

When analyzing ICIQ score change before/after the study drug administration by previous anticholinergic therapy, subjects who had received anticholinergic therapy showed the mean decrease of 6.89±5.52, which was statistically significant (p<0.0001). There was no change in the score before/after the study drug administration in subjects without previous anticholinergic therapy. Difference in ICIQ score changes between the groups was not statistically significant (p=0.2162) (Table 53).

When analyzing ICIQ score change before/after the study drug administration by previous use of sacral neuromodulation therapy, no change was found in subjects who had received sacral neuromodulation therapy. Subjects without previous sacral neuromodulation therapy showed the mean decrease of 6.89±5.52, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.2162) (Table 53).

When analyzing ICIQ score change before/after the study drug administration by past treatment history with the study drug for other indication or other botulinum toxin, the mean decrease of 4.55±6.76 were found in subjects who had used the study drug or other botolimum toxin, which was statistically significant (p=0.0498). Subjects who had not been previously treated with BOTOX or other botulinum toxin showed the mean decrease of 7.04±5.40, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.1526) (Table 53).

Table 53. Effectiveness evaluation by past treatment history (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Previous Anticholinergic Therapy	Yes	133	-6.89± 5.52	-7.00	-21.00~ 10.00	<0.0001	0.2162
	No	1	0.00	0.00	0.00~ 0.00		
Previous Use of Sacral Neuromodulation Therapy	Yes	1	0.00	0.00	0.00~ 0.00		0.2162
	No	133	-6.89± 5.52	-7.00	-21.00~ 10.00	<0.0001	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	11	-4.55± 6.76	-1.00	-21.00~ 2.00	0.0498	0.1526
	None	123	-7.04± 5.40	-7.00	-21.00~ 10.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

C. Medical history

When analyzing ICIQ score change before/after the study drug administration by medical history including surgeries and complications of underlying diseases, the mean decrease of 6.69±5.96 was found in subjects with medical history, which was statistically significant (p<0.0001). Subjects without medical history showed the mean decrease of 7.27±3.99, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.5277) (Table 54).

ICIQ score change before/after the study drug administration by medical history type (multiple counting allowed) are presented in the table below (Table 54).

When analyzing ICIQ score change before/after the study drug administration by allergy history, the mean decrease of 5.13±5.46 was found in subjects with allergy history, which was statistically significant (p=0.0328). Subjects without allergy history showed the mean decrease of 6.94±5.54, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.3691) (Table 54).

ICIQ score change before/after the study drug administration by allergen (multiple counting allowed) are presented in the table below (Table 54).

Table 54. Effectiveness evaluation by medical history (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	101	-6.69± 5.96	-7.00	-21.00~ 10.00	<0.0001	0.5277
	None	33	-7.27± 3.99	-7.00	-18.00~ 0.00	<0.0001	
	Details for Medical History by dictionary (Overlapped¶)						
	Diseases of the circulatory system	37	-6.00± 5.89	-8.00	-18.00~ 10.00	<0.0001	
	Factors influencing health status and contact with health services	24	-6.21± 7.95	-5.50	-21.00~ 10.00	0.0009	
	Endocrine, nutritional and metabolic diseases	25	-7.20± 5.66	-7.00	-16.00~ 10.00	<0.0001	
	Diseases of the genitourinary system	22	-5.95± 7.44	-5.00	-21.00~ 9.00	0.0012	
	Diseases of the digestive system	28	-6.18± 7.08	-5.50	-18.00~ 10.00	<0.0001	
	Diseases of the musculoskeletal system and connective tissue	14	-5.21± 8.98	-5.50	-21.00~ 10.00	0.0489	
	Neoplasms	9	-4.11± 5.01	-6.00	-10.00~ 2.00	0.0392	
	Mental and behavioural disorders	13	-5.15± 7.43	-4.00	-21.00~ 2.00	0.0278	
	Diseases of the nervous system	36	-6.75± 6.65	-5.00	-21.00~ 3.00	<0.0001	
	Diseases of the respiratory system	7	-5.14± 6.20	-5.00	-15.00~ 2.00	0.0707	
	Diseases of the eye and adnexa	2	-3.00± 18.38	-3.00	-16.00~ 10.00	0.8556	
	Injury, poisoning and certain other consequences of external causes	8	-4.75± 7.55	0.00	-16.00~ 2.00	0.1186	
	Certain infectious and parasitic diseases	2	-3.00± 4.24	-3.00	-6.00~ 0.00	0.5000	
	Diseases of the skin and subcutaneous tissue	8	-8.00± 6.89	-8.00	-17.00~ 0.00	0.0134	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2	-6.50± 3.54	-6.50	-9.00~ -4.00	0.2338	
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	13	-4.54± 6.08	-2.00	-17.00~ 2.00	0.0196	
History of Allergies	Yes	8	-5.13± 5.46	-5.50	-15.00~ 2.00	0.0328	0.3691
	None	126	-6.94± 5.54	-7.00	-21.00~ 10.00	<0.0001	
	Details for History of Allergies by dictionary						
	Factors influencing health status and contact with health services	6	-6.17± 5.49	-6.50	-15.00~ 0.00	0.0403	
	Injury, poisoning and certain other consequences of external causes	2	-2.00± 5.66	-2.00	-6.00~ 2.00	0.7048	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

D. Concomitant medications

When analyzing ICIQ score change before/after the study drug administration by use of concomitant medications, the mean decrease 6.78±5.53 was found in subjects with concomitant medications, which was statistically significant (p<0.0001). Subjects without concomitant medications showed the mean decrease of 9.33±6.51, which was not statistically significant (p=0.1309). Difference in ICIQ score changes between the groups was not statistically significant (p=0.4312) (Table 55).

ICIQ score change before/after the study drug administration by concomitant medication type (multiple counting allowed) are presented in the table below (Table 55).

Table 55. Effectiveness evaluation by concomitant medications (Neurogenic Detrusor Overactivity)

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Yes	131	-6.78± 5.53	-7.00	-21.00~ 10.00	<0.0001	0.4312
No	3	-9.33± 6.51	-9.00	-16.00~ -3.00	0.1309	
Details for Concomitant Medication by dictionary (Overlapped¶)						
Anaesthetics- Local & General	119	-6.73± 5.45	-7.00	-21.00~ 10.00	<0.0001	
Anaesthetics - Local & General	119	-6.73± 5.45	-7.00	-21.00~ 10.00	<0.0001	
Central Nervous System	89	-7.12± 5.61	-7.00	-21.00~ 9.00	<0.0001	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	26	-9.23± 6.43	-8.50	-21.00~ 3.00	<0.0001	
Analgesics (Non-Opioid) & Antipyretics	41	-8.59± 4.62	-8.00	-21.00~ 2.00	<0.0001	
Analgesics (Opioid)	27	-6.78± 6.46	-6.00	-18.00~ 2.00	<0.0001	
Hypnotics & Sedatives	11	-4.91± 7.30	0.00	-18.00~ 2.00	0.0498	
Antidepressants	25	-6.56± 6.47	-7.00	-21.00~ 9.00	<0.0001	
Drugs For Neuropathic Pain	31	-7.58± 4.08	-8.00	-15.00~ 0.00	<0.0001	
Anxiolytics	15	-8.00± 5.64	-8.00	-18.00~ 2.00	<0.0001	
Anticonvulsants	21	-8.24± 5.17	-8.00	-21.00~ 2.00	<0.0001	
Neurodegenerative Disease Drugs	1	-21.00	-21.00	-21.00~ -21.00		
Antiparkinsonian Drugs	2	-18.00± 4.24	-18.00	-21.00~ -15.00	0.1051	
Antipsychotics	2	-8.00± 14.14	-8.00	-18.00~ 2.00	0.5704	
Gastrointestinal & Hepatobiliary System	85	-7.24± 5.39	-7.00	-21.00~ 9.00	<0.0001	
Antacids, Antireflux Agents & Antiulcerants	55	-7.91± 4.94	-8.00	-21.00~ 3.00	<0.0001	
GIT Regulators, Antiflatulents & Anti-inflammatories	39	-6.08± 4.79	-7.00	-16.00~ 9.00	<0.0001	
Digestives	7	-9.14± 7.36	-10.00	-18.00~ 2.00	0.0167	
Laxatives, Purgatives	32	-7.84± 5.35	-7.50	-18.00~ 2.00	<0.0001	
Antiemetics	11	-8.64± 6.12	-6.00	-18.00~ 1.00	0.0009	
Antispasmodics	6	-10.33± 4.23	-9.00	-16.00~ -6.00	0.0019	
Antidiarrheals	1	-9.00	-9.00	-9.00~ -9.00		
Cholagogues, Cholelitholytics & Hepatic Protectors	2	-5.00± 7.07	-5.00	-10.00~ 0.00	0.5000	
Cardiovascular & Hematopoietic System	26	-5.58± 5.79	-6.00	-18.00~ 10.00	<0.0001	
Dyslipidaemic Agents	6	-7.17± 3.25	-6.50	-12.00~ -4.00	0.0029	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	7	-4.14± 8.71	-2.00	-17.00~ 10.00	0.2548	
Calcium Antagonists	7	-2.14± 6.15	-4.00	-9.00~ 10.00	0.3921	
Angiotensin II Antagonists	2	4.50± 7.78	4.50	-1.00~ 10.00	0.5635	
Other Antihypertensives	5	-7.40± 2.61	-7.00	-10.00~ -4.00	0.0032	
Beta-Blockers	1	-10.00	-10.00	-10.00~ -10.00		
Peripheral Vasodilators & Cerebral Activators	2	-6.00± 1.41	-6.00	-7.00~ -5.00	0.1051	
Other Cardiovascular Drugs	1	-7.00	-7.00	-7.00~ -7.00		
Vasoconstrictors	3	-8.67± 9.50	-9.00	-18.00~ 1.00	0.2550	
Phlebitis & Varicose Preparations	1	-2.00	-2.00	-2.00~ -2.00		
Antidiuretics	2	0.00± 0.00	0.00	0.00~ 0.00		
Musculo-Skeletal System	40	-7.10± 5.61	-7.00	-18.00~ 10.00	<0.0001	
Muscle Relaxants	38	-7.37± 4.88	-7.00	-18.00~ 3.00	<0.0001	
Neuromuscular Disorder Drugs	5	-12.40± 4.28	-15.00	-16.00~ -6.00	0.0029	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	1	10.00	10.00	10.00~ 10.00		
Hyperuricemia & Gout Preparations	1	-14.00	-14.00	-14.00~ -14.00		
Endocrine & Metabolic System	14	-4.71± 6.40	-4.50	-17.00~ 10.00	0.0164	
Antidiabetic Agents	9	-3.00± 5.45	-4.00	-9.00~ 10.00	0.1375	
Other Agents Affecting Metabolism	2	-10.00± 1.41	-10.00	-11.00~ -9.00	0.0635	
Agents Affecting Bone Metabolism	3	-6.33± 10.07	-5.00	-17.00~ 3.00	0.3896	
Intravenous & Other Sterile Solutions	14	-7.86± 5.65	-8.00	-18.00~ 1.00	0.0002	

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Intravenous & other sterile solutions	14	-7.86± 5.65	-8.00	-18.00~ 1.00	0.0002	
Genito-Urinary System	19	-6.63± 7.69	-5.00	-21.00~ 9.00	0.0014	
Drugs for Bladder & Prostate Disorders	18	-7.00± 7.74	-5.50	-21.00~ 9.00	0.0013	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	2	4.50± 6.36	4.50	0.00~ 9.00	0.5000	
Respiratory System	13	-9.00± 7.35	-6.00	-18.00~ 2.00	0.0008	
Antiasthmatic & COPD Preparations	8	-8.25± 7.15	-5.00	-18.00~ 1.00	0.0138	
Cough & Cold Preparations	11	-7.45± 6.90	-5.00	-18.00~ 2.00	0.0050	
Nasal Decongestant & Other Nasal Preparations	1	-17.00	-17.00	-17.00~ -17.00		
Oncology	4	-5.75± 4.19	-6.50	-10.00~ 0.00	0.0712	
Supportive Care Therapy	4	-5.75± 4.19	-6.50	-10.00~ 0.00	0.0712	
Vitamins & Minerals	15	-6.73± 7.19	-5.00	-21.00~ 3.00	0.0027	
Calcium / with Vitamins	11	-5.73± 6.93	-4.00	-18.00~ 3.00	0.0208	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	2	-4.00± 2.83	-4.00	-6.00~ -2.00	0.2952	
Vitamin B-complex / with C	2	-3.00± 8.49	-3.00	-9.00~ 3.00	0.7048	
Vitamins &/or Minerals	1	-5.00	-5.00	-5.00~ -5.00		
Vitamin C	1	-2.00	-2.00	-2.00~ -2.00		
Vitamins & Minerals (Geriatric)	1	-21.00	-21.00	-21.00~ -21.00		
Anti-infectives (systemic)	9	-6.56± 6.19	-6.00	-17.00~ 1.00	0.0130	
Cephalosporins	5	-3.00± 4.74	-2.00	-11.00~ 1.00	0.2302	
Quinolones	4	-7.50± 4.20	-7.00	-13.00~ -3.00	0.0376	
Antivirals	1	-17.00	-17.00	-17.00~ -17.00		
Antibacterial Combinations	1	-2.00	-2.00	-2.00~ -2.00		
Allergy & Immune System	3	-11.00± 9.54	-16.00	-17.00~ 0.00	0.1839	
Antihistamines & Antiallergics	1	0.00	0.00	0.00~ 0.00		
Immunosuppressants	2	-16.50± 0.71	-16.50	-17.00~ -16.00	0.0193	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	5	-5.80± 7.16	-4.00	-18.00~ 1.00	0.1441	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	5	-5.80± 7.16	-4.00	-18.00~ 1.00	0.1441	
Hormones	3	-9.67± 10.12	-15.00	-16.00~ 2.00	0.2397	
Corticosteroid Hormones	2	-15.50± 0.71	-15.50	-16.00~ -15.00	0.0205	
Other Drugs Affecting Hormonal Regulation	1	2.00	2.00	2.00~ 2.00		
Nutrition	10	-10.80± 6.44	-12.00	-18.00~ 2.00	0.0005	
Parenteral Nutritional Products	8	-11.63± 4.87	-12.00	-18.00~ -4.00	0.0003	
Electrolytes	6	-11.17± 5.53	-11.50	-18.00~ -4.00	0.0043	
Appetite Enhancers	1	2.00	2.00	2.00~ 2.00		
Supplements & Adjuvant Therapy	1	-17.00	-17.00	-17.00~ -17.00		
Eye	3	-7.67± 6.43	-5.00	-15.00~ -3.00	0.1749	
Ophthalmic Lubricants	2	-4.00± 1.41	-4.00	-5.00~ -3.00	0.1560	
Eye Anti-infectives & Antiseptics	1	-15.00	-15.00	-15.00~ -15.00		
Dermatologicals	2	-3.50± 2.12	-3.50	-5.00~ -2.00	0.2578	
Topical Corticosteroids	1	-5.00	-5.00	-5.00~ -5.00		
Topical Antifungals & Antiparasites	1	-2.00	-2.00	-2.00~ -2.00		

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

E. Special population

Subjects of '65 or/and over' were classified into elderly group. When analyzing ICIQ score change before/after the study drug administration in elderly and non-elderly groups, the mean

decrease of 8.79±4.85 was found in the group of '65 or/and over', which was statistically significant (p<0.0001). The mean decrease of 6.41±5.60 was found in the group of 'below 65 years', which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.0557) (Table 56).

When analyzing ICIQ score change before/after the study drug administration by presence of renal impairment, the mean decrease of 4.33±8.50 was found in subjects with renal impairment, which was not statistically significant (p=0.4706), and the mean decrease of 6.89±5.48 was found in subjects without renal impairment, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.4303) (Table 56).

When analyzing ICIQ score change before/after the study drug administration by hepatic impairment, the mean increase of 0.50±0.71 was found in subjects with hepatic impairment, which was not statistically significant (p=0.5000). Subjects without hepatic impairment showed the mean decrease of 6.95±5.50, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.0586) (Table 56).

Table 56. Effectiveness evaluation in special population (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Elderly	below 65 years	110	-6.41± 5.60	-7.00	-21.00~ 10.00	<0.0001	0.0557
	65 or/and over	24	-8.79± 4.85	-8.00	-21.00~ 0.00	<0.0001	
Renal impairment	Yes	3	-4.33± 8.50	-1.00	-14.00~ 2.00	0.4706	0.4303
	No	131	-6.89± 5.48	-7.00	-21.00~ 10.00	<0.0001	
Hepatic impairment	Yes	2	0.50± 0.71	0.50	0.00~ 1.00	0.5000	0.0586
	No	132	-6.95± 5.50	-7.00	-21.00~ 10.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

F. Information of the study drug administration

When analyzing ICIQ score change before/after the study drug administration by the number of injection sites and total injection dose, all subjects in the effectiveness population received total 200 U in 30 sites and their ICIQ score change before/after the study drug administration was the same as that of the effectiveness population (Table 57).

When analyzing ICIQ score change before/after the study drug administration by use of anesthesia at the study drug administration, the mean decrease of 9.18±4.98 was found in 'None' anesthesia group, which was statistically significant (p=0.0001). The mean decrease of 6.52±5.04 was found in 'Local' anesthesia group, which was statistically significant (p=0.0001). The mean decrease of 7.04±7.26 was found in 'General' anesthesia group, which was statistically significant (p<0.0001). Difference in ICIQ score changes between the groups was not statistically significant (p=0.3131) (Table 57).

When analyzing the ICIQ score change by use of prophylactic antibiotics before, during, and after the study drug administration, the mean decrease of 6.91±5.46 was found in subjects with

antibiotics, which was statistically significant (p<0.0001). Subjects without antibiotics showed the mean decrease of 5.00±7.68, which was not statistically significant (p=0.2192). Difference in ICIQ score changes between the groups was not statistically significant (p=0.4517) (Table 57).

Table 57. Effectiveness evaluation by the information of study drug administration (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Number of Injection Sites	20	0					NA
	30	134	-6.84± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Total Units Injected	100	0					NA
	200	134	-6.84± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Anesthesia	None	11	-9.18± 4.98	-8.00	-17.00~ -3.00	0.0001	0.3131
	Local	97	-6.52± 5.04	-7.00	-21.00~ 10.00	<0.0001	
	General	26	-7.04± 7.26	-4.50	-18.00~ 2.00	<0.0001	
Prophylactic Antibiotic Use	Yes	129	-6.91± 5.46	-7.00	-21.00~ 10.00	<0.0001	0.4517
	No	5	-5.00± 7.68	-1.00	-18.00~ 0.00	0.2192	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

G. Clean intermittent catheterization

When analyzing ICIQ score change before/after the study drug administration by use of urinary catheterization before the study drug administration, the mean decrease of 6.75±5.22 was found in subjects with clean intermittent catheterization, which was statistically significant (p<0.0001). Subjects without clean intermittent catheterization showed the mean decrease of 7.39±7.42, which was statistically significant (p=0.0006). Difference in ICIQ score changes between the groups was not statistically significant (p=0.7286) (Table 58).

When analyzing ICIQ score change before/after the study drug administration by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, the mean decrease of 6.00±6.78 was found in subjects with urinary catheterization, which was statistically significant (p=0.0409). Subjects without urinary catheterization showed the mean decrease of 8.50±8.07, which was statistically significant (p=0.0088). Difference in ICIQ score changes between the groups was not statistically significant (p=0.4943). Among the subjects with urinary catheterization, the mean decrease of 13.00±4.36 was found in subjects who initiated catheterization due to urinary retention (p=0.0355) and the mean decrease of 1.80±3.49 was found in subjects who initiated catheterization due to other reason (p=0.3134) (Table 58).

Table 58. Effectiveness evaluation by use of clean intermittent catheterization (Neurogenic Detrusor Overactivity)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Routine Urinary Catheterization(before BOTOX)	Yes	116	-6.75± 5.22	-7.00	-21.00~ 10.00	<0.0001	0.7286
	No	18	-7.39± 7.42	-7.00	-21.00~ 2.00	0.0006	
Initiation of CIC after BOTOX injection§	Yes	8	-6.00± 6.78	-5.50	-16.00~ 2.00	0.0409	0.4943**
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	3	-13.00± 4.36	-15.00	-16.00~ -8.00	0.0355	
	initiated CIC due to "Other Reason"	5	-1.80± 3.49	0.00	-6.00~ 2.00	0.3134	
	No	10	-8.50± 8.07	-9.50	-21.00~ 2.00	0.0088	

The p-value(a) is about that the ICIQ Score change by the subject characteristics
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change
(a): Paired t-test
(b): T-test or ANOVA
**The p-value is about that relation between Yes/No and the amount of ICIQ Score Change.

H. Factors that may affect effectiveness

For the effectiveness evaluation in this PMS, evaluation was conducted by age, sex, treatment setting, pregnancy status, underlying neurological conditions, past treatment history, medical history, concomitant medications, and the study information of study drug administration as well as in special population such as the elderly and subjects with renal or hepatic impairment. In the evaluation results, there was no factor that significantly affected the effectiveness.

Ⅳ. Discussion on Results and Further Measures (Neurogenic Detrusor Overactivity)

4. Discussion on Results and Further Measures (Neurogenic Detrusor Overactivity)

During the re-examination period, CRFs were collected from a total of 173 subjects. Among the subjects, 161 subjects were included in the safety evaluation, except 5 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), and 1 subject who violate the dosage (ie, subject received an unapproved dosage). Among the safety population, 134 subjects were included in the effectiveness evaluation, except 27 subjects whose ICIQ Scores at the baseline or follow-up on the CRF are not recorded.

During the PMS period, 27 AEs occurred in 19 out of 161 subjects in the safety population, which indicated that incidence of AEs was 11.80%. Examining the AEs by PT, 'URINARY TRACT INFECTION' occurred in 2.98% (5/168 subjects), followed by 'URINARY RETENTION', 'DYSURIA', 'HEADACHE', and 'MYALGIA' each in 1.19% (2/168 subjects) and 'HAEMATURIA', 'PYURIA', and 'DIFFICULTY IN MICTURITION' each in 0.60% (1/168 subjects).

Among them, 11 events occurred in 10 subjects (5.95%) were ADRs which cannot rule out the relationship to the study drug.

Examining the ADRs by PT, 'URINARY RETENTION', 'DYSURIA', 'URINARY TRACT INFECTION', and 'MYALGIA' occurred in 1.19% (2/168 subjects) each, followed by 'DIFFICULTY IN MICTURITION', 'CONSTIPATION', and 'TESTIS DISORDER' each in 0.60% (1/168 subjects).

During the PMS period, a total of 9 unexpected AEs were reported from 8 subjects (4.97%) in the safety population. Examining the unexpected AEs by PT, 'HEADACHE' occurred in 1.24% (2/161 subjects), followed by 'DYSPEPSIA', 'PELVIC PAIN', and 'PAIN IN LIMB' each in 0.62% (1/161 subjects). Among them, 1 event of 'TESTIS DISORDER' was an unexpected ADR which cannot rule out the relationship to the study drug. But the causal relationship between 'TESTIS DISORDER' and the study drug could not be established based on the study data.

During the PMS period, no SAE was reported in the safety population.

When classifying and evaluating the expectedness of AEs, 'Expected AE' accounted for 66.67% (18/27 events) and 'Unexpected AE' accounted for 33.33% (9/27 events).

When classifying and evaluating the seriousness of AEs into two of 'Serious' and 'Non-serious', all AEs were 'Non-serious'.

When classifying and evaluating the severity of AEs, 'Mild' occurred in 66.67% (18/27 events), 'Moderate' in 33.33% (9/27 events) and none were severe.

When classifying and evaluating the outcome of AEs, 'Resolved without sequelae' was reported in 92.59% (25/27 events) and 'Ongoing' in 7.41% (2/27 events). No fatal outcome has been reported.

When classifying and evaluating the causal relationship of AEs to the study drug, 'Unlikely' was

reported in 62.96% (17/27 events), 'Possible' and 'Unassessable/Unclassifiable' was reported in 11.11% (3/27 events) each, and 'Certain' was reported in 7.41% (2/27 events).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure, 'Unlikely' was 77.78% (21/27 events), and 'Possible' and 'Unassessable/Unclassifiable' was 11.11% (3/27 events) each.

When comparing and analyzing the ICIQ score change before/after the study drug administration, the mean decrease of 6.84±5.53 was found from baseline, and it was statistically significant ($p<0.0001$).

In conclusion, the PMS study results showed no specific trend comparing to previously reported AE incidence and no specific matter that may affect the safety and effectiveness. There were no events of distant spread of toxin reported. Therefore, we will continuously monitor the use of BOTOX through routine pharmacovigilence activities.

B. Overactive Bladder

Ⅰ. General Matters of Investigation (Overactive Bladder)

1. General Matters of Investigation (Overactive Bladder)

1.1 Re-examination period (Overactive Bladder)

31 Aug 2012 ~ 30 Aug 2016

1.2 Number of subjects (Overactive Bladder)

During the re-examination period, CRFs were collected from a total of 564 subjects. Among the subjects whose CRFs were retrieved, a total of 525 subjects were included in the safety evaluation except 28 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 2 subjects lost to follow-up, and 9 subjects who violate the dosage (ie, subjects received an unapproved dosage). Among the safety population, 478 subjects were included in the effectiveness evaluation, except 47 subjects whose record ICIQ Scores at the baseline or follow-up on the CRF are not completed.

Number of subjects whose CRFs were retrieved	564
Number of subjects included in safety evaluation	525
Number of subjects included in effectiveness evaluation	478

Number of sites	From 31 Aug 2012 to 30 Aug 2016, CRFs were collected from 564 subjects by 41 Investigators in 40 hospitals.
Method of investigation	This PMS was done in a manner that subjects who received Botox Inj. following the signed date were asked to successively participate in the PMS, up to the requested number of subjects, and it was pooled with post-marketing clinical tiral (Phase 4) data for analysis.
CRF format	Appendix 2
Point to be investigated with priority	There was no specific focus in this surveillance since no specific issues had been identified in clinical study results during the development phase as well as in post-marketing experiences in other countries. During this re-examination period, very rarely occurring AEs and unexpected AEs of which causal relationship to the study drug had not been established were to be monitored and investigated with particular interest.

1.3 PMS management chart (Overactive Bladder)

Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled
[redacted]									

Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled

Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled
[redacted]									

Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled
			Hospital						
Total								1,110	564

* CRFs of subjects in the sites were collected through post-marketing clinical trial (Phase 4).
** Contracted number of cases includes both Neurogenic Detrusor Overactivity and Overactive Bladder.

Ⅱ. Overview of PMS Results (Overactive Bladder)

2. Overview of PMS Results (Overactive Bladder)

2.1 Overview and purpose of PMS (Overactive Bladder)

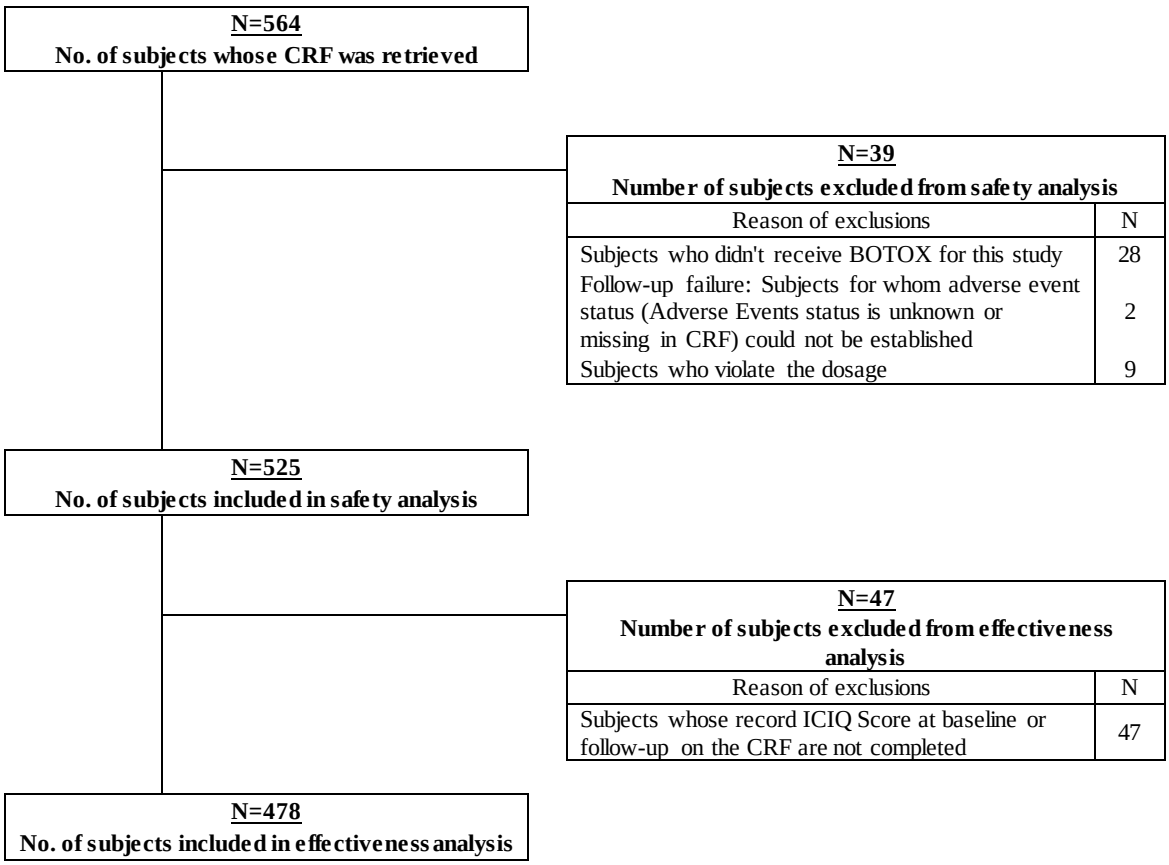
This PMS was conducted to examine whether unexpected AEs and SAEs occurred, frequency of AEs and the variations, and factors likely to influence safety and effectiveness under the post-marketing uses of BOTOX in subjects of 'Treatment of Overactive Bladder with urge urinary incontinence, urgency, and frequency in adults aged 18 years or over an inadequate response to or are intolerant of an anticholinergic therapy (hereafter 'Overactive Bladder')' who received Botox Inj. (hereafter the 'study drug').

This PMS investigated subjects' fundamental demographic data, follow-up duration, past treatment history, medical history, special population, information of study drug administration, use of clean intermittent catheterization, safety, and effectiveness. This PMS was planned to investigate all types of AEs, which were incurred during the investigation period including AEs whose causal relationship to BOTOX Inj. has not been established yet and unexpected AEs/ADRs. The purpose of this study was toevaluate the safety and effectiveness of BOTOX for the treatment of OAB through active surveillance under routine clinical practice after the launch of BOTOX in Korea..

2.2 Analysis set of PMS (Overactive Bladder)

During this PMS, CRFs were collected from 564 subjects. Among the subjects, 525 subjects were included in the safety evaluation except 28 subjects who didin’t received Botox for this study due to consent withdrawal or other reasons, 2 subjects of follow-up failured, and 9 subjects who violate the dosage (ie, subjects received an unapproved dosage),. Among the safety population, 478 subjects were included in the effectiveness evaluation, except 47 subjects whose record ICIQ Score at baseline or follow-up on the CRF are not completed (Figure 2).

Figure 2. Analysis set of PMS (Overactive Bladder)



2.3 Fundamental demographic data of subjects (Overactive Bladder)

2.3.1 All subjects

Of 564 subjects with CRFs collected, the mean age was 62.66±14.36 years, ranged from 19 to 89 years of age. The largest subject age group was '≥ 70 years' in 38.12% (215/564 subjects), followed by '≥ 60 years to < 70 years' in 23.76% (134/564 subjects), '≥ 50 years to < 60 years' in 19.68% (111/564 subjects), and '≥ 50 years' in 18.44% (104/564 subjects) (Table 59).

In all subjects, 'Male' accounted for 21.10% (119/564 subjects) and 'Female' accounted for 78.90% (445/564 subjects) (Table 59).

In all subjects, the mean height was 157.57±7.99 cm, ranged from 133.00 to 185.00 cm (Table 59).

In all subjects, the mean body weight was 60.50±10.43 kg, ranged from 32.50 to 100.00 kg (Table 59).

When classifying all subjects by treatment setting, 'Outpatient' was 39.18% (221/564 subjects) and 'Inpatient' was 60.82% (343/564 subjects) (Table 59).

The mean duration after diagnosis in all subjects was 4.82±5.27 years and the most common

symptom (multiple counting allowed) was 'Frequency' in 72.52% (409/564 subjects), followed by 'Urge urinary incontinence' in 70.74% (399/564 subjects), 'Urgency' in 66.49% (375/564 subjects), and 'Other' in 17.73% (100/564 subjects). Symptoms belonging to 'Other' included 'Nocturia' and 'Stress urinary incontinence' (Table 59).

Among female subjects, there was no pregnant subject (Table 59).

Table 59. Demographic data in all subjects (Overactive Bladder)

		Total n(%)
Age	mean±std (years)	62.66± 14.36
	median	65.00
	min ~ max	19.00~ 89.00
	< 50 years	104(18.44)
	≥ 50 years to < 60 years	111(19.68)
	≥ 60 years to < 70 years	134(23.76)
	≥ 70 years	215(38.12)
	Total	564(100.00)
Sex	Male	119(21.10)
	Female	445(78.90)
	Total	564(100.00)
Height	n	558
	mean±std (cm)	157.57± 7.99
	median	158.00
	min ~ max	133.00~ 185.00
Weight	n	559
	mean±std (kg)	60.50± 10.43
	median	60.00
	min ~ max	32.50~ 100.00
Treatment Setting	Outpatient	221(39.18)
	Inpatient	343(60.82)
	Total	564(100.00)
Currently pregnant	Yes	0(0.00)
* for female	No	445(100.00)
	Total	445(100.00)
Duration since OAB diagnosis	n	542
	mean±std (years)	4.82± 5.27
	median	3.00
	min ~ max	0.00~ 40.00
Symptoms	Urge urinary incontinence	399(70.74)
* for patients with OAB	Urgency	375(66.49)
Overlapped¶	Frequency	409(72.52)
	Other	100(17.73)
	Total	564(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
Unkown: 6 (Height), 5 (Weight), 22 (Duration since OAB diagnosis)

2.3.2 Safety population

Of 525 subjects in the safety population, the mean age was 62.54±14.54 years, ranged from 19 to 89 years of age. The largest subject age group was '≥ 70 years' in 38.67% (203/525 subjects), followed by '≥ 60 years to < 70 years' in 23.24% (122/525 subjects), '≥ 50 years to < 60 years' in 19.24% (101/525 subjects), and '≥ 50 years' in 18.86% (99/525 subjects) (Table 60).

In the safety population, 'Male' accounted for 21.33% (112/525 subjects) and 'Female' accounted for 78.67% (413/525 subjects) (Table 60).

In the safety population, the mean height was 157.52±8.05 cm, ranged from 133.00 to 185.00 cm (Table 60).

In the safety population, the mean body weight was 60.46±10.48 kg, ranged from 32.50 to 100.00 kg (Table 60).

When classifying safety population by treatment setting, 'Outpatient' was 40.38% (212/525 subjects) and 'Inpatient' was 59.62% (313/525 subjects) (Table 60).

The mean duration after diagnosis in the safety population was 4.84±5.35 years and the most common symptom (multiple counting allowed) was 'Frequency' in 73.33% (385/525 subjects), followed by 'Urge urinary incontinence' in 71.62% (376/525 subjects), 'Urgency' in 66.29% (348/525 subjects), and 'Other' in 18.86% (99/525 subjects) (Table 60).

Among female subjects, there was no pregnant subject (Table 60).

Table 60. Demographic data in the safety population (Overactive Bladder)

		Total n(%)
Age	mean±std (years)	62.54± 14.54
	median	65.00
	min ~ max	19.00~ 89.00
	< 50 years	99(18.86)
	≥ 50 years to < 60 years	101(19.24)
	≥ 60 years to < 70 years	122(23.24)
	≥ 70 years	203(38.67)
	Total	525(100.00)
Sex	Male	112(21.33)
	Female	413(78.67)
	Total	525(100.00)
Height	n	523
	mean±std (cm)	157.52± 8.05
	median	158.00
	min ~ max	133.00~ 185.00
Weight	n	524
	mean±std (kg)	60.46± 10.48
	median	60.00
	min ~ max	32.50~ 100.00
Treatment Setting	Outpatient	212(40.38)
	Inpatient	313(59.62)
	Total	525(100.00)
Currently pregnant	Yes	0(0.00)

		Total n(%)
* for female	No	413(100.00)
	Total	413(100.00)
Duration since OAB diagnosis	n	505
	mean±std (years)	4.84± 5.35
	median	3.00
	min ~ max	0.00~ 40.00
Symptoms	Urge urinary incontinence	376(71.62)
* for patients with OAB	Urgency	348(66.29)
Overlapped¶	Frequency	385(73.33)
	Other	99(18.86)
	Total	525(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
Unkown: 2 (Height), 1 (Weight), 20 (Duration since OAB diagnosis)

39 subjects were excluded in the safety evaluation for the following reasons: 28 subjects who didin't received Botox for this study due to consent withdrawal or other reasons, 2 subjects of follow-up failure, and 9 subjects who violate the dosage (ie, subjects received an unapproved dosage).

2.4 Follow-up duration (Overactive Bladder)

2.4.1 All subjects

During the PMS period, the mean follow-up duration in all subjects was 62.54±39.11 days (Table 61).

Table 61. Follow-up duration in all subjects (Overactive Bladder)

	Total (N=564)
n	534
mean±std (days)	62.54± 39.11
median	51.00
min ~ max	17.00~ 485.00

Length of follow-up = Date of follow-up - Date of initial visit
Missing: 30

2.4.2 Safety population

During the PMS period, the mean follow-up duration in the safety population was 62.73±39.35 days (Table 62).

Table 62. Follow-up duration in the safety population (Overactive Bladder)

	Total (N=525)
n	525
mean±std (days)	62.73± 39.35
median	51.00
min ~ max	17.00~ 485.00

Length of follow-up = Date of follow-up - Date of initial visit + 1

2.5 Past treatment history (Overactive Bladder)

2.5.1 All subjects

In all subjects, 97.99% (536/547 subjects) had received anticholinergic therapy and 56.02% (307/548 subjects) had used other OAB drugs after anticholinergic therapy (Table 63). Other OAB drugs included 'mirabegron', 'tamsulosin' and 'imipramine'.

Proportion of subjects who had received sacral neuromodulation therapy was 1.82% (10/548 subjects) and proportion of subjects who had used the study drug or other botulinum toxin was 4.20% (23/548 subjects) (Table 63).

Table 63. Past treatment history in all subjects (Overactive Bladder)

		Total n(%)
Previous Anticholinergic Therapy	Yes	536(97.99)
	No	11(2.01)
	Total	547(100.00)
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	307(56.02)
	No	241(43.98)
	Total	548(100.00)
Previous Use of Sacral Neuromodulation Therapy	Yes	10(1.82)
	No	538(98.18)
	Total	548(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	23(4.20)
	None	525(95.80)
	Total	548(100.00)

The denominator is number of total subjects.
Missing: 17 (Previous Anticholinergic Therapy), 16 (Another OAB drug also used after anticholinergic therapy), 16 (Previous Use of Sacral Neuromodulation Therapy), 16 (Previous BOTOX or Other Botulinum Toxin Treatment)

2.5.2 Safety population

In the safety population, 98.10% (515/525 subjects) had received anticholinergic therapy and 56.00% (294/525 subjects) had used other OAB drugs after anticholinergic therapy (Table 64).

Proportion of subjects who had received sacral neuromodulation therapy was 1.71% (9/525 subjects) and proportion of subjects who had used the study drug or other botulinum toxin was

3.81% (20/525 subjects) (Table 64).

Table 64. Past treatment history in the safety population (Overactive Bladder)

		Total n(%)
Previous Anticholinergic Therapy	Yes	515(98.10)
	No	10(1.90)
	Total	525(100.00)
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	294(56.00)
	No	231(44.00)
	Total	525(100.00)
Previous Use of Sacral Neuromodulation Therapy	Yes	9(1.71)
	No	516(98.29)
	Total	525(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	20(3.81)
	None	505(96.19)
	Total	525(100.00)

The denominator is number of total subjects.

2.6 Medical history (Overactive Bladder)

2.6.1 All subjects

In all subjects, 85.69% (467/545 subjects) had medical history including surgeries and complications of underlying diseases (Table 65).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 54.60% (255/467 subjects), followed by 'Factors influencing health status and contact with health services' in 46.90% (219/467 subjects), and 'Endocrine, nutritional and metabolic diseases' in 37.69% (176/467 subjects) (Table 65).

In total, 5.14% (29/564 subjects) of subjects had allergy history (Table 65).

When analyzing the type of allergy history, 'Injury, poisoning and certain other consequences of external causes' accounted for 55.17% (16/29 subjects), followed by 'Factors influencing health status and contact with health services' in 44.83% (13/29 subjects), and the allergens included 'contrast medium' and 'UK' (Table 65).

Table 65. Medical history in all subjects (Overactive Bladder)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	467(85.69)
	None	78(14.31)
	Total	545(100.00)
	Details for Medical History by dictionary (Overlapped¶)	

		Total n(%)
	Diseases of the circulatory system	255(54.60)
	Factors influencing health status and contact with health services	219(46.90)
	Endocrine, nutritional and metabolic diseases	176(37.69)
	Diseases of the genitourinary system	126(26.98)
	Diseases of the digestive system	113(24.20)
	Diseases of the musculoskeletal system and connective tissue	126(26.98)
	Neoplasms	95(20.34)
	Mental and behavioural disorders	90(19.27)
	Diseases of the nervous system	53(11.35)
	Diseases of the respiratory system	46(9.85)
	Diseases of the eye and adnexa	45(9.64)
	Injury, poisoning and certain other consequences of external causes	35(7.49)
	Certain infectious and parasitic diseases	36(7.71)
	Diseases of the skin and subcutaneous tissue	20(4.28)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	12(2.57)
	Diseases of the ear and mastoid process	11(2.36)
	Congenital malformations, deformations and chromosomal abnormalities	5(1.07)
	Pregnancy, childbirth and the puerperium	1(0.21)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	53(11.35)
History of Allergies	Yes	29(5.14)
	None	535(94.86)
	Total	564(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	13(44.83)
	Injury, poisoning and certain other consequences of external causes	16(55.17)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Missing: 15 (Medical History, Including Surgeries and Complications of Underlying Diseases)
Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

2.6.2 Safety population

In the safety population, 85.99% (448/521 subjects) had medical history including surgeries and complications of underlying diseases (Table 66).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 54.46% (244/448 subjects), followed by 'Factors influencing health status and contact with health services' in 46.88% (210/448 subjects) and 'Endocrine, nutritional and metabolic diseases' in 37.05% (166/448 subjects) (Table 66).

In total, 5.14% (27/525 subjects) of subjects had allergy history (Table 66).

When analyzing the type of allergy history, 'Injury, poisoning and certain other consequences of external causes' accounted for 59.26% (16/27 subjects), followed by 'Factors influencing health status and contact with health services' in 40.74% (11/27 subjects) (Table 66).

Table 66. Medical history in the safety population (Overactive Bladder)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	448(85.99)
	None	73(14.01)
	Total	521(100.00)
	Details for Medical History by dictionary (Overlapped¶)	
	Diseases of the circulatory system	244(54.46)
	Factors influencing health status and contact with health services	210(46.88)
	Endocrine, nutritional and metabolic diseases	166(37.05)
	Diseases of the genitourinary system	119(26.56)
	Diseases of the digestive system	109(24.33)
	Diseases of the musculoskeletal system and connective tissue	120(26.79)
	Neoplasms	90(20.09)
	Mental and behavioural disorders	86(19.20)
	Diseases of the nervous system	52(11.61)
	Diseases of the respiratory system	46(10.27)
	Diseases of the eye and adnexa	40(8.93)
	Injury, poisoning and certain other consequences of external causes	34(7.59)
	Certain infectious and parasitic diseases	34(7.59)
	Diseases of the skin and subcutaneous tissue	19(4.24)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	12(2.68)
	Diseases of the ear and mastoid process	11(2.46)
	Congenital malformations, deformations and chromosomal abnormalities	5(1.12)
	Pregnancy, childbirth and the puerperium	1(0.22)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	52(11.61)
History of Allergies	Yes	27(5.14)
	None	498(94.86)
	Total	525(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	11(40.74)
	Injury, poisoning and certain other consequences of external causes	16(59.26)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

2.7 Concomitant medications (Overactive Bladder)

2.7.1 All subjects

Subjects who received concomitant medications accounted for 92.84% (506/545 subjects) (Table 67).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 87.94% (445/506 subjects), followed by 'Central Nervous System' in 68.58% (347/506 subjects) and 'Gastrointestinal & Hepatobiliary System' in 55.73% (282/506 subjects) (Table 67).

Table 67. Concomitant medications in all subjects (Overactive Bladder)

	Total n(%)
Yes	506(92.84)
No	39(7.16)
Total	545(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	445(87.94)
Anaesthetics - Local & General	445(87.94)
Central Nervous System	347(68.58)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	174(34.39)
Analgesics (Non-Opioid) & Antipyretics	125(24.70)
Analgesics (Opioid)	88(17.39)
Hypnotics & Sedatives	71(14.03)
Antidepressants	49(9.68)
Drugs For Neuropathic Pain	20(3.95)
Anxiolytics	37(7.31)
Anticonvulsants	26(5.14)
Nootropics & Neurotonics	33(6.52)
Neurodegenerative Disease Drugs	22(4.35)
Antiparkinsonian Drugs	17(3.36)
Antipsychotics	12(2.37)
Antivertigo Drugs	4(0.79)
Antimigraine Preparations	2(0.40)
Other CNS Drugs & Agents for ADHD	1(0.20)
Gastrointestinal & Hepatobiliary System	282(55.73)
Antacids, Antireflux Agents & Antiulcerants	187(36.96)
GIT Regulators, Antiflatulents & Anti-inflammatories	82(16.21)
Digestives	78(15.42)
Laxatives, Purgatives	42(8.30)
Antiemetics	23(4.55)
Antispasmodics	17(3.36)
Antidiarrheals	11(2.17)
Cholagogues, Cholelitholytics & Hepatic Protectors	7(1.38)
Other Gastrointestinal Agents	1(0.20)
Miscellaneous	4(0.79)
Cardiovascular & Hematopoietic System	233(46.05)
Dyslipidaemic Agents	88(17.39)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	85(16.80)
Calcium Antagonists	63(12.45)
Angiotensin II Antagonists	53(10.47)
Other Antihypertensives	34(6.72)
Haemostatics	38(7.51)
Beta-Blockers	34(6.72)
Peripheral Vasodilators & Cerebral Activators	21(4.15)
Diuretics	16(3.16)

	Total n(%)
Anti-Anginal Drugs	16(3.16)
Other Cardiovascular Drugs	12(2.37)
Vasoconstrictors	6(1.19)
Cardiac Drugs	6(1.19)
Phlebitis & Varicose Preparations	3(0.59)
Antidiuretics	1(0.20)
Haematopoietic Agents	2(0.40)
ACE Inhibitors/Direct Renin Inhibitors	1(0.20)
Miscellaneous	7(1.38)
Musculo-Skeletal System	60(11.86)
Muscle Relaxants	23(4.55)
Neuromuscular Disorder Drugs	31(6.13)
Other Drugs Acting on the Musculo-Skeletal System	18(3.56)
Anti-Inflammatory Enzymes	13(2.57)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	4(0.79)
Endocrine & Metabolic System	95(18.77)
Antidiabetic Agents	65(12.85)
Other Agents Affecting Metabolism	20(3.95)
Thyroid Hormones	13(2.57)
Agents Affecting Bone Metabolism	7(1.38)
Insulin Preparations	6(1.19)
Antithyroid Agents	1(0.20)
Miscellaneous	1(0.20)
Intravenous & Other Sterile Solutions	72(14.23)
Intravenous & other sterile solutions	72(14.23)
Genito-Urinary System	61(12.06)
Drugs for Bladder & Prostate Disorders	59(11.66)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	4(0.79)
Other Drugs Acting on the Genito-Urinary System	1(0.20)
Respiratory System	44(8.70)
Antiasthmatic & COPD Preparations	29(5.73)
Cough & Cold Preparations	21(4.15)
Nasal Decongestant & Other Nasal Preparations	3(0.59)
Oncology	51(10.08)
Supportive Care Therapy	44(8.70)
Hormonal Chemotherapy	5(0.99)
Cytotoxic Chemotherapy	2(0.40)
Vitamins & Minerals	35(6.92)
Calcium / with Vitamins	17(3.36)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	9(1.78)
Vitamin B-complex / with C	7(1.38)
Vitamins &/or Minerals	7(1.38)
Vitamins A, D & E	1(0.20)
Miscellaneous	1(0.20)
Anti-infectives (systemic)	21(4.15)
Cephalosporins	8(1.58)
Quinolones	5(0.99)
Antivirals	5(0.99)
Antifungals	5(0.99)
Antiamoebics	1(0.20)
Macrolides	2(0.40)
Aminoglycosides	1(0.20)

	Total n(%)
Anti-TB Agents	1(0.20)
Tetracyclines	1(0.20)
Allergy & Immune System	24(4.74)
Antihistamines & Antiallergics	21(4.15)
Immunosuppressants	2(0.40)
Vaccines, Antisera & Immunologicals	1(0.20)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16(3.16)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16(3.16)
Hormones	16(3.16)
Corticosteroid Hormones	12(2.37)
Oestrogens & Progesterones & Related Synthetic Drugs	3(0.59)
Other Drugs Affecting Hormonal Regulation	1(0.20)
Trophic Hormones & Related Synthetic Drugs	1(0.20)
Nutrition	9(1.78)
Parenteral Nutritional Products	5(0.99)
Electrolytes	2(0.40)
Appetite Enhancers	2(0.40)
Enteral / Nutritional Products	1(0.20)
Eye	9(1.78)
Ophthalmic Lubricants	3(0.59)
Eye Anti-infectives & Antiseptics	2(0.40)
Eye Corticosteroids	2(0.40)
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2(0.40)
Other Eye Preparations	2(0.40)
Antiglaucoma Preparations	1(0.20)
Mydriatic Drugs	1(0.20)
Dermatologicals	9(1.78)
Topical Corticosteroids	4(0.79)
Other Dermatologicals	2(0.40)
Topical Antibiotics	2(0.40)
Topical Antifungals & Antiparasites	1(0.20)
Emollients & Skin Protectives	1(0.20)
Psoriasis, Seborrhea & Ichthyosis Preparations	1(0.20)
Skin Antiseptics & Disinfectants	1(0.20)
Topical Anti-infectives with Corticosteroids	1(0.20)
Ear & Mouth / Throat	1(0.20)
Mouth / Throat Preparations	1(0.20)
Miscellaneous	8(1.58)
Miscellaneous	8(1.58)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS
Missing: 19

2.7.2 Safety population

In the safety population, subjects who received concomitant medications accounted for 93.52% (491/525 subjects) (Table 68).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 88.80% (436/491 subjects), followed by 'Central Nervous System' in 69.45% (341/491 subjects) and 'Gastrointestinal & Hepatobiliary System' in 56.42% (277/491 subjects) (Table 68).

Table 68. Concomitant medications in the safety population (Overactive Bladder)

	Total n(%)
Yes	491(93.52)
No	34(6.48)
Total	525(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	436(88.80)
Anaesthetics - Local & General	436(88.80)
Central Nervous System	341(69.45)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	170(34.62)
Analgesics (Non-Opioid) & Antipyretics	124(25.25)
Analgesics (Opioid)	88(17.92)
Hypnotics & Sedatives	71(14.46)
Antidepressants	49(9.98)
Drugs For Neuropathic Pain	20(4.07)
Anxiolytics	37(7.54)
Anticonvulsants	25(5.09)
Nootropics & Neurotonics	33(6.72)
Neurodegenerative Disease Drugs	21(4.28)
Antiparkinsonian Drugs	17(3.46)
Antipsychotics	12(2.44)
Antivertigo Drugs	4(0.81)
Antimigraine Preparations	2(0.41)
Other CNS Drugs & Agents for ADHD	1(0.20)
Gastrointestinal & Hepatobiliary System	277(56.42)
Antacids, Antireflux Agents & Antiulcerants	185(37.68)
GIT Regulators, Antiflatulents & Anti-inflammatories	82(16.70)
Digestives	77(15.68)
Laxatives, Purgatives	40(8.15)
Antiemetics	22(4.48)
Antispasmodics	17(3.46)
Antidiarrheals	11(2.24)
Cholagogues, Cholelitholytics & Hepatic Protectors	7(1.43)
Other Gastrointestinal Agents	1(0.20)
Miscellaneous	4(0.81)
Cardiovascular & Hematopoietic System	226(46.03)
Dyslipidaemic Agents	84(17.11)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	82(16.70)
Calcium Antagonists	60(12.22)
Angiotensin II Antagonists	52(10.59)
Other Antihypertensives	33(6.72)
Haemostatics	38(7.74)
Beta-Blockers	34(6.92)
Peripheral Vasodilators & Cerebral Activators	21(4.28)
Diuretics	15(3.05)

	Total n(%)
Anti-Anginal Drugs	16(3.26)
Other Cardiovascular Drugs	12(2.44)
Vasoconstrictors	6(1.22)
Cardiac Drugs	6(1.22)
Phlebitis & Varicose Preparations	3(0.61)
Antidiuretics	1(0.20)
Haematopoietic Agents	2(0.41)
ACE Inhibitors/Direct Renin Inhibitors	1(0.20)
Miscellaneous	7(1.43)
Musculo-Skeletal System	60(12.22)
Muscle Relaxants	23(4.68)
Neuromuscular Disorder Drugs	31(6.31)
Other Drugs Acting on the Musculo-Skeletal System	18(3.67)
Anti-Inflammatory Enzymes	13(2.65)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	4(0.81)
Endocrine & Metabolic System	93(18.94)
Antidiabetic Agents	64(13.03)
Other Agents Affecting Metabolism	19(3.87)
Thyroid Hormones	13(2.65)
Agents Affecting Bone Metabolism	7(1.43)
Insulin Preparations	5(1.02)
Antithyroid Agents	1(0.20)
Miscellaneous	1(0.20)
Intravenous & Other Sterile Solutions	72(14.66)
Intravenous & other sterile solutions	72(14.66)
Genito-Urinary System	60(12.22)
Drugs for Bladder & Prostate Disorders	58(11.81)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	4(0.81)
Other Drugs Acting on the Genito-Urinary System	1(0.20)
Respiratory System	42(8.55)
Antiasthmatic & COPD Preparations	28(5.70)
Cough & Cold Preparations	20(4.07)
Nasal Decongestant & Other Nasal Preparations	3(0.61)
Oncology	49(9.98)
Supportive Care Therapy	43(8.76)
Hormonal Chemotherapy	4(0.81)
Cytotoxic Chemotherapy	2(0.41)
Vitamins & Minerals	33(6.72)
Calcium / with Vitamins	15(3.05)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	9(1.83)
Vitamin B-complex / with C	7(1.43)
Vitamins &/or Minerals	7(1.43)
Vitamins A, D & E	1(0.20)
Miscellaneous	1(0.20)
Anti-infectives (systemic)	21(4.28)
Cephalosporins	8(1.63)
Quinolones	5(1.02)
Antivirals	5(1.02)
Antifungals	5(1.02)
Antiamoebics	1(0.20)
Macrolides	2(0.41)
Aminoglycosides	1(0.20)

	Total n(%)
Anti-TB Agents	1(0.20)
Tetracyclines	1(0.20)
Allergy & Immune System	24(4.89)
Antihistamines & Antiallergics	21(4.28)
Immunosuppressants	2(0.41)
Vaccines, Antisera & Immunologicals	1(0.20)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16(3.26)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16(3.26)
Hormones	16(3.26)
Corticosteroid Hormones	12(2.44)
Oestrogens & Progesterones & Related Synthetic Drugs	3(0.61)
Other Drugs Affecting Hormonal Regulation	1(0.20)
Trophic Hormones & Related Synthetic Drugs	1(0.20)
Nutrition	9(1.83)
Parenteral Nutritional Products	5(1.02)
Electrolytes	2(0.41)
Appetite Enhancers	2(0.41)
Enteral / Nutritional Products	1(0.20)
Eye	9(1.83)
Ophthalmic Lubricants	3(0.61)
Eye Anti-infectives & Antiseptics	2(0.41)
Eye Corticosteroids	2(0.41)
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2(0.41)
Other Eye Preparations	2(0.41)
Antiglaucoma Preparations	1(0.20)
Mydriatic Drugs	1(0.20)
Dermatologicals	9(1.83)
Topical Corticosteroids	4(0.81)
Other Dermatologicals	2(0.41)
Topical Antibiotics	2(0.41)
Topical Antifungals & Antiparasites	1(0.20)
Emollients & Skin Protectives	1(0.20)
Psoriasis, Seborrhea & Ichthyosis Preparations	1(0.20)
Skin Antiseptics & Disinfectants	1(0.20)
Topical Anti-infectives with Corticosteroids	1(0.20)
Ear & Mouth / Throat	1(0.20)
Mouth / Throat Preparations	1(0.20)
Miscellaneous	8(1.63)
Miscellaneous	8(1.63)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS

2.8 Special population (Overactive Bladder)

2.8.1 All subjects

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 51.06% (288/564 subjects) were included in elderly group (Table 69).

A total of 1.06% (6/564 subjects) had renal impairment and the renal impairment included 'chronic kideney disease', 'chronic kideney failure', 'chronic renal failure', and 'hydronephrosis' (Table 69).

A total of 1.60% (9/564 subjects) had hepatic impairment and the hepatic impairment included 'liver cirrhosis', 'hepatitis B', and 'fatty liver' (Table 69).

Table 69. Special population in all subjects (Overactive Bladder)

		Total n(%)
Elderly	below 65 years	276(48.94)
	65 or/and over	288(51.06)
	Total	564(100.00)
Renal impairment	Yes	6(1.06)
	No	558(98.94)
	Total	564(100.00)
Hepatic impairment	Yes	9(1.60)
	No	555(98.40)
	Total	564(100.00)

The denominator is number of total subjects.

2.8.2 Safetyp population

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 51.62% (271/525 subjects) in the safety population were included in elderly group. Subjects with renal impairment accounted for 0.95% (5/525 subjects) and subjects with hepatic impairment accounted for 1.33% (7/525 subjects) (Table 70).

Table 70. Special population in the safety population (Overactive Bladder)

		Total n(%)
Elderly	below 65 years	254(48.38)
	65 or/and over	271(51.62)
	Total	525(100.00)
Renal impairment	Yes	5(0.95)
	No	520(99.05)
	Total	525(100.00)
Hepatic impairment	Yes	7(1.33)
	No	518(98.67)
	Total	525(100.00)

The denominator is number of total subjects.

2.9 Information of the study drug administration (Overactive Bladder)

2.9.1 All subjects

When analyzing the number of injection sites of study drug in all subjects, 20 sites accounted for 98.32% (527/536 subjects), followed by 30 sites in 1.31% (7/536 subjects) and others in 0.37% (2/536 subjects) (Table 71).

When analyzing the total units injected, 100 U accounted for 98.51% (528/536 subjects), followed by 200 U in 1.31% (7/536 subjects) and 50 U in 0.19% (1/536 subjects) (Table 71).

When investigating anesthesia upon the study drug administration, 'Local' accounted for 60.82% (326/536 subjects), 'General' 26.68% (143/536 subjects), and 'None' 12.50% (67/536 subjects) (Table 71).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 89.94% (483/537 subjects) (Table 71).

Table 71. Information of the study drug administration in all subjects (Overactive Bladder)

		Total n(%)
Number of Injection Sites	20	527(98.32)
	30	7(1.31)
	Other	2(0.37)
	Total	536(100.00)
Total Units Injected	50	1(0.19)
	100	528(98.51)
	200	7(1.31)
	Total	536(100.00)
Anesthesia	None	67(12.50)
	Local	326(60.82)
	General	143(26.68)
	Total	536(100.00)
Prophylactic Antibiotic Use	Yes	483(89.94)
	No	54(10.06)
	Total	537(100.00)

The denominator is number of total subjects.
Missing: 28 (Number of Injection Sites), 28 (Total Units Injected), 28 (Anesthesia), 27 (Prophylactic Antibiotic Use)

2.9.2 Safety population

When analyzing the number of injection sites of study drug and total units injected in the safety population, all subjects received total 100 U in 20 sites (Table 72).

When investigating anesthesia upon the study drug administration, 'Local' accounted for 60.95% (320/525 subjects), 'General' 26.48% (139/525 subjects), and 'None' 12.57% (66/525 subjects) (Table 72).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 90.48% (475/525 subjects) (Table 72).

Table 72. Information of the study drug administration in the safety population (Overactive Bladder)

		Total n(%)
Number of Injection Sites	20	525(100.00)
	30	0(0.00)
	Total	525(100.00)
Total Units Injected	100	525(100.00)
	200	0(0.00)
	Total	525(100.00)
Anesthesia	None	66(12.57)
	Local	320(60.95)
	General	139(26.48)
	Total	525(100.00)
Prophylactic Antibiotic Use	Yes	475(90.48)
	No	50(9.52)
	Total	525(100.00)

The denominator is number of total subjects.

2.10 Clean intermittent catheterization (Overactive Bladder)

2.10.1 All subjects

In all subjects, 21.81% (123/564 subjects) received clean intermittent catheterization before the study drug administration and 78.19% (441/564 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean PVR urine volume prior to BOTOX treatment was 32.42±51.67 mL (Table 73).

Among the subjects not performing clean intermittent catheterization before the study drug administration, 24.82% (106/427 subjects) received catheterization after the study drug administration including 3.75% (16/427 subjects) who initiated catheterization due to urinary retention and 21.31% (91/427 subjects) who initiated catheterization due to other reason (Table 73).

Table 73. Clean intermittent catheterization in all subjects (Overactive Bladder)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	123(21.81)
	No	441(78.19)
	Total	564(100.00)
Post-Void Residual Urine Volume(before BOTOX)*	n	423
* In subjects not performing CIC before BOTOX	mean±std (mL)	32.42± 51.67
	median	16.00
	min ~ max	0.00~ 430.00

		Total n(%)
Initiation of CIC after BOTOX injection§ § In subjects not performing CIC before BOTOX	Yes	106(24.82)
	initiated CIC due to "Urinary Retention"	16(3.75)
	initiated CIC due to "Other Reason"	91(21.31)
	No	321(75.18)
	Total	427(100.00)

The denominator is number of total subjects.
Missing: 27(Catheterization after BOTOX injection)
Not Done: 5(Post-Void Residual Urine Volume(before BOTOX))
Unknown: 13(Post-Void Residual Urine Volume(before BOTOX))
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

2.10.2 Safety population

In the safety population, 20.76% (109/525 subjects) received clean intermittent catheterization before the study drug administration and 79.24% (416/525 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean PVR urine volume prior to BOTOX treatment was 31.83±48.89 mL (Table 74).

Among the subjects not performing clean intermittent catheterization before the study drug administration, 25.00% (104/416 subjects) received catheterization after the study drug administration including 3.61% (15/416 subjects) who initiated catheterization due to urinary retention and 21.63% (90/416 subjects) who initiated catheterization due to other reason (Table 74).

Table 74. Clean intermittent catheterization in the safety population (Overactive Bladder)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	109(20.76)
	No	416(79.24)
	Total	525(100.00)
Post-Void Residual Urine Volume(before BOTOX)* * In subjects not performing CIC before BOTOX	n	399
	mean±std (mL)	31.83± 48.89
	median	16.00
	min ~ max	0.00~ 430.00
Initiation of CIC after BOTOX injection§ § In subjects not performing CIC before BOTOX	Yes	104(25.00)
	initiated CIC due to "Urinary Retention"	15(3.61)
	initiated CIC due to "Other Reason"	90(21.63)
	No	312(75.00)

	Total	416(100.00)

The denominator is number of total subjects.
Not Done: 5(Post-Void Residual Urine Volume(before BOTOX))
Unknown: 12(Post-Void Residual Urine Volume(before BOTOX))
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

Ⅲ. Results of Post-marketing Surveillance (Overactive Bladder)

3. Results of Post-marketing Surveillance (Overactive Bladder)

3.1 Incidence of Adverse Events (Overactive Bladder)

Source: Post-marketing Surveillance
Events to be reported: All AEs occurring to subjects during the entire surveillance period were to be included in the report, regardless of their causal relationship to the study drug.

It was specified that any AEs, which occurred during the PMS period, should be reported by the physician (investigator) to Allergan Korea Ltd. irrespective of their causal relationship to the study drug, and of these, any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to a series of procedure as soon as they are reported.

In this report, classification of AEs was presented in accordance with the WHO-ART 092 classification criteria.

During the PMS period, 51 AEs occurred in 40 out of 525 subjects in the safety population, which indicated that incidence of AEs was 7.62% (Table 75).

Table 75. Incidence of AEs (Overactive Bladder)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)
Total	40(7.62)	(5.35, 9.89)	51	525(100.00)

† The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects of safety analysis sets) * 100%
‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.

3.1.1 Serious AEs/ADRs

It was specified that any SAEs, which occurred during the PMS period, should be reported irrespective of their causal relationship to the study drug, and any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to the procedure as soon as they are reported.

During the PMS period, a total of 9 SAEs were reported in 8 of all 534 subjects (1.50%) except those who had not received the study drug or those of follow-up failure (Table 76).

The SAEs included "Gastro-intestinal system disorders" - 'ANAL PAIN', "Resistance mechanism disorders" - 'CYSTITIS', 'PYELONEPHRITIS', "Central & peripheral nervous system disorders" - 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', "Musculo-skeletal system disorders" - 'ARTHRALGIA', 'ARTHRITIS', "Metabolic and nutritional disorders" - 'HYPONATRAEMIA', and "Secondary terms - events" - 'ALCOHOL PROBLEM' each in 0.19% (1/534 subjects) (Table 76).

Among them, 1 event occurred in 1 subject (0.19%) was an SADR which cannot rule out the relationship to the study drug: "Resistance mechanism disorder" - 'PYELONEPHRITIS' (Table 76).

Individual SAEs are presented in the table below (Table 77).

Table 76. SAEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Gastro-intestinal system disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.37)	(0.00, 0.89)	2	1(0.19)	(0.00, 0.55)	1
CYSTITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Central & peripheral nervous system disorders	1(0.19)	(0.00, 0.55)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.37)	(0.00, 0.89)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Total	8(1.50)	(0.47, 2.53)	9	1(0.19)	(0.00, 0.55)	1

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of SAE' = (No. subjects of SAE/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%
The percentage of 'Incidence rate of SADR' = (No. subjects of SADR/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%
95% Confidence Interval for SAE/SADR incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)
Dictionary: WHO-ART 092

Table 77. Details of SAEs incurred in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

During the PMS period, 9 SAEs were reported from 8 subjects (1.52%) in the safety population (Table 78).

The SAEs included "Gastro-intestinal system disorders" - 'ANAL PAIN', "Resistance mechanism disorders" - 'CYSTITIS', 'PYELONEPHRITIS', "Central & peripheral nervous system disorders" - 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', "Musculo-skeletal system disorders" - 'ARTHRALGIA', 'ARTHRITIS', "Metabolic and nutritional disorders" - 'HYPONATRAEMIA', and "Secondary terms - events" - 'ALCOHOL PROBLEM' each in 0.19% (1/525 subjects) (Table 78).

Among them, 1 event occurred in 1 subject (0.19%) was an SADR which cannot rule out the relationship to the study drug: "Resistance mechanism disorders" - 'PYELONEPHRITIS' (Table 78).

Individual SAEs are presented in the table below (Table 79).

Table 78. SAEs onset status incurred in the safety population (Overactive Bladder)

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Gastro-intestinal system disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.38)	(0.00, 0.91)	2	1(0.19)	(0.00, 0.56)	1
CYSTITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Central & peripheral nervous system disorders	1(0.19)	(0.00, 0.56)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Total	8(1.52)	(0.48, 2.57)	9	1(0.19)	(0.00, 0.56)	1

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of SAE' = (No. subjects of SAE/No. subjects of safety analysis sets)*100%
The percentage of 'Incidence rate of SADR' = (No. subjects of SADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for SAE/SADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 79. Details of SAEs incurred in the safety population (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE

During the PMS period, no SAE was reported in the subjects excluded from the safety population.

3.1.2 Unexpected AEs/ADRs

During the PMS period, a total of 21 unexpected AEs were reported in 18 of all 534 subjects (3.37%) except those who didn't receive the study drug or those of follow-up failure (Table 80).

Examining the unexpected AEs by SOC, the most common unexpected AE was 'Gastro-intestinal system disorders' in 0.75% (4/534 subjects), followed by 'Body as a whole - general disorders' and 'Musculo-skeletal system disorders ' each in 0.56% (3/534 subjects) and 'Central & peripheral nervous system disorders' and 'Secondary terms - events' each in 0.37% (2/534 subjects). Examining the unexpected AEs by PT, 'URINARY HESITATION' and other accounted for 0.19% (1/534 subjects) each (Table 80).

Among them, 2 events occurred in 2 subjects (0.37%) were unexpected ADRs which cannot rule out the relationship to the study drug (Table 80).

Examining the unexpected ADRs, "Urinary system disorders" - 'URINARY HESITATION' and "Reproductive disorders, male" - 'PERINEAL PAIN MALE' accounted for 0.19% (1/534 subjects) each (Table 80).

Individual unexpected AEs are presented in the table below (Table 81).

Table 80. Unexpected AEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
URINARY HESITATION	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Gastro-intestinal system disorders	4(0.75)	(0.02, 1.48)	4	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	3(0.56)	(0.00, 1.20)	3	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(0.37)	(0.00, 0.89)	3	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.56)	(0.00, 1.20)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
HYPONATRAEMIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
PERINEAL PAIN MALE	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Endocrine disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.37)	(0.00, 0.89)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Total	18(3.37)	(1.84, 4.90)	21	2(0.37)	(0.00, 0.89)	2

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%
The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

Table 81. Details of unexpected AEs incurred in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

During the PMS period, 21 cases of unexpected AE were reported from 18 subjects in the safety population (3.43%) (Table 82).

Examining the unexpected AEs by SOC, the highest incidence was found in 'Gastro-intestinal system disorders' in 0.76% (4/525 subjects), followed by 'Body as a whole - general disorders' and 'Musculo-skeletal system disorders' each in 0.57% (3/525 subjects) and 'Central & peripheral nervous system disorders' and 'Secondary terms - events' each in 0.38% (2/525 subjects). Examining the unexpected AEs by PT, 'URINARY HESITATION' and others occurred in 0.19% (1/525 subjects) each (Table 82).

Among them, 2 events occurred in 2 subjects (0.38%) were unexpected ADRs which cannot rule out the relationship to the study drug (Table 82).

Examining the unexpected ADRs, "Urinary system disorders" - 'URINARY HESITATION' and "Reproductive disorders, male" - 'PERINEAL PAIN MALE' accounted for 0.19% (1/525 subjects) each (Table 82).

Individual unexpected AEs are presented in the table below (Table 83).

Table 82. Unexpected AEs onset status in the safety population (Overactive Bladder)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Gastro-intestinal system disorders	4(0.76)	(0.02, 1.51)	4	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	3(0.57)	(0.00, 1.22)	3	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	2(0.38)	(0.00, 0.91)	3	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.57)	(0.00, 1.22)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
PERINEAL PAIN MALE	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Endocrine disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Total	18(3.43)	(1.87, 4.99)	21	2(0.38)	(0.00, 0.91)	2

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE / No. subjects of safety analysis sets) * 100%
The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 83. Details of unexpected AEs incurred in the safety population (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No

During the PMS period, no unexpected AE was reported in the subjects excluded from the safety population.

3.1.3 AEs/ADRs

During the PMS period, a total of 51 AEs were reported in 40 of all 534 subjects (7.49%) except those who had not received the study drug or those of follow-up failure (Table 84).

Examining the AEs by SOC, the highest incidence was found in 'Urinary system disorders' in 3.18% (17/534 subjects), followed by 'Gastro-intestinal system disorders' in 1.12% (6/534 subjects), and 'Resistance mechanism disorders' and 'Body as a whole - general disorders' in 0.94% (5/534 subjects) each. Examining the AEs by PT, 'URINARY RETENTION' accounted for 1.50% (8/534 subjects), followed by 'DYSURIA' in 0.56% (3/534 subjects) and 'HAEMATURIA', 'URODYNIA', 'NAUSEA', 'INFECTION', 'CYSTITIS', and 'DIZZINESS' each in 0.37% (2/534 subjects) (Table 84).

Among them, 20 events occurred in 17 subjects (3.18%) were ADRs which cannot rule out the relationship to the study drug (Table 84).

Examining the ADRs by SOC, 'Urinary system disorders' occurred in 2.62% (14/534 subjects), 'Resistance mechanism disorders' 0.37%(2/534 subjects), followed by 'Gastro-intestinal system disorders', and 'Reproductive disorders, male' each in 0.19% (1/534 subjects). Examining the ADRs by PT, 'URINARY RETENTION' occurred in 1.50% (8/534 subjects), followed by 'DYSURIA' in 0.56% (3/534 subjects) and others in 0.19% (1/534 subjects) each (Table 84).

Individual AEs are presented in the table below (Table 85).

Table 84. AEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	17(3.18)	(1.69, 4.67)	19	14(2.62)	(1.27, 3.98)	16
URINARY RETENTION	8(1.50)	(0.47, 2.53)	8	8(1.50)	(0.47, 2.53)	8
DYSURIA	3(0.56)	(0.00, 1.20)	3	3(0.56)	(0.00, 1.20)	3
HAEMATURIA	2(0.37)	(0.00, 0.89)	2	1(0.19)	(0.00, 0.55)	1
PYURIA	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
URODYNIA	2(0.37)	(0.00, 0.89)	2	1(0.19)	(0.00, 0.55)	1
URETHRAL PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
URINARY HESITATION	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Gastro-intestinal system disorders	6(1.12)	(0.23, 2.02)	6	1(0.19)	(0.00, 0.55)	1
NAUSEA	2(0.37)	(0.00, 0.89)	2	1(0.19)	(0.00, 0.55)	1
ANAL PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	5(0.94)	(0.12, 1.75)	5	2(0.37)	(0.00, 0.89)	2
URINARY TRACT INFECTION	2(0.37)	(0.00, 0.89)	2	0(0.00)	(0.00, 0.00)	0

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
CYSTITIS	2(0.37)	(0.00, 0.89)	2	1(0.19)	(0.00, 0.55)	1
PYELONEPHRITIS	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Body as a whole - general disorders	5(0.94)	(0.12, 1.75)	5	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	4(0.75)	(0.02, 1.48)	5	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.37)	(0.00, 0.89)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.56)	(0.00, 1.20)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
PERINEAL PAIN MALE	1(0.19)	(0.00, 0.55)	1	1(0.19)	(0.00, 0.55)	1
Endocrine disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.37)	(0.00, 0.89)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.55)	1	0(0.00)	(0.00, 0.00)	0
Total	40(7.49)	(5.26, 9.72)	51	17(3.18)	(1.69, 4.67)	20

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'

The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%

The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects who enrolled this study and received BOTOX and received BOTOX)*100%

95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).

Dictionary: WHO-ART 092

Table 85. Details of AEs incurred in all subjects except those who didn't received the study drug or those of follow-up failure (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	URODYNIA	2015-04-16		Mild	None	Ongoing	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-05-05	2015-05-15	Mild	Not applicable	Resolved without sequelae	Conditional/unclassified	Conditional/unclassified	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2016-03-21	2016-04-01	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2014-10-27		Moderate	Not applicable	Ongoing	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	PYURIA	2014-10-27		Moderate	Not applicable	Ongoing	Certain	Certain	Yes	Expected AE
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2014-09-22	2014-10-05	Moderate	Not applicable	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY FREQUENCY	2014-11-11		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2016-02-04	2016-02-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Possible	No	Expected AE
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-07-23	2015-08-20	Mild	Not applicable	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-10-19		Moderate	Not applicable	Ongoing	Probable/likely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-19	2015-12-29	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-04-01	2016-04-06	Mild	Not applicable	Resolved without sequelae	Possible	Probable/likely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-03-17		Mild	Not applicable	Ongoing	Possible	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-13	2015-11-14	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Skin and appendages disorders	DRUG ERUPTION	2016-03-14	2016-04-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Body as a whole - general disorders	WEAKNESS GENERALIZED	2016-07-19	2016-07-19	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-22	2016-01-31	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-29		Moderate	None	Ongoing	Certain	Unlikely	No	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-05	2016-05-09	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URETHRAL PAIN	2016-04-12	2016-04-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2016-03-01	2016-03-01	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-06-02	2016-06-02	Moderate	None	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No	Unexpected AE
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-20	2016-05-24	Moderate	None	Resolved without sequelae	Certain	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-31	2016-01-27	Mild	None	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-03	2016-05-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included)

During the PMS period, a total of 51 AEs were reported from 40 subjects (7.62%) in the safety population (Table 86).

Examining the AEs by SOC, the highest incidence was found in 'Urinary system disorders' in 3.24% (17/525 subjects), followed by 'Gastro-intestinal system disorders' in 1.14% (6/525 subjects) and 'Resistance mechanism disorders', and 'Body as a whole - general disorders' each in 0.95% (5/525 subjects). Examining the AEs by PT, 'URINARY RETENTION' occurred in 1.52% (8/525 subjects), followed by 'DYSURIA' in 0.57% (3/525 subjects) and 'HAEMATURIA', 'URODYNIA', 'NAUSEA', 'INFECTION', 'CYSTITIS', and 'DIZZINESS' each in 0.38% (2/525 subjects) (Table 86).

Among them, 20 events occurred in 17 subjects (3.24%) were ADRs which cannot rule out the relationship to the study drug (Table 86).

Examining the ADRs by SOC, the highest incidence was found in 'Urinary system disorders' in 2.67% (14/525 subjects), followed by 'Resistance mechanism disorders' in 0.38% (2/525 subjects) and 'Gastro-intestinal system disorders', and 'Reproductive disorders, male' each in

0.19% (1/525 subjects). Examining the ADRs by PT, 'URINARY RETENTION' occurred in 1.52% (8/525 subjects), followed by 'DYSURIA' in 0.57% (3/525 subjects) and others in 0.19% (1/525 subjects) each (Table 86).

Individual AEs are presented in the table below (Table 87).

Table 86. AEs onset status in the safety population (Overactive Bladder)

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	17(3.24)	(1.72, 4.75)	19	14(2.67)	(1.29, 4.04)	16
URINARY RETENTION	8(1.52)	(0.48, 2.57)	8	8(1.52)	(0.48, 2.57)	8
DYSURIA	3(0.57)	(0.00, 1.22)	3	3(0.57)	(0.00, 1.22)	3
HAEMATURIA	2(0.38)	(0.00, 0.91)	2	1(0.19)	(0.00, 0.56)	1
PYURIA	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
URODYNIA	2(0.38)	(0.00, 0.91)	2	1(0.19)	(0.00, 0.56)	1
URETHRAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Gastro-intestinal system disorders	6(1.14)	(0.23, 2.05)	6	1(0.19)	(0.00, 0.56)	1
NAUSEA	2(0.38)	(0.00, 0.91)	2	1(0.19)	(0.00, 0.56)	1
ANAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	5(0.95)	(0.12, 1.78)	5	2(0.38)	(0.00, 0.91)	2
URINARY TRACT INFECTION	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
CYSTITIS	2(0.38)	(0.00, 0.91)	2	1(0.19)	(0.00, 0.56)	1
PYELONEPHRITIS	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Body as a whole - general disorders	5(0.95)	(0.12, 1.78)	5	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	4(0.76)	(0.02, 1.51)	5	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.57)	(0.00, 1.22)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
PERINEAL PAIN MALE	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1
Endocrine disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Total	40(7.62)	(5.35, 9.89)	51	17(3.24)	(1.72, 4.75)	20

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects of safety analysis sets)*100%
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 87. Details of AEs incurred in the safety population (Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	URODYNIA	2015-04-16		Mild	None	Ongoing	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-05-05	2015-05-15	Mild	Not applicable	Resolved without sequelae	Conditional/unclassified	Conditional/unclassified	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2016-03-21	2016-04-01	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2014-10-27		Moderate	Not applicable	Ongoing	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	PYURIA	2014-10-27		Moderate	Not applicable	Ongoing	Certain	Certain	Yes	Expected AE
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2014-09-22	2014-10-05	Moderate	Not applicable	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY FREQUENCY	2014-11-11		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Body as a whole - general disorders	FEVER	2016-02-04	2016-02-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Possible	No	Expected AE
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-07-23	2015-08-20	Mild	Not applicable	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-10-19		Moderate	Not applicable	Ongoing	Probable/likely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-19	2015-12-29	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-04-01	2016-04-06	Mild	Not applicable	Resolved without sequelae	Possible	Probable/likely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-03-17		Mild	Not applicable	Ongoing	Possible	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-13	2015-11-14	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Skin and appendages disorders	DRUG ERUPTION	2016-03-14	2016-04-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Body as a whole - general disorders	WEAKNESS GENERALIZED	2016-07-19	2016-07-19	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-22	2016-01-31	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-29		Moderate	None	Ongoing	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-05	2016-05-09	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URETHRAL PAIN	2016-04-12	2016-04-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2016-03-01	2016-03-01	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-06-02	2016-06-02	Moderate	None	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No	Unexpected AE
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-20	2016-05-24	Moderate	None	Resolved without sequelae	Certain	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-31	2016-01-27	Mild	None	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-03	2016-05-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE

During the PMS period, no AE was reported in the subjects excluded from the safety population.

3.1.4 Classification of AEs/ADRs by severity

A. Severity of AEs

When classifying and evaluating the severity of AEs reported in all 534 subjects except those who didn't receive the study drug or those of 'follow-up failure', 'Mild' occurred in 4.68% (25/534 subjects), 'Moderate' in 3.00% (16/534 subjects) and none were severe (Table 88).

Table 88. Severity of AEs in all subjects except those who didn't received the study drug or those of follow-up failure by AE type (Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	8(1.50)	(0.47, 2.53)	8	10(1.87)	(0.72, 3.02)	11	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.56)	(0.00, 1.19)	3	5(0.94)	(0.12, 1.76)	5	0(0.00)	(0.00, 0.00)	0
DYSURIA	0(0.00)	(0.00, 0.00)	0	3(0.56)	(0.00, 1.19)	3	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URETHRAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	6(1.12)	(0.23, 2.01)	6	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.37)	(0.00, 0.88)	2	3(0.56)	(0.00, 1.19)	3	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	4(0.75)	(0.02, 1.48)	4	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	3(0.56)	(0.00, 1.19)	4	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	1(0.19)	(0.00, 0.56)	1	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Reproductive disorders, male	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Endocrine disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	25(4.68)	(2.89, 6.47)	32	16(3.00)	(1.55, 4.45)	19	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects who enrolled this study and received BOTOX)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

When classifying and evaluating the severity of AEs reported in the safety population, 'Mild' occurred in 4.76% (25/525 subjects), 'Moderate' in 3.05% (16/525 subjects) and none were severe (Table 89).

Table 89. Severity of AEs in the safety population by AE type (Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	8(1.52)	(0.47, 2.57)	8	10(1.90)	(0.73, 3.07)	11	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.57)	(0.00, 1.21)	3	5(0.95)	(0.12, 1.78)	5	0(0.00)	(0.00, 0.00)	0
DYSURIA	0(0.00)	(0.00, 0.00)	0	3(0.57)	(0.00, 1.21)	3	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.19)	(0.00, 0.56)	1	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URETHRAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	6(1.14)	(0.23, 2.05)	6	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.38)	(0.00, 0.91)	2	3(0.57)	(0.00, 1.21)	3	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	4(0.76)	(0.02, 1.50)	4	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
FEVER	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	3(0.57)	(0.00, 1.21)	4	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	1(0.19)	(0.00, 0.56)	1	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Endocrine disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	25(4.76)	(2.94, 6.58)	32	16(3.05)	(1.58, 4.52)	19	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

No AE was reported in the subjects excluded from the safety population.

B. Severity of ADRs

When classifying and evaluating the severity of ADRs reported in all 534 subjects except those who didn't receive the study drug or those of 'follow-up failure', 'Moderate' occurred in 2.25% (12/534 subjects), 'Mild' in 1.12% (6/534 subjects) and none were severe (Table 90).

Table 90. Severity of ADRs in all subjects except those who didn't received the study drug or those of follow-up failure by ADR type (Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	5(0.94)	(0.12, 1.76)	5	10(1.87)	(0.72, 3.02)	11	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.56)	(0.00, 1.19)	3	5(0.94)	(0.12, 1.76)	5	0(0.00)	(0.00, 0.00)	0
DYSURIA	0(0.00)	(0.00, 0.00)	0	3(0.56)	(0.00, 1.19)	3	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	0(0.00)	(0.00, 0.00)	0	2(0.37)	(0.00, 0.88)	2	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Total	6(1.12)	(0.23, 2.01)	6	12(2.25)	(0.99, 3.51)	14	0(0.00)	(0.00, 0.00)	0

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects who enrolled this study and received BOTOX)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

When classifying and evaluating the severity of ADRs reported in the safety population, 'Moderate' occurred in 2.29% (12/525 subjects), 'Mild' in 1.14% (6/525 subjects) and none were severe (Table 91).

Table 91. Severity of ADRs in the safety population by ADR type (Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	5(0.95)	(0.12, 1.78)	5	10(1.90)	(0.73, 3.07)	11	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.57)	(0.00, 1.21)	3	5(0.95)	(0.12, 1.78)	5	0(0.00)	(0.00, 0.00)	0
DYSURIA	0(0.00)	(0.00, 0.00)	0	3(0.57)	(0.00, 1.21)	3	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	0(0.00)	(0.00, 0.00)	0	2(0.38)	(0.00, 0.91)	2	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
CYSTITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.19)	(0.00, 0.56)	1	0(0.00)	(0.00, 0.00)	0
Total	6(1.14)	(0.23, 2.05)	6	12(2.29)	(1.01, 3.57)	14	0(0.00)	(0.00, 0.00)	0

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

No ADR was reported in the subjects excluded from the safety population.

3.1.5 Classification of AEs in the safety population

The 51 AEs reported in the safety population were analyzed in detail.

When classifying and evaluating the expectedness of AEs into two of 'Expected AE' and 'Unexpected AE', 'Expected AE' accounted for 58.82% (30/51 events) and 'Unexpected AE' accounted for 41.18% (21/51 events) (Table 92).

When classifying and evaluating the seriousness of AEs into two of 'Serious' and 'Non-serious', 'Non-serious' accounted for 82.35% (42/51 events) and 'Serious' accounted for 17.65% (9/51 events) (Table 92).

When classifying and evaluating the severity of AEs into three of 'Mild', 'Moderate', and 'Severe', 'Mild' occurred in 62.75% (32/51 events) and 'Moderate' in 37.25% (19/51 events) (Table 92).

When classifying and evaluating the outcome of AEs incurred into four of 'Ongoing', 'Resolved without sequelae', 'Resolved with sequelae', and 'Death', 'Resolved without sequelae' was reported in 58.82% (30/51 events), 'Ongoing' in 37.25% (19/51 events), and 'Resolved with sequelae' in 3.92% (2/51 events) (Table 92).

When classifying and evaluating the causal relationship of AEs to the study drug into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and 'Unassessable/Unclassifiable', 'Unlikely' was reported in 60.78% (31/51 events); 'Possible' in 17.65% (9/51 events); 'Certain' and 'Probable/Likely' in 9.80% (5/51 events) each; and 'Conditional/Unclassified' in 1.96% (1/51 events) (Table 92).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and 'Unassessable/Unclassifiable', 'Unlikely' was reported in 72.55% (37/51 events); 'Possible' in 13.73% (7/51 events); 'Probable/Likely' in 9.80% (5/51 events); and 'Certain' and 'Conditional/Unclassified' in 1.96% (1/51 events) each (Table 92).

When classifying and evaluating the change in the study drug administration after AEs into four

of 'None', 'Regimen changed', 'Discontinued', and 'Not applicable', 'Not applicable' was 54.90% (28/51 cases) and 'None' was 45.10% (23/51 cases) (Table 92).

When classifying and evaluating use of AE treatment into two of 'Yes' and 'No', 'Yes' accounted for 66.67% (34/51 events) and 'No' accounted for 33.33% (17/51 events) (Table 92).

Table 92. Classification of AEs in the safety population (Overactive Bladder)

		Total n(%)
Expected	Expected AE	30(58.82)
	Unexpected AE	21(41.18)
Seriousness	Serious	9(17.65)
	Non-serious	42(82.35)
Severity	Mild	32(62.75)
	Moderate	19(37.25)
	Severe	0(0.00)
Current Status	Ongoing	19(37.25)
	Resolved without sequelae	30(58.82)
	Resolved with sequelae	2(3.92)
	Death	0(0.00)
Causal Relationship	Certain	5(9.80)
	Probable/Likely	5(9.80)
	Possible	9(17.65)
	Unlikely	31(60.78)
	Conditional/Unclassified	1(1.96)
	Unassessable/Unclassifiable	0(0.00)
BOTOX Injection procedure	Certain	1(1.96)
	Probable/Likely	5(9.80)
	Possible	7(13.73)
	Unlikely	37(72.55)
	Conditional/Unclassified	1(1.96)
	Unassessable/Unclassifiable	0(0.00)
Change in BOTOX treatment after AE	None	23(45.10)
	Regimen changed	0(0.00)
	Discontinued	0(0.00)
	Not applicable	28(54.90)
Treatment received	Yes	34(66.67)
	No	17(33.33)
Total		51(100.00)

The denominator is number of total AE counts.

A. Expectedness

Incidence of AEs based on the expectedness is presented by AE type in the table below (Table 93).

Table 93. AEs onset status based on the expectedness by AE type (Overactive Bladder)

	Expected AE n(%)	Unexpected AE n(%)	Total n(%)
Urinary system disorders	18(94.74)	1(5.26)	19(37.25)
URINARY RETENTION	8(100.00)	0(0.00)	8(15.69)
DYSURIA	3(100.00)	0(0.00)	3(5.88)
HAEMATURIA	2(100.00)	0(0.00)	2(3.92)
PYURIA	1(100.00)	0(0.00)	1(1.96)
URODYNIA	2(100.00)	0(0.00)	2(3.92)
URETHRAL PAIN	1(100.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	1(100.00)	0(0.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.96)
Gastro-intestinal system disorders	2(33.33)	4(66.67)	6(11.76)
NAUSEA	2(100.00)	0(0.00)	2(3.92)
ANAL PAIN	0(0.00)	1(100.00)	1(1.96)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.96)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.96)
HEARTBURN	0(0.00)	1(100.00)	1(1.96)
Resistance mechanism disorders	5(100.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	2(100.00)	0(0.00)	2(3.92)
CYSTITIS	2(100.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	2(40.00)	3(60.00)	5(9.80)
FEVER	1(100.00)	0(0.00)	1(1.96)
PELVIC PAIN	0(0.00)	1(100.00)	1(1.96)
PAIN GROIN	0(0.00)	1(100.00)	1(1.96)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.96)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	2(40.00)	3(60.00)	5(9.80)
DIZZINESS	2(100.00)	0(0.00)	2(3.92)
DEMENTIA	0(0.00)	1(100.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	1(100.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	1(100.00)	1(1.96)
Musculo-skeletal system disorders	0(0.00)	3(100.00)	3(5.88)
ARTHRALGIA	0(0.00)	1(100.00)	1(1.96)
ARTHRITIS	0(0.00)	1(100.00)	1(1.96)
BACK PAIN	0(0.00)	1(100.00)	1(1.96)
Metabolic and nutritional disorders	0(0.00)	1(100.00)	1(1.96)
HYPONATRAEMIA	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, male	0(0.00)	1(100.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	1(1.96)
Endocrine disorders	0(0.00)	1(100.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	1(100.00)	1(1.96)
Neoplasms	0(0.00)	1(100.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, female	0(0.00)	1(100.00)	1(1.96)
VAGINITIS	0(0.00)	1(100.00)	1(1.96)
Skin and appendages disorders	1(100.00)	0(0.00)	1(1.96)
DRUG ERUPTION	1(100.00)	0(0.00)	1(1.96)
Secondary terms - events	0(0.00)	2(100.00)	2(3.92)
ALCOHOL PROBLEM	0(0.00)	1(100.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.96)

Total	30(58.82)	21(41.18)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

B. Seriousness

Incidence of AEs based on the seriousness is presented by AE type in the table below (Table 94).

Table 94. AEs onset status based on the seriousness by AE type (Overactive Bladder)

	Serious n(%)	Non-serious n(%)	Total n(%)
Urinary system disorders	0(0.00)	19(100.00)	19(37.25)
URINARY RETENTION	0(0.00)	8(100.00)	8(15.69)
DYSURIA	0(0.00)	3(100.00)	3(5.88)
HAEMATURIA	0(0.00)	2(100.00)	2(3.92)
PYURIA	0(0.00)	1(100.00)	1(1.96)
URODYNIA	0(0.00)	2(100.00)	2(3.92)
URETHRAL PAIN	0(0.00)	1(100.00)	1(1.96)
URINARY FREQUENCY	0(0.00)	1(100.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.96)
Gastro-intestinal system disorders	1(16.67)	5(83.33)	6(11.76)
NAUSEA	0(0.00)	2(100.00)	2(3.92)
ANAL PAIN	1(100.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.96)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.96)
HEARTBURN	0(0.00)	1(100.00)	1(1.96)
Resistance mechanism disorders	2(40.00)	3(60.00)	5(9.80)
URINARY TRACT INFECTION	0(0.00)	2(100.00)	2(3.92)
CYSTITIS	1(50.00)	1(50.00)	2(3.92)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	0(0.00)	5(100.00)	5(9.80)
FEVER	0(0.00)	1(100.00)	1(1.96)
PELVIC PAIN	0(0.00)	1(100.00)	1(1.96)
PAIN GROIN	0(0.00)	1(100.00)	1(1.96)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.96)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	1(1.96)
Central & peripheral nervous system disorders	2(40.00)	3(60.00)	5(9.80)
DIZZINESS	0(0.00)	2(100.00)	2(3.92)
DEMENTIA	1(100.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	1(100.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	2(66.67)	1(33.33)	3(5.88)
ARTHRALGIA	1(100.00)	0(0.00)	1(1.96)
ARTHRITIS	1(100.00)	0(0.00)	1(1.96)
BACK PAIN	0(0.00)	1(100.00)	1(1.96)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	1(100.00)	0(0.00)	1(1.96)
Reproductive disorders, male	0(0.00)	1(100.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	1(1.96)

	Serious n(%)	Non-serious n(%)	Total n(%)
Endocrine disorders	0(0.00)	1(100.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	1(100.00)	1(1.96)
Neoplasms	0(0.00)	1(100.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, female	0(0.00)	1(100.00)	1(1.96)
VAGINITIS	0(0.00)	1(100.00)	1(1.96)
Skin and appendages disorders	0(0.00)	1(100.00)	1(1.96)
DRUG ERUPTION	0(0.00)	1(100.00)	1(1.96)
Secondary terms - events	1(50.00)	1(50.00)	2(3.92)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.96)
Total	9(17.65)	42(82.35)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

C. Severity of AEs

Incidence of AEs based on the severity is presented in the table below (Table 95).

Table 95. AEs onset status based on the severity by AE type (Overactive Bladder)

	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)
Urinary system disorders	8(42.11)	11(57.89)	0(0.00)	19(37.25)
URINARY RETENTION	3(37.50)	5(62.50)	0(0.00)	8(15.69)
DYSURIA	0(0.00)	3(100.00)	0(0.00)	3(5.88)
HAEMATURIA	1(50.00)	1(50.00)	0(0.00)	2(3.92)
PYURIA	0(0.00)	1(100.00)	0(0.00)	1(1.96)
URODYNIA	2(100.00)	0(0.00)	0(0.00)	2(3.92)
URETHRAL PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	0(0.00)	1(100.00)	0(0.00)	1(1.96)
URINARY HESITATION	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Gastro-intestinal system disorders	6(100.00)	0(0.00)	0(0.00)	6(11.76)
NAUSEA	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ANAL PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	1(1.96)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HEARTBURN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Resistance mechanism disorders	2(40.00)	3(60.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	2(100.00)	0(0.00)	0(0.00)	2(3.92)
CYSTITIS	0(0.00)	2(100.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	0(0.00)	1(100.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	4(80.00)	1(20.00)	0(0.00)	5(9.80)
FEVER	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PELVIC PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PAIN GROIN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	1(1.96)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	4(80.00)	1(20.00)	0(0.00)	5(9.80)

	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)
DIZZINESS	2(100.00)	0(0.00)	0(0.00)	2(3.92)
DEMENTIA	1(100.00)	0(0.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	1(100.00)	0(0.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	1(33.33)	2(66.67)	0(0.00)	3(5.88)
ARTHRALGIA	0(0.00)	1(100.00)	0(0.00)	1(1.96)
ARTHRITIS	0(0.00)	1(100.00)	0(0.00)	1(1.96)
BACK PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, male	0(0.00)	1(100.00)	0(0.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	0(0.00)	1(1.96)
Endocrine disorders	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Neoplasms	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CERVICAL CARCINOMA	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, female	1(100.00)	0(0.00)	0(0.00)	1(1.96)
VAGINITIS	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Skin and appendages disorders	1(100.00)	0(0.00)	0(0.00)	1(1.96)
DRUG ERUPTION	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Secondary terms - events	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Total	32(62.75)	19(37.25)	0(0.00)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

D. Outcome of AEs

Incidence of AEs by AE type based on the outcome is presented in the table below (Table 96).

Table 96. Outcome of AEs by AE type (Overactive Bladder)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
Urinary system disorders	8(42.11)	11(57.89)	0(0.00)	0(0.00)	19(37.25)
URINARY RETENTION	3(37.50)	5(62.50)	0(0.00)	0(0.00)	8(15.69)
DYSURIA	1(33.33)	2(66.67)	0(0.00)	0(0.00)	3(5.88)
HAEMATURIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
PYURIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URODYNIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
URETHRAL PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Gastro-intestinal system disorders	2(33.33)	4(66.67)	0(0.00)	0(0.00)	6(11.76)
NAUSEA	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ANAL PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
HEARTBURN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Resistance mechanism disorders	0(0.00)	4(80.00)	1(20.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
CYSTITIS	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	2(40.00)	3(60.00)	0(0.00)	0(0.00)	5(9.80)
FEVER	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PELVIC PAIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
PAIN GROIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	2(40.00)	3(60.00)	0(0.00)	0(0.00)	5(9.80)
DIZZINESS	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
DEMENTIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	1(33.33)	2(66.67)	0(0.00)	0(0.00)	3(5.88)
ARTHRALGIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ARTHRITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
BACK PAIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, male	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
PERINEAL PAIN MALE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Endocrine disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Neoplasms	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
CERVICAL CARCINOMA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, female	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
VAGINITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Skin and appendages disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
DRUG ERUPTION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Secondary terms - events	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(3.92)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Total	19(37.25)	30(58.82)	2(3.92)	0(0.00)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

E. Relationship to the study drug

Incidence of AEs based on the relationship to the study drug is presented by AE type in the table below (Table 97).

Table 97. AEs onset status based on the relationship to the study drug by AE type (Overactive Bladder)

	Certain n(%)	Probable/Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessible/Unclassifiable n(%)	Total n(%)
Urinary system disorders	5(26.32)	5(26.32)	5(26.32)	3(15.79)	1(5.26)	0(0.00)	19(37.25)
URINARY RETENTION	4(50.00)	2(25.00)	2(25.00)	0(0.00)	0(0.00)	0(0.00)	8(15.69)
DYSURIA	0(0.00)	1(33.33)	2(66.67)	0(0.00)	0(0.00)	0(0.00)	3(5.88)
HAEMATURIA	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
PYURIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URODYNIA	0(0.00)	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(3.92)
URETHRAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	1(16.67)	5(83.33)	0(0.00)	0(0.00)	6(11.76)
NAUSEA	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
FAECAL INCONTINENCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HEARTBURN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Resistance mechanism disorders	0(0.00)	0(0.00)	2(40.00)	3(60.00)	0(0.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
CYSTITIS	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	0(0.00)	0(0.00)	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(9.80)
FEVER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PAIN GROIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
UROGENITAL PROLAPSE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
WEAKNESS GENERALIZED	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(9.80)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(5.88)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, male	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)

	Certain n(%)	Probable/Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessible/Unclassifiable n(%)	Total n(%)
Secondary terms - events	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Total	5(9.80)	5(9.80)	9(17.65)	31(60.78)	1(1.96)	0(0.00)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

F. Relationship to the study drug administration procedure

Incidence of AEs based on the relationship to the study drug administration procedure is presented by AE type in the table below (Table 98).

Table 98. AEs onset status based on the relationship to the study drug administration procedure by AE type (Overactive Bladder)

	Certain n(%)	Probable/Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessible/Unclassifiable n(%)	Total n(%)
Urinary system disorders	1(5.26)	5(26.32)	3(15.79)	9(47.37)	1(5.26)	0(0.00)	19(37.25)
URINARY RETENTION	0(0.00)	2(25.00)	0(0.00)	6(75.00)	0(0.00)	0(0.00)	8(15.69)
DYSURIA	0(0.00)	1(33.33)	2(66.67)	0(0.00)	0(0.00)	0(0.00)	3(5.88)
HAEMATURIA	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
PYURIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URODYNIA	0(0.00)	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(3.92)
URETHRAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	0(0.00)	6(100.00)	0(0.00)	0(0.00)	6(11.76)
NAUSEA	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
FAECAL INCONTINENCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HEARTBURN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Resistance mechanism disorders	0(0.00)	0(0.00)	2(40.00)	3(60.00)	0(0.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
CYSTITIS	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	0(0.00)	0(0.00)	1(20.00)	4(80.00)	0(0.00)	0(0.00)	5(9.80)
FEVER	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
PAIN GROIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
UROGENITAL PROLAPSE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
WEAKNESS GENERALIZED	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(9.80)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)

	Certain	Probable/Likely	Possible	Unlikely	Conditional/ Unclassified	Unassessible/Unclassifiable	Total
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(5.88)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, male	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Secondary terms - events	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(3.92)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.96)
Total	1(1.96)	5(9.80)	7(13.73)	37(72.55)	1(1.96)	0(0.00)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

G. Change in the study drug administration after AE

Incidence of AEs based on change in the study drug administration after AE is presented by AE type in the table below (Table 99).

Table 99. AEs onset status based on the actions taken to the study drug by AE type (Overactive Bladder)

	None	Regimen changed	Discontinued	Not applicable	Total
	n(%)	n(%)	n(%)	n(%)	n(%)
Urinary system disorders	9(47.37)	0(0.00)	0(0.00)	10(52.63)	19(37.25)
URINARY RETENTION	4(50.00)	0(0.00)	0(0.00)	4(50.00)	8(15.69)
DYSURIA	2(66.67)	0(0.00)	0(0.00)	1(33.33)	3(5.88)
HAEMATURIA	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(3.92)
PYURIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
URODYNIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(3.92)
URETHRAL PAIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
URINARY HESITATION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Gastro-intestinal system disorders	5(83.33)	0(0.00)	0(0.00)	1(16.67)	6(11.76)
NAUSEA	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(3.92)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
HEARTBURN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)

	None	Regimen changed	Discontinued	Not applicable	Total
	n(%)	n(%)	n(%)	n(%)	n(%)
Resistance mechanism disorders	2(40.00)	0(0.00)	0(0.00)	3(60.00)	5(9.80)
URINARY TRACT INFECTION	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(3.92)
CYSTITIS	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(3.92)
PYELONEPHRITIS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	3(60.00)	0(0.00)	0(0.00)	2(40.00)	5(9.80)
FEVER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
PAIN GROIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	3(60.00)	0(0.00)	0(0.00)	2(40.00)	5(9.80)
DIZZINESS	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(3.92)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
GAIT DISTURBANCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Musculo-skeletal system disorders	0(0.00)	0(0.00)	0(0.00)	3(100.00)	3(5.88)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, male	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
Secondary terms - events	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(3.92)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.96)
CLOSED HEAD INJURY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.96)
Total	23(45.10)	0(0.00)	0(0.00)	28(54.90)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

H. AE treatment

Incidence of AEs based on the use of AE treatment is presented by AE type in the table below (Table 100).

Table 100. AEs onset status based on the use of AE treatment by AE type (Overactive Bladder)

	Yes	No	Total
	n(%)	n(%)	n(%)
Urinary system disorders	13(68.42)	6(31.58)	19(37.25)

	Yes n(%)	No n(%)	Total n(%)
URINARY RETENTION	5(62.50)	3(37.50)	8(15.69)
DYSURIA	3(100.00)	0(0.00)	3(5.88)
HAEMATURIA	1(50.00)	1(50.00)	2(3.92)
PYURIA	1(100.00)	0(0.00)	1(1.96)
URODYNIA	1(50.00)	1(50.00)	2(3.92)
URETHRAL PAIN	1(100.00)	0(0.00)	1(1.96)
URINARY FREQUENCY	1(100.00)	0(0.00)	1(1.96)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.96)
Gastro-intestinal system disorders	2(33.33)	4(66.67)	6(11.76)
NAUSEA	1(50.00)	1(50.00)	2(3.92)
ANAL PAIN	1(100.00)	0(0.00)	1(1.96)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.96)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.96)
HEARTBURN	0(0.00)	1(100.00)	1(1.96)
Resistance mechanism disorders	5(100.00)	0(0.00)	5(9.80)
URINARY TRACT INFECTION	2(100.00)	0(0.00)	2(3.92)
CYSTITIS	2(100.00)	0(0.00)	2(3.92)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.96)
Body as a whole - general disorders	1(20.00)	4(80.00)	5(9.80)
FEVER	0(0.00)	1(100.00)	1(1.96)
PELVIC PAIN	0(0.00)	1(100.00)	1(1.96)
PAIN GROIN	0(0.00)	1(100.00)	1(1.96)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.96)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	1(1.96)
Central & peripheral nervous system disorders	4(80.00)	1(20.00)	5(9.80)
DIZZINESS	1(50.00)	1(50.00)	2(3.92)
DEMENTIA	1(100.00)	0(0.00)	1(1.96)
GAIT DISTURBANCE	1(100.00)	0(0.00)	1(1.96)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	1(1.96)
Musculo-skeletal system disorders	3(100.00)	0(0.00)	3(5.88)
ARTHRALGIA	1(100.00)	0(0.00)	1(1.96)
ARTHRITIS	1(100.00)	0(0.00)	1(1.96)
BACK PAIN	1(100.00)	0(0.00)	1(1.96)
Metabolic and nutritional disorders	1(100.00)	0(0.00)	1(1.96)
HYPONATRAEMIA	1(100.00)	0(0.00)	1(1.96)
Reproductive disorders, male	1(100.00)	0(0.00)	1(1.96)
PERINEAL PAIN MALE	1(100.00)	0(0.00)	1(1.96)
Endocrine disorders	1(100.00)	0(0.00)	1(1.96)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	1(1.96)
Neoplasms	0(0.00)	1(100.00)	1(1.96)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.96)
Reproductive disorders, female	1(100.00)	0(0.00)	1(1.96)
VAGINITIS	1(100.00)	0(0.00)	1(1.96)
Skin and appendages disorders	1(100.00)	0(0.00)	1(1.96)
DRUG ERUPTION	1(100.00)	0(0.00)	1(1.96)
Secondary terms - events	1(50.00)	1(50.00)	2(3.92)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	1(1.96)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.96)
Total	34(66.67)	17(33.33)	51(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

3.1.6 Adverse events by factors

The 51 AEs reported in the safety population were analyzed by factor.

A. Background factors

When analyzing AE incidence by age group, it was 8.87% (18/203 subjects, 27 events) in '≥ 70 years', 7.38% (9/122 subjects, 10 events) in '≥ 60 years to < 70 years', 7.07% (7/99 subjects, 7 events) in '< 50 years', and 5.94% (6/101 subjects, 7 events) in '≥ 50 years to < 60 years'. Difference in AE incidences between the groups was not statistically significant (p=0.8240) (Table 101).

When analyzing AE incidence by sex, incidence of AEs was 6.25% (7/112 subjects, 9 events) in 'Male' and 7.99% (33/413 subjects, 42 events) in 'Female', and difference in AE incidences between the groups was not statistically significant (p=0.5381) (Table 101).

When analyzing AE incidence by treatment setting, incidence of AEs was 7.55% (16/212 subjects, 20 events) in 'Outpatient' and 7.67% (24/313 subjects, 31 events) in 'Inpatient', and difference in AE incidences between the groups was not statistically significant (p=0.9593) (Table 101).

When analyzing AE incidence by symptoms in the safety population (multiple counting allowed), incidence of AEs was 9.31% (35/376 subjects, 46 events) in 'Urge urinary incontinence', 8.62% (30/348 subjects, 38 events) in 'Urgency', 7.27% (28/385 subjects, 36 events) in 'Frequency', and 7.07% (7/99 subjects, 8 events) in 'Other' (Table 101).

Among female subjects, there was no pregnant subject (Table 101).

Table 101. AEs onset status by background factor (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Age	< 50 years	7(7.07)	(2.02, 12.12)	7	99(18.86)	0.8240
	≥ 50 years to < 60 years	6(5.94)	(1.33, 10.55)	7	101(19.24)	Chi-square test
	≥ 60 years to < 70 years	9(7.38)	(2.74, 12.02)	10	122(23.24)	
	≥ 70 years	18(8.87)	(4.96, 12.78)	27	203(38.67)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Sex	Male	7(6.25)	(1.77, 10.73)	9	112(21.33)	0.5381
	Female	33(7.99)	(5.38, 10.61)	42	413(78.67)	Chi-square test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Treatment Setting	Outpatient	16(7.55)	(3.99, 11.10)	20	212(40.38)	0.9593
	Inpatient	24(7.67)	(4.72, 10.62)	31	313(59.62)	Chi-square test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Currently pregnant	Yes	0(0.00)	(0.00, 0.00)	0	0(0.00)	NA
* for female	No	33(7.99)	(5.38, 10.61)	42	413(100.00)	
	Total	33(7.99)	(5.38, 10.61)	42	413(100.00)	

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Symptoms	Urge urinary incontinence	35(9.31)	(6.37, 12.25)	46	376(71.62)	NA
* for patients with OAB	Urgency	30(8.62)	(5.67, 11.57)	38	348(66.29)	
Overlapped¶	Frequency	28(7.27)	(4.68, 9.87)	36	385(73.33)	
	Other	7(7.07)	(2.02, 12.12)	8	99(18.86)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

B. Past treatment history

When analyzing AE incidence by previous anticholinergic therapy, it was 7.77% (40/515 subjects, 51 events) in subjects who had received anticholinergic therapy, and no AE was reported in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 102).

When analyzing AE incidence by use of other OAB drugs after anticholinergic therapy, it was 8.84% (26/294 subjects, 32 events) in subjects who had used other OAB drugs and 6.06% (14/231 subjects, 19 events) in subjects who had not. The difference in AE incidences between the groups was not statistically significant (p=0.2328) (Table 102).

When analyzing AE incidence by previous use of sacral neuromodulation therapy, it was 22.22% (2/9 subjects, 2 events) in a subject who had received sacral neuromodulation therapy and 7.36% (38/516 subjects, 49 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.1450) (Table 102).

When analyzing AE incidence by past treatment history with the study drug or other botulinum toxin, it was 10.00% (2/20 subjects, 2 events) in subjects who had used the study drug or other botolinum toxin and 7.52% (38/505 subjects, 49 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.6588) (Table 102).

Table 102. AEs onset status by past treatment history (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Previous Anticholinergic Therapy	Yes	40(7.77)	(5.46, 10.08)	51	515(98.10)	1.0000
	No	0(0.00)	(0.00, 0.00)	0	10(1.90)	Fisher's Exact test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Another OAB drug also used after anticholinergic therapy	Yes	26(8.84)	(5.60, 12.09)	32	294(56.00)	0.2328
* for patients with OAB	No	14(6.06)	(2.98, 9.14)	19	231(44.00)	Chi-square test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Previous Use of Sacral Neuromodulation Therapy	Yes	2(22.22)	(0.00, 49.38)	2	9(1.71)	0.1450
	No	38(7.36)	(5.11, 9.62)	49	516(98.29)	Fisher's Exact test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	2(10.00)	(0.00, 23.15)	2	20(3.81)	0.6588
	None	38(7.52)	(5.22, 9.83)	49	505(96.19)	Fisher's Exact test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

C. Medical history

When analyzing AE incidence by medical history including surgeries and complications of underlying diseases, it was 8.26% (37/448 subjects, 48 events) in subjects with medical history and 4.11% (3/73 subjects, 3 events) in subjects without medical history. Difference in AE incidences between the groups was not statistically significant (p=0.2169) (Table 103).

When analyzing AE incidence by the type of medical history (multiple counting allowed), it was 36.36% (4/11 subjects, 7 events) in 'Diseases of the ear and mastoid process', followed by 'Injury, poisoning and certain other consequences of external causes' in 17.65% (6/34 subjects, 8 events) and ‘Symptoms, signs and abnormal clinical and laboratory findings, NEC' in 15.38% (8/52 subjects, 12 events) (Table 103).

When analyzing AE incidence by allergy history, it was 7.41% (2/27 subjects, 4 events) in subjects with allergy history and 7.63% (38/498 subjects, 47 events) in subject without allergy history. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 103).

When analyzing AE incidence by the type of allergy history, all were ‘Factors influencing health status and contact with health services’ (Table 103).

Table 103. AEs onset status by medical history (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	37(8.26)	(5.71, 10.81)	48	448(85.99)	0.2169
	None	3(4.11)	(0.00, 8.66)	3	73(14.01)	Chi-square test
	Total	40(7.68)	(5.39, 9.96)	51	521(100.00)	
	Details for Medical History by dictionary (Overlapped¶)					
	Diseases of the circulatory system	20(8.20)	(4.75, 11.64)	27	244(54.46)	

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
	Factors influencing health status and contact with health services	20(9.52)	(5.55, 13.49)	27	210(46.88)	
	Endocrine, nutritional and metabolic diseases	11(6.63)	(2.84, 10.41)	17	166(37.05)	
	Diseases of the genitourinary system	11(9.24)	(4.04, 14.45)	15	119(26.56)	
	Diseases of the digestive system	8(7.34)	(2.44, 12.24)	12	109(24.33)	
	Diseases of the musculoskeletal system and connective tissue	14(11.67)	(5.92, 17.41)	19	120(26.79)	
	Neoplasms	5(5.56)	(0.82, 10.29)	7	90(20.09)	
	Mental and behavioural disorders	9(10.47)	(4.00, 16.93)	13	86(19.20)	
	Diseases of the nervous system	4(7.69)	(0.45, 14.94)	7	52(11.61)	
	Diseases of the respiratory system	3(6.52)	(0.00, 13.66)	4	46(10.27)	
	Diseases of the eye and adnexa	6(15.00)	(3.93, 26.07)	9	40(8.93)	
	Injury, poisoning and certain other consequences of external causes	6(17.65)	(4.83, 30.46)	8	34(7.59)	
	Certain infectious and parasitic diseases	2(5.88)	(0.00, 13.79)	3	34(7.59)	
	Diseases of the skin and subcutaneous tissue	1(5.26)	(0.00, 15.30)	2	19(4.24)	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1(8.33)	(0.00, 23.97)	1	12(2.68)	
	Diseases of the ear and mastoid process	4(36.36)	(7.94, 64.79)	7	11(2.46)	
	Congenital malformations, deformations and chromosomal abnormalities	0(0.00)	(0.00, 0.00)	0	5(1.12)	
	Pregnancy, childbirth and the puerperium	0(0.00)	(0.00, 0.00)	0	1(0.22)	
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	8(15.38)	(5.58, 25.19)	12	52(11.61)	
History of Allergies	Yes	2(7.41)	(0.00, 17.29)	4	27(5.14)	1.0000 Fisher's Exact test
	None	38(7.63)	(5.30, 9.96)	47	498(94.86)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
	Details for History of Allergies by dictionary					
	Factors influencing health status and contact with health services	2(18.18)	(0.00, 40.97)	4	11(40.74)	
	Injury, poisoning and certain other consequences of external causes	0(0.00)	(0.00, 0.00)	0	16(59.26)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

Dictionary: KCD 7 and ICD 10

Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

D. Concomitant medications

When analyzing AE incidence by use of concomitant medications, it was 8.15% (40/491 subjects, 51 events) in subjects with concomitant medications, and no AE was reported in subjects without concomitant medications. Difference in AE incidences between the groups was not statistically significant (p=0.0976) (Table 104).

When analyzing AE incidence by concomitant medications (multiple counting allowed), it was 47.62% (10/21 subjects, 16 events) in 'Anti-infectives (systemic)', followed by 'Dermatologicals' in 33.33% (3/9 subjects, 4 events) and 'Hormones' in 25.00% (4/16 subjects, 6 events) (Table 104).

Table 104. AEs onset status by concomitant medications (Overactive Bladder)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Yes	40(8.15)	(5.73, 10.57)	51	491(93.52)	0.0976
No	0(0.00)	(0.00, 0.00)	0	34(6.48)	Fisher's Exact test
Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Details for Concomitant Medication by dictionary (Overlapped¶)					
Anaesthetics- Local & General	36(8.26)	(5.67, 10.84)	46	436(88.80)	
Anaesthetics - Local & General	36(8.26)	(5.67, 10.84)	46	436(88.80)	
Central Nervous System	31(9.09)	(6.04, 12.14)	40	341(69.45)	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	19(11.18)	(6.44, 15.91)	25	170(34.62)	
Analgesics (Non-Opioid) & Antipyretics	13(10.48)	(5.09, 15.88)	19	124(25.25)	
Analgesics (Opioid)	6(6.82)	(1.55, 12.08)	7	88(17.92)	
Hypnotics & Sedatives	6(8.45)	(1.98, 14.92)	8	71(14.46)	
Antidepressants	7(14.29)	(4.49, 24.08)	10	49(9.98)	
Drugs For Neuropathic Pain	2(10.00)	(0.00, 23.15)	2	20(4.07)	
Anxiolytics	5(13.51)	(2.50, 24.53)	8	37(7.54)	
Anticonvulsants	3(12.00)	(0.00, 24.74)	4	25(5.09)	
Nootropics & Neurotonics	2(6.06)	(0.00, 14.20)	4	33(6.72)	
Neurodegenerative Disease Drugs	2(9.52)	(0.00, 22.08)	3	21(4.28)	
Antiparkinsonian Drugs	0(0.00)	(0.00, 0.00)	0	17(3.46)	
Antipsychotics	2(16.67)	(0.00, 37.75)	3	12(2.44)	
Antivertigo Drugs	1(25.00)	(0.00, 67.44)	3	4(0.81)	
Antimigraine Preparations	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Other CNS Drugs & Agents for ADHD	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Gastrointestinal & Hepatobiliary System	28(10.11)	(6.56, 13.66)	37	277(56.42)	
Antacids, Antireflux Agents & Antiulcerants	19(10.27)	(5.90, 14.64)	26	185(37.68)	
GIT Regulators, Antiflatulents & Anti-inflammatories	9(10.98)	(4.21, 17.74)	12	82(16.70)	
Digestives	6(7.79)	(1.80, 13.78)	9	77(15.68)	
Laxatives, Purgatives	6(15.00)	(3.93, 26.07)	8	40(8.15)	
Antiemetics	2(9.09)	(0.00, 21.10)	2	22(4.48)	
Antispasmodics	1(5.88)	(0.00, 17.07)	2	17(3.46)	
Antidiarrheals	0(0.00)	(0.00, 0.00)	0	11(2.24)	
Cholagogues, Cholelitholytics & Hepatic Protectors	2(28.57)	(0.00, 62.04)	3	7(1.43)	
Other Gastrointestinal Agents	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	4(0.81)	
Cardiovascular & Hematopoietic System	20(8.85)	(5.15, 12.55)	26	226(46.03)	
Dyslipidaemic Agents	7(8.33)	(2.42, 14.24)	10	84(17.11)	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	6(7.32)	(1.68, 12.95)	10	82(16.70)	
Calcium Antagonists	5(8.33)	(1.34, 15.33)	7	60(12.22)	
Angiotensin II Antagonists	3(5.77)	(0.00, 12.11)	4	52(10.59)	
Other Antihypertensives	2(6.06)	(0.00, 14.20)	2	33(6.72)	
Haemostatics	2(5.26)	(0.00, 12.36)	2	38(7.74)	
Beta-Blockers	3(8.82)	(0.00, 18.36)	4	34(6.92)	
Peripheral Vasodilators & Cerebral Activators	2(9.52)	(0.00, 22.08)	3	21(4.28)	
Diuretics	1(6.67)	(0.00, 19.29)	2	15(3.05)	
Anti-Anginal Drugs	1(6.25)	(0.00, 18.11)	1	16(3.26)	
Other Cardiovascular Drugs	3(25.00)	(0.50, 49.50)	4	12(2.44)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Vasoconstrictors	2(33.33)	(0.00, 71.05)	3	6(1.22)	
Cardiac Drugs	1(16.67)	(0.00, 46.49)	2	6(1.22)	
Phlebitis & Varicose Preparations	2(66.67)	(13.32, 100.00)	2	3(0.61)	
Antidiuretics	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Haematopoietic Agents	0(0.00)	(0.00, 0.00)	0	2(0.41)	
ACE Inhibitors/Direct Renin Inhibitors	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	7(1.43)	
Musculo-Skeletal System	8(13.33)	(4.73, 21.93)	9	60(12.22)	
Muscle Relaxants	3(13.04)	(0.00, 26.81)	4	23(4.68)	
Neuromuscular Disorder Drugs	5(16.13)	(3.18, 29.08)	5	31(6.31)	
Other Drugs Acting on the Musculo-Skeletal System	2(11.11)	(0.00, 25.63)	2	18(3.67)	
Anti-Inflammatory Enzymes	0(0.00)	(0.00, 0.00)	0	13(2.65)	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	0(0.00)	(0.00, 0.00)	0	4(0.81)	
Endocrine & Metabolic System	5(5.38)	(0.79, 9.96)	9	93(18.94)	
Antidiabetic Agents	4(6.25)	(0.32, 12.18)	8	64(13.03)	
Other Agents Affecting Metabolism	0(0.00)	(0.00, 0.00)	0	19(3.87)	
Thyroid Hormones	0(0.00)	(0.00, 0.00)	0	13(2.65)	
Agents Affecting Bone Metabolism	0(0.00)	(0.00, 0.00)	0	7(1.43)	
Insulin Preparations	1(20.00)	(0.00, 55.06)	1	5(1.02)	
Antithyroid Agents	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Intravenous & Other Sterile Solutions	7(9.72)	(2.88, 16.57)	9	72(14.66)	
Intravenous & other sterile solutions	7(9.72)	(2.88, 16.57)	9	72(14.66)	
Genito-Urinary System	6(10.00)	(2.41, 17.59)	6	60(12.22)	
Drugs for Bladder & Prostate Disorders	6(10.34)	(2.51, 18.18)	6	58(11.81)	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	1(25.00)	(0.00, 67.44)	1	4(0.81)	
Other Drugs Acting on the Genito-Urinary System	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Respiratory System	2(4.76)	(0.00, 11.20)	3	42(8.55)	
Antiasthmatic & COPD Preparations	2(7.14)	(0.00, 16.68)	3	28(5.70)	
Cough & Cold Preparations	1(5.00)	(0.00, 14.55)	1	20(4.07)	
Nasal Decongestant & Other Nasal Preparations	0(0.00)	(0.00, 0.00)	0	3(0.61)	
Oncology	8(16.33)	(5.98, 26.68)	11	49(9.98)	
Supportive Care Therapy	8(18.60)	(6.97, 30.24)	11	43(8.76)	
Hormonal Chemotherapy	0(0.00)	(0.00, 0.00)	0	4(0.81)	
Cytotoxic Chemotherapy	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Vitamins & Minerals	3(9.09)	(0.00, 18.90)	4	33(6.72)	
Calcium / with Vitamins	0(0.00)	(0.00, 0.00)	0	15(3.05)	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	0(0.00)	(0.00, 0.00)	0	9(1.83)	
Vitamin B-complex / with C	1(14.29)	(0.00, 40.21)	1	7(1.43)	
Vitamins &/or Minerals	2(28.57)	(0.00, 62.04)	3	7(1.43)	
Vitamins A, D & E	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Anti-infectives (systemic)	10(47.62)	(26.26, 68.98)	16	21(4.28)	
Cephalosporins	7(87.50)	(64.58, 100.00)	12	8(1.63)	
Quinolones	5(100.00)	(100.00, 100.00)	7	5(1.02)	
Antivirals	0(0.00)	(0.00, 0.00)	0	5(1.02)	
Antifungals	1(20.00)	(0.00, 55.06)	1	5(1.02)	
Antiamoebics	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Macrolides	1(50.00)	(0.00, 100.00)	1	2(0.41)	
Aminoglycosides	1(100.00)	(100.00, 100.00)	1	1(0.20)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Anti-TB Agents	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Tetracyclines	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Allergy & Immune System	2(8.33)	(0.00, 19.39)	2	24(4.89)	
Antihistamines & Antiallergics	2(9.52)	(0.00, 22.08)	2	21(4.28)	
Immunosuppressants	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Vaccines, Antisera & Immunologicals	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	3(18.75)	(0.00, 37.88)	6	16(3.26)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	3(18.75)	(0.00, 37.88)	6	16(3.26)	
Hormones	4(25.00)	(3.78, 46.22)	6	16(3.26)	
Corticosteroid Hormones	3(25.00)	(0.50, 49.50)	5	12(2.44)	
Oestrogens & Progesterones & Related Synthetic Drugs	1(33.33)	(0.00, 86.68)	1	3(0.61)	
Other Drugs Affecting Hormonal Regulation	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Trophic Hormones & Related Synthetic Drugs	1(100.00)	(100.00, 100.00)	3	1(0.20)	
Nutrition	0(0.00)	(0.00, 0.00)	0	9(1.83)	
Parenteral Nutritional Products	0(0.00)	(0.00, 0.00)	0	5(1.02)	
Electrolytes	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Appetite Enhancers	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Enteral / Nutritional Products	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Eye	2(22.22)	(0.00, 49.38)	4	9(1.83)	
Ophthalmic Lubricants	0(0.00)	(0.00, 0.00)	0	3(0.61)	
Eye Anti-infectives & Antiseptics	1(50.00)	(0.00, 100.00)	2	2(0.41)	
Eye Corticosteroids	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Other Eye Preparations	1(50.00)	(0.00, 100.00)	2	2(0.41)	
Antiglaucoma Preparations	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Mydriatic Drugs	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Dermatologicals	3(33.33)	(2.53, 64.13)	4	9(1.83)	
Topical Corticosteroids	1(25.00)	(0.00, 67.44)	1	4(0.81)	
Other Dermatologicals	0(0.00)	(0.00, 0.00)	0	2(0.41)	
Topical Antibiotics	1(50.00)	(0.00, 100.00)	2	2(0.41)	
Topical Antifungals & Antiparasites	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Emollients & Skin Protectives	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Psoriasis, Seborrhea & Ichthyosis Preparations	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Skin Antiseptics & Disinfectants	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Topical Anti-infectives with Corticosteroids	1(100.00)	(100.00, 100.00)	1	1(0.20)	
Ear & Mouth / Throat	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Mouth / Throat Preparations	0(0.00)	(0.00, 0.00)	0	1(0.20)	
Miscellaneous	1(12.50)	(0.00, 35.42)	2	8(1.63)	
Miscellaneous	1(12.50)	(0.00, 35.42)	2	8(1.63)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

Dictionary: KIMS

E. Special population

When classifying and analyzing AE incidence in elderly group who was '65 or/and over', it was 8.86% (24/271 subjects, 34 events) in subjects of '65 or/and over' and 6.30% (16/254 subjects, 17 events) in subjects of 'below 65 years'. Difference in AE incidences between the groups was not statistically significant (p=0.2698) (Table 105).

When analyzing AE incidence by renal impairment, no AE was reported in subjects with renal impairment, and it was 7.69% (40/520 subjects, 51 events) in subjects without renal impairment. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 105).

When analyzing AE incidence by hepatic impairment, it was 14.29% (1/7 subjects, 1 event) in subjects with hepatic impairment and 7.53% (39/518 subjects, 50 events) in subjects without hepatic impairment. Difference in AE incidences between the groups was not statistically significant (p=0.4277) (Table 105).

Details of AE in subjects with hepatic impairment are presented in the table below (Table 106).

Table 105. AEs onset status in special population (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value
Elderly	below 65 years	16(6.30)	(3.31, 9.29)	17	254(48.38)	0.2698 Chi-square test
	65 or/and over	24(8.86)	(5.47, 12.24)	34	271(51.62)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Renal impairment	Yes	0(0.00)	(0.00, 0.00)	0	5(0.95)	1.0000 Fisher's Exact test
	No	40(7.69)	(5.40, 9.98)	51	520(99.05)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Hepatic impairment	Yes	1(14.29)	(0.00, 40.21)	1	7(1.33)	0.4277 Fisher's Exact test
	No	39(7.53)	(5.26, 9.80)	50	518(98.67)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

Table 106. AEs onset status in the subjects with hepatic impairment (Overactive Bladder)

caseno	Liver	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	r/o toxic liver injury;r/o non-alcoholic steatohepatitis	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE

F. Information of the study drug administration

When analyzing AE incidence by the number of injection sites of the study drug and total units injected, all subjects received total 100 U of the study drug in 20 sites and thus the AE incidence was the same as that in the safety population (Table 107).

When analyzing AE incidence by use of anesthesia at the study drug administration, it was 9.06% (29/320 subjects, 37 events) in 'Local', followed by 'None' in 6.06% (4/66 subjects, 5 events) and 'General' in 5.04% (7/139 subjects, 9 events). Difference in AE incidences among the groups was not statistically significant (p=0.2876) (Table 107).

When analyzing AE incidence by use of prophylactic antibiotics before, during, and after the study drug administration, it was 8.42% (40/475 subjects, 51 events) in subjects with antibiotics, and no AE was reported in subjects without antibiotics. The difference in AE incidences between the groups was statistically significant (p=0.0240) (Table 107).

Table 107. AEs onset status based on the information of study drug administration (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Number of Injection Sites	20	40(7.62)	(5.35, 9.89)	51	525(100.00)	NA
	30	0(0.00)	(0.00, 0.00)	0	0(0.00)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Total Units Injected	100	40(7.62)	(5.35, 9.89)	51	525(100.00)	NA
	200	0(0.00)	(0.00, 0.00)	0	0(0.00)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Anesthesia	None	4(6.06)	(0.30, 11.82)	5	66(12.57)	0.2876 Chi-square test
	Local	29(9.06)	(5.92, 12.21)	37	320(60.95)	
	General	7(5.04)	(1.40, 8.67)	9	139(26.48)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Prophylactic Antibiotic Use	Yes	40(8.42)	(5.92, 10.92)	51	475(90.48)	0.0240 Fisher's Exact test
	No	0(0.00)	(0.00, 0.00)	0	50(9.52)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

G. Clean intermittent catheterization

When analyzing AE incidence by use of clean intermittent catheterization before the study drug administration, it was 6.42% (7/109 subjects, 9 events) in subjects with clean intermittent catheterization and 7.93% (33/416 subjects, 42 events) in subjects without clean intermittent catheterization. The difference in AE incidences between the groups was not statistically

significant (p=0.5967) (Table 108).

When analyzing AE incidence by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, it was 15.38% (16/104 subjects, 19 events) in subjects with urinary catheterization and 5.45% (17/312 subjects, 23 events) in subjects without urinary catheterization, and difference in AE incidences between the groups was statistically significant (p=0.0012). Among the subjects with urinary catheterization, AE incidence was 40.00% (6/15 subjects, 6 events) in subjects who initiated catheterization due to urinary retention and 12.22% (11/90 subjects, 14 events) in subjects who initiated catheterization due to other reason (Table 108).

Table 108. AEs onset status by clean intermittent catheterization (Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Routine Urinary Catheterization(before BOTOX)	Yes	7(6.42)	(1.82, 11.02)	9	109(20.76)	0.5967
	No	33(7.93)	(5.34, 10.53)	42	416(79.24)	Chi-square test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Initiation of CIC after BOTOX injection§	Yes	16(15.38)	(8.45, 22.32)	19	104(25.00)	0.0012**
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	6(40.00)	(15.2, 164.79)	6	15(3.61)	Chi-square test
	initiated CIC due to "Other Reason"	11(12.22)	(5.46, 18.99)	14	90(21.63)	
	No	17(5.45)	(2.93, 7.97)	23	312(75.00)	
	Total	33(7.93)	(5.34, 10.53)	42	416(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%
‡ 95% Confidence Interval for adverse event incidence rate
95% Confidence Interval was calculated using the normal approximation method.
* The p-value is about that relation between Category and incidence rate of AEs
**The p-value is about that relation between Yes/No and incidence rate of AEs
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

H. Factors that may affect safety

Regarding the safety in this PMS, incidence of AEs was investigated by age, sex, treatment setting, pregnancy status, symptoms, past treatment history, medical history, concomitant medications, information of the study drug administration, and clean intermittent catheterization as well as in special population such as the elderly, subjects with renal or hepatic impairment.

The analysis results showed statistically significant difference in AE incidence by 2 factors: use of prophylactic antibiotics before, during, and after the study drug administration (p=0.0240), and use of urinary catheterization after the study drug administration in subjects who had not used urinary catheterization before the study drug administration (p=0.0012).

When analyzing AE incidence by use of prophylactic antibiotics before, during, and after the study drug administration, it was 8.42% (40/475 subjects, 51 events) in subjects with antibiotics, and no AE was reported in subjects without antibiotics (0/50 subjects, 0 events), and the difference in AE incidences between the groups was statistically significant (p=0.0240). Since so few patients did not use antibiotics, it is difficult to draw any conclusions or determine clinical significance from this analysis., but

When analyzing AE incidence by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, it was 15.38% (16/104 subjects, 19 events) in subjects with urinary catheterization and 5.45% (17/312 subjects, 23 events) in subjects without urinary catheterization, and difference in AE incidences between the groups was statistically significant (p=0.0012). It should be noted that subjects who initiate catheterization are at increased risk to develop a urinary tract infection. However, as the analysis did not specify the type of AEs experienced in the group of patients who initiated catheterization after BOTOX treatment, it is difficult to draw any conclusions or determine clinical significance from this analysis.

3.1.7 Other AEs

No distant spread of toxin was identified.

3.2 Effectiveness data (Overactive Bladder)

3.2.1 Effectiveness evaluation

Effectiveness evaluation was conducted by the subject using incontinence questionnaire (ICIQ-SF) before the study drug administration and 1 ~ 4 month(s) after the study drug administration. Evaluation should be carried out based on the change in total score before and after the study drug administration. A decrease in score represents an improvement.

When comparing and analyzing changes in the ICIQ score in 478 subjects of the effectiveness population, the mean score decreased by 6.00±6.41 from 12.20±6.56 before the study drug administration to 6.19±6.27 after the study drug administration. The mean change in ICIQ from baseline was statistically significant (p<0.0001) (Table 109).

Table 109. Change in ICIQ score (Overactive Bladder)

	n	mean± std	median	min~ max
before BOTOX injection	478	12.20± 6.56	14.00	0.00~ 21.00
after BOTOX injection	478	6.19± 6.27	5.00	0.00~ 21.00

	n	mean± std	median	min~ max
after BOTOX injection - before BOTOX injection	478	-6.00± 6.41	-5.00	-21.00~ 13.00
p-value(paired t-test)		<0.0001		

When analyzing changes in ICIQ scores in the effectiveness population by range, it was '< -5' in 47.28% (226/478 subjects), '≥ 0 to < 5' in 25.52% (122/478 subjects), '≥ -5 to < 0' in 25.10% (120/478 subjects), and '≥ 5' in 2.09% (10/478 subjects) (Table 110).

Table 110. Change in ICIQ Score by range (Overactive Bladder)

	Total n(%)
< -5	226(47.28)
≥ -5 to < 0	120(25.10)
≥ 0 to < 5	122(25.52)
≥ 5	10(2.09)
Total	478(100.00)

The denominator is number of total subjects.

The mean time to ICIQ assessment completion from baseline was 64.62±123.36 days (Table 111).

Table 111. Time to ICIQ assessment completion (Overactive Bladder)

	Total (N=478)
n	478
mean±std (days)	64.62± 123.36
median	45.00
min ~ max	17.00~ 2,184.00

Duration between baseline and follow-up ICIQ completion = Date of after BOTOX treatment - Date of before BOTOX treatment + 1

When investigating the degree of urine leaks before/after the study drug administration by multiple counting, 'Never-urine does not leak' accounted for 16.24% (77/474 subjects) before the study drug administration, but it accounted for 43.04% (204/474 subjects) after the study drug administration (Table 112).

'Leaks before you can get to the toilet' accounted for 51.90% (246/474 subjects) before the study drug administration, but it accounted for 27.43% (130/474 subjects) after the study drug administration (Table 112).

'Leaks when you cough or sneeze' accounted for 30.80% (146/474 subjects) before the study drug administration, but it accounted for 16.67% (79/474 subjects) after the study drug administration (Table 112). Note that 'Leaks when you cough or sneeze' is a symptom of stress

incontinence, which is not indicated for BOTOX.

'Leaks when you are asleep' accounted for 19.41% (92/474 subjects) before the study drug administration, but it accounted for 11.18% (53/474 subjects) after the study drug administration (Table 112).

'Leaks when are physically active/exercising' accounted for 19.62% (93/474 subjects) before the study drug administration, but it accounted for 9.28% (44/474 subjects) after the study drug administration (Table 112). Note that 'Leaks when are physically active/exercising' is a symptom of stress incontinence, which is not indicated for BOTOX.

'Leaks when you have finished urinating and are dressed' accounted for 15.40% (73/474 subjects) before the study drug administration, but it accounted for 9.28% (44/474 subjects) after the study drug administration (Table 112).

'Leaks for no obvious reason' accounted for 37.34% (177/474 subjects) before the study drug administration, but it accounted for 19.41% (92/474 subjects) after the study drug administration (Table 112).

'Leaks all the time' accounted for 15.61% (74/474 subjects) before the study drug administration, but it accounted for 4.64% (22/474 subjects) after the study drug administration (Table 112).

Table 112. Degree of urine leaks before/after the study drug administration (Overactive Bladder)

Overlapped¶	Before BOTOX n(%)	After BOTOX n(%)
Never-urine does not leak	77(16.24)	204(43.04)
Leaks before you can get to the toilet	246(51.90)	130(27.43)
Leaks when you cough or sneeze	146(30.80)	79(16.67)
Leaks when you are asleep	92(19.41)	53(11.18)
Leaks when are physically active/exercising	93(19.62)	44(9.28)
Leaks when you have finished urinating and are dressed	73(15.40)	44(9.28)
Leaks for no obvious reason	177(37.34)	92(19.41)
Leaks all the time	74(15.61)	22(4.64)
Total	474(100.00)	474(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
Missing: 4 (Before BOTOX), 4 (After BOTOX)

3.2.2 Effectiveness evaluation by factor

A. Background factors

When analyzing ICIQ score change before/after the study drug administration by age, the mean decrease of 6.13±5.87 was found in subjects '< 50 years', and it was statistically significant ($p<0.0001$). The mean decrease of 6.31±6.67 was found in '≥ 50 years to < 60 years', which was

statistically significant (p<0.0001). The mean decrease of 5.20±6.47 was found in '≥ 60 years to < 70 years', which was statistically significant (p<0.0001). The mean decrease of 6.25±6.49 was found in '≥ 70 years', which was statistically significant (p<0.0001). Difference in ICIQ score change from baseline among the groups was not statistically significant (p=0.5316) (Table 113).

When analyzing ICIQ score change before/after the study drug administration by sex, the mean decrease of 4.58±5.83 was found in 'Male' subjects, and it was statistically significant (p<0.0001). The mean decrease of 6.42±6.52 was found in 'Female' subjects, which was statistically significant (p<0.0001). Difference in ICIQ score change from baseline between the groups was statistically significant (p=0.0090) (Table 113).

When analyzing ICIQ score change before/after the study drug administration by treatment setting, the mean decrease of 6.62±6.45 was found in 'Outpatient' subjects, and it was statistically significant (p<0.0001). The mean decrease of 5.65±6.38 was found in 'Inpatient', which was statistically significant (p<0.0001). Difference in ICIQ score change from baseline between the groups was not statistically significant (p=0.1114) (Table 113).

When analyzing ICIQ score change before/after the study drug administration by symptoms (multiple counting allowed) in subjects, subjects with 'Urge urinary incontinence' showed the mean decrease of 7.02±6.48, which was statistically significant (p<0.0001). The mean decrease of 5.77±6.34 was found in 'Urgency', which was statistically significant (p<0.0001). The mean decrease of 5.71±6.18 was found in 'Frequency', which was statistically significant (p<0.0001). The mean decrease of 4.66±5.61 was found in 'Other', which was statistically significant (p<0.0001) (Table 113).

Among female subjects, there was no pregnant subject (Table 113).

Table 113. Effectiveness evaluation by background factor (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Age	< 50 years	83	-6.13± 5.87	-4.00	-21.00~ 5.00	<0.0001	0.5316
	≥ 50 years to < 60 years	94	-6.31± 6.67	-5.00	-21.00~ 7.00	<0.0001	
	≥ 60 years to < 70 years	108	-5.20± 6.47	-3.00	-20.00~ 8.00	<0.0001	
	≥ 70 years	193	-6.25± 6.49	-6.00	-21.00~ 13.00	<0.0001	
Sex	Male	107	-4.58± 5.83	-3.00	-21.00~ 7.00	<0.0001	0.0090
	Female	371	-6.42± 6.52	-6.00	-21.00~ 13.00	<0.0001	
Treatment Setting	Outpatient	173	-6.62± 6.45	-5.00	-21.00~ 9.00	<0.0001	0.1114
	Inpatient	305	-5.65± 6.38	-4.00	-21.00~ 13.00	<0.0001	
Currently pregnant	Yes	0					NA
* for female	No	371	-6.42± 6.52	-6.00	-21.00~ 13.00	<0.0001	
Symptoms	Urge urinary incontinence	351	-7.02± 6.48	-6.00	-21.00~ 13.00	<0.0001	NA
* for patients with OAB	Urgency	320	-5.77± 6.34	-5.00	-21.00~ 13.00	<0.0001	
Overlapped¶	Frequency	348	-5.71± 6.18	-4.00	-21.00~ 13.00	<0.0001	
	Other	86	-4.66± 5.61	-3.00	-18.00~ 7.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.

B. Past treatment history

When analyzing ICIQ score change before/after the study drug administration by previous anticholinergic therapy, subjects who had received anticholinergic therapy showed the mean decrease of 6.10±6.40, which was statistically significant (p<0.0001). Subjects without previous anticholinergic therapy showed the mean decrease of 5.78±7.24, which was statistically significant (p=0.0436). Difference in ICIQ score change between the groups was not statistically significant (p=0.9150) (Table 114).

When analyzing ICIQ score change before/after the study drug administration by past use of other OAB drugs after anticholinergic therapy in subjects diagnosed with OAB in the safety population, subjects who had used OAB drug showed the mean decrease of 5.61±6.17, which was statistically significant (p<0.0001). Subjects without experience of other treatments showed the mean decrease of 6.47±6.67, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1441) (Table 114).

When analyzing ICIQ score change before/after the study drug administration by previous use of sacral neuromodulation therapy, subjects who had received sacral neuromodulation therapy showed the mean decrease of 7.88±6.94, which was statistically significant (p=0.0148). Subjects without previous sacral neuromodulation therapy showed the mean decrease of 5.97±6.41, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.4059) (Table 114).

When analyzing ICIQ score change before/after the study drug administration by past treatment history with the study drug for other indication or other botulinum toxin, the mean decrease of 4.37±5.07 were found in subjects who had used the study drug or other botolimum toxin, which was statistically significant (p=0.0014). Subjects who had not been previously treated with BOTOX or other botulinum toxin showed the mean decrease of 6.07±6.46, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.2570) (Table 114).

Table 114. Effectiveness evaluation by past treatment history (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Previous Anticholinergic Therapy	Yes	469	-6.01± 6.40	-5.00	-21.00~ 13.00	<0.0001	0.9150
	No	9	-5.78± 7.24	-2.00	-16.00~ 3.00	0.0436	
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	259	-5.61± 6.17	-4.00	-21.00~ 9.00	<0.0001	0.1441
	No	219	-6.47± 6.67	-6.00	-21.00~ 13.00	<0.0001	
Previous Use of Sacral Neuromodulation Therapy	Yes	8	-7.88± 6.94	-10.50	-18.00~ 0.00	0.0148	0.4059
	No	470	-5.97± 6.41	-5.00	-21.00~ 13.00	<0.0001	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	19	-4.37± 5.07	-3.00	-12.00~ 1.00	0.0014	0.2570
	None	459	-6.07± 6.46	-5.00	-21.00~ 13.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

C. Medical history

When analyzing ICIQ score change before/after the study drug administration by medical history including surgeries and complications of underlying diseases, the mean decrease of 6.02±6.48 was found in subjects with medical history, which was statistically significant (p<0.0001). Subjects without medical history showed the mean decrease of 5.52±5.87, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.5747) (Table 115).

ICIQ score change before/after the study drug administration by medical history type (multiple counting allowed) are presented in the table below (Table 115).

When analyzing ICIQ score change before/after the study drug administration by allergy history, the mean decrease of 5.08±7.13 was found in subjects with allergy history, which was statistically significant (p=0.0013). Subjects without allergy history showed the mean decrease of 6.06±6.37, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.4489) (Table 15).

ICIQ score change before/after the study drug administration by allergen (multiple counting allowed) are presented in the table below (Table 115).

Table 115. Effectiveness evaluation by medical history (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	417	-6.02± 6.48	-5.00	-21.00~ 13.00	<0.0001	0.5747
	None	58	-5.52± 5.87	-3.50	-21.00~ 2.00	<0.0001	
	Details for Medical History by dictionary (Overlapped¶)						
	Diseases of the circulatory system	235	-6.29± 6.22	-6.00	-21.00~ 9.00	<0.0001	
	Factors influencing health status and contact with health services	201	-6.23± 6.53	-5.00	-21.00~ 7.00	<0.0001	
	Endocrine, nutritional and metabolic diseases	158	-6.12± 6.27	-6.00	-21.00~ 8.00	<0.0001	
	Diseases of the genitourinary system	108	-4.80± 5.61	-3.00	-21.00~ 7.00	<0.0001	
	Diseases of the digestive system	102	-5.80± 6.78	-4.00	-21.00~ 13.00	<0.0001	
	Diseases of the musculoskeletal system and connective tissue	117	-5.93± 6.22	-5.00	-21.00~ 7.00	<0.0001	
	Neoplasms	89	-5.97± 7.04	-5.00	-21.00~ 13.00	<0.0001	
	Mental and behavioural disorders	82	-6.05± 6.52	-7.00	-21.00~ 13.00	<0.0001	
	Diseases of the nervous system	51	-5.84± 7.20	-3.00	-21.00~ 13.00	<0.0001	
	Diseases of the respiratory system	45	-5.78± 6.67	-3.00	-21.00~ 5.00	<0.0001	
	Diseases of the eye and adnexa	40	-4.93± 6.08	-4.00	-18.00~ 7.00	<0.0001	
	Injury, poisoning and certain other consequences of external causes	33	-6.03± 5.96	-5.00	-19.00~ 3.00	<0.0001	
	Certain infectious and parasitic diseases	33	-6.27± 6.33	-5.00	-21.00~ 1.00	<0.0001	
	Diseases of the skin and subcutaneous tissue	19	-5.89± 7.17	-3.00	-19.00~ 1.00	0.0021	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	12	-5.25± 4.92	-5.00	-14.00~ 1.00	0.0035	

	Diseases of the ear and mastoid process	11	-5.82± 5.88	-3.00	-15.00~ 1.00	0.0083	
	Congenital malformations, deformations and chromosomal abnormalities	5	-6.80± 4.32	-7.00	-12.00~ -2.00	0.0245	
.	Pregnancy, childbirth and the puerperium	1	-18.00	-18.00	-18.00~ -18.00		
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	52	-5.79± 6.18	-5.00	-19.00~ 5.00	<0.0001	
History of Allergies	Yes	26	-5.08± 7.13	-3.50	-20.00~ 7.00	0.0013	0.4489
	None	452	-6.06± 6.37	-5.00	-21.00~ 13.00	<0.0001	
	Details for History of Allergies by dictionary						
	Factors influencing health status and contact with health services	11	-5.00± 6.54	-3.00	-20.00~ 1.00	0.0296	
	Injury, poisoning and certain other consequences of external causes	15	-5.13± 7.75	-4.00	-17.00~ 7.00	0.0225	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Unknown: 3 (Medical History, Including Surgeries and Complications of Underlying Diseases)

D. Concomitant medications

When analyzing ICIQ score change before/after the study drug administration by use of concomitant medications, the mean decrease 6.12±6.42 was found in subjects with concomitant medications, which was statistically significant (p<0.0001). Subjects without concomitant medications showed the mean decrease of 4.04±6.04, which was statistically significant (p=0.0022). Difference in ICIQ score change between the groups was not statistically significant (p=0.1081) (Table 116).

ICIQ score change before/after the study drug administration by concomitant medication type (double counting allowed) are presented in the table below (Table 116).

Table 116. Effectiveness evaluation by concomitant medications (Overactive Bladder)

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Yes	452	-6.12± 6.42	-5.00	-21.00~ 13.00	<0.0001	0.1081
No	26	-4.04± 6.04	-4.50	-18.00~ 9.00	0.0022	
Details for Concomitant Medication by dictionary						
Anaesthetics- Local & General	403	-6.19± 6.42	-5.00	-21.00~ 13.00	<0.0001	
Anaesthetics - Local & General	403	-6.19± 6.42	-5.00	-21.00~ 13.00	<0.0001	
Central Nervous System	307	-6.34± 6.49	-6.00	-21.00~ 13.00	<0.0001	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	139	-6.74± 6.18	-7.00	-21.00~ 7.00	<0.0001	
Analgesics (Non-Opioid) & Antipyretics	115	-6.27± 6.88	-6.00	-21.00~ 7.00	<0.0001	
Analgesics (Opioid)	88	-5.85± 6.38	-5.00	-21.00~ 7.00	<0.0001	
Hypnotics & Sedatives	70	-4.20± 6.39	-2.00	-21.00~ 13.00	<0.0001	
Antidepressants	47	-7.17± 6.54	-8.00	-19.00~ 13.00	<0.0001	
Drugs For Neuropathic Pain	17	-6.71± 5.95	-5.00	-21.00~ 1.00	0.0003	
Anxiolytics	31	-6.35± 6.45	-8.00	-18.00~ 13.00	<0.0001	
Anticonvulsants	23	-7.43± 9.02	-7.00	-21.00~ 13.00	0.0007	

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Nootropics & Neurotonics	33	-6.12± 5.70	-7.00	-18.00~ 5.00	<0.0001	
Neurodegenerative Disease Drugs	21	-4.81± 6.13	-3.00	-21.00~ 3.00	0.0018	
Antiparkinsonian Drugs	17	-6.59± 7.24	-6.00	-21.00~ 3.00	0.0017	
Antipsychotics	12	-7.83± 7.11	-7.50	-18.00~ 1.00	0.0029	
Antivertigo Drugs	4	-3.00± 6.00	0.00	-12.00~ 0.00	0.3910	
Antimigraine Preparations	2	-8.00± 2.83	-8.00	-10.00~ -6.00	0.1560	
Other CNS Drugs & Agents for ADHD	1	-18.00	-18.00	-18.00~ -18.00		
Gastrointestinal & Hepatobiliary System	244	-6.33± 6.60	-5.00	-21.00~ 13.00	<0.0001	
Antacids, Antireflux Agents & Antiulcerants	157	-5.98± 6.80	-5.00	-21.00~ 13.00	<0.0001	
GIT Regulators, Antiflatulents & Anti-inflammatories	72	-5.64± 6.35	-5.50	-21.00~ 13.00	<0.0001	
Digestives	63	-7.21± 6.90	-6.00	-21.00~ 5.00	<0.0001	
Laxatives, Purgatives	38	-7.39± 7.19	-6.00	-21.00~ 2.00	<0.0001	
Antiemetics	21	-6.38± 7.22	-4.00	-21.00~ 2.00	0.0006	
Antispasmodics	16	-2.31± 5.69	0.00	-17.00~ 7.00	0.1248	
Antidiarrheals	11	-7.36± 7.71	-6.00	-20.00~ 0.00	0.0100	
Cholagogues, Cholelitholytics & Hepatic Protectors	7	-8.29± 8.50	-5.00	-21.00~ 2.00	0.0418	
Other Gastrointestinal Agents	1	-18.00	-18.00	-18.00~ -18.00		
Miscellaneous	4	-9.25± 6.80	-10.50	-16.00~ 0.00	0.0725	
Cardiovascular & Hematopoietic System	218	-6.43± 6.22	-6.00	-21.00~ 7.00	<0.0001	
Dyslipidaemic Agents	82	-6.67± 6.23	-7.00	-21.00~ 7.00	<0.0001	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	82	-7.09± 6.10	-6.00	-21.00~ 5.00	<0.0001	
Calcium Antagonists	60	-5.63± 5.67	-4.50	-19.00~ 3.00	<0.0001	
Angiotensin II Antagonists	50	-6.86± 5.59	-7.00	-21.00~ 3.00	<0.0001	
Other Antihypertensives	33	-6.03± 5.02	-5.00	-17.00~ 1.00	<0.0001	
Haemostatics	34	-4.12± 4.91	-2.50	-13.00~ 7.00	<0.0001	
Beta-Blockers	32	-5.22± 6.11	-4.50	-21.00~ 3.00	<0.0001	
Peripheral Vasodilators & Cerebral Activators	21	-8.52± 6.93	-9.00	-19.00~ 1.00	<0.0001	
Diuretics	14	-5.79± 6.17	-3.50	-19.00~ 0.00	0.0038	
Anti-Anginal Drugs	15	-6.07± 5.19	-6.00	-16.00~ 0.00	0.0005	
Other Cardiovascular Drugs	12	-9.92± 6.36	-9.50	-21.00~ -1.00	0.0002	
Vasoconstrictors	5	-2.80± 4.32	-2.00	-9.00~ 2.00	0.2212	
Cardiac Drugs	6	-3.67± 6.35	-1.50	-16.00~ 1.00	0.2161	
Phlebitis & Varicose Preparations	3	-10.00± 11.79	-13.00	-20.00~ 3.00	0.2796	
Antidiuretics	1	-7.00	-7.00	-7.00~ -7.00		
Haematopoietic Agents	2	-0.50± 0.71	-0.50	-1.00~ 0.00	0.5000	
ACE Inhibitors/Direct Renin Inhibitors	1	-18.00	-18.00	-18.00~ -18.00		
Miscellaneous	7	-7.86± 7.56	-11.00	-17.00~ 0.00	0.0333	
Musculo-Skeletal System	57	-7.67± 7.11	-7.00	-21.00~ 7.00	<0.0001	
Muscle Relaxants	22	-5.23± 6.80	-4.00	-21.00~ 7.00	0.0017	
Neuromuscular Disorder Drugs	30	-8.00± 6.73	-8.50	-21.00~ 0.00	<0.0001	
Other Drugs Acting on the Musculo-Skeletal System	17	-6.53± 8.19	-5.00	-21.00~ 7.00	0.0046	
Anti-Inflammatory Enzymes	12	-9.75± 7.07	-9.00	-21.00~ 0.00	0.0006	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	4	-4.25± 4.99	-3.50	-11.00~ 1.00	0.1871	
Endocrine & Metabolic System	88	-5.93± 6.22	-5.50	-21.00~ 7.00	<0.0001	
Antidiabetic Agents	64	-6.95± 5.96	-7.00	-21.00~ 5.00	<0.0001	
Other Agents Affecting Metabolism	15	-1.80± 4.59	0.00	-10.00~ 7.00	0.1507	
Thyroid Hormones	12	-8.08± 8.05	-10.00	-19.00~ 7.00	0.0052	
Agents Affecting Bone Metabolism	7	-4.57± 4.96	-4.00	-11.00~ 2.00	0.0506	
Insulin Preparations	5	-7.20± 7.16	-6.00	-18.00~ 0.00	0.0876	
Antithyroid Agents	1	-2.00	-2.00	-2.00~ -2.00		
Miscellaneous	1	0.00	0.00	0.00~ 0.00		

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Intravenous & Other Sterile Solutions	72	-6.47± 6.50	-7.00	-21.00~ 5.00	<0.0001	
Intravenous & other sterile solutions	72	-6.47± 6.50	-7.00	-21.00~ 5.00	<0.0001	
Genito-Urinary System	48	-6.04± 5.48	-5.50	-21.00~ 2.00	<0.0001	
Drugs for Bladder & Prostate Disorders	46	-6.24± 5.51	-6.00	-21.00~ 2.00	<0.0001	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	4	-7.00± 7.07	-6.00	-16.00~ 0.00	0.1421	
Other Drugs Acting on the Genito-Urinary System	1	-11.00	-11.00	-11.00~ -11.00		
Respiratory System	41	-5.41± 7.71	-4.00	-21.00~ 7.00	<0.0001	
Antiasthmatic & COPD Preparations	28	-5.46± 8.18	-3.50	-21.00~ 7.00	0.0015	
Cough & Cold Preparations	19	-8.11± 7.90	-7.00	-21.00~ 7.00	0.0003	
Nasal Decongestant & Other Nasal Preparations	2	2.00± 7.07	2.00	-3.00~ 7.00	0.7578	
Oncology	48	-6.63± 5.16	-7.00	-18.00~ 2.00	<0.0001	
Supportive Care Therapy	42	-6.62± 5.40	-7.00	-18.00~ 2.00	<0.0001	
Hormonal Chemotherapy	4	-6.50± 2.89	-6.50	-10.00~ -3.00	0.0204	
Cytotoxic Chemotherapy	2	-7.00± 5.66	-7.00	-11.00~ -3.00	0.3305	
Vitamins & Minerals	32	-7.44± 5.16	-8.00	-21.00~ 0.00	<0.0001	
Calcium / with Vitamins	15	-7.13± 4.24	-8.00	-13.00~ 0.00	<0.0001	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	8	-5.75± 4.50	-5.50	-11.00~ 0.00	0.0085	
Vitamin B-complex / with C	7	-7.86± 5.34	-9.00	-16.00~ 0.00	0.0080	
Vitamins &/or Minerals	7	-9.00± 6.46	-9.00	-21.00~ 0.00	0.0102	
Vitamins A, D & E	1	-12.00	-12.00	-12.00~ -12.00		
Miscellaneous	1	-14.00	-14.00	-14.00~ -14.00		
Anti-infectives (systemic)	18	-5.94± 7.16	-2.50	-21.00~ 2.00	0.0026	
Cephalosporins	7	-6.71± 8.48	-6.00	-21.00~ 2.00	0.0810	
Quinolones	4	-5.00± 8.08	-3.00	-16.00~ 2.00	0.3040	
Antivirals	4	-3.75± 3.59	-2.50	-9.00~ -1.00	0.1282	
Antifungals	4	-3.75± 5.56	-1.50	-12.00~ 0.00	0.2702	
Macrolides	1	-12.00	-12.00	-12.00~ -12.00		
Anti-TB Agents	1	-16.00	-16.00	-16.00~ -16.00		
Tetracyclines	1	0.00	0.00	0.00~ 0.00		
Allergy & Immune System	23	-7.00± 5.30	-7.00	-19.00~ 0.00	<0.0001	
Antihistamines & Antiallergics	20	-7.05± 5.55	-5.50	-19.00~ 0.00	<0.0001	
Immunosuppressants	2	-5.50± 4.95	-5.50	-9.00~ -2.00	0.3608	
Vaccines, Antisera & Immunologicals	1	-9.00	-9.00	-9.00~ -9.00		
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16	-6.25± 6.46	-5.00	-21.00~ 1.00	0.0015	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	16	-6.25± 6.46	-5.00	-21.00~ 1.00	0.0015	
Hormones	15	-7.00± 5.96	-9.00	-19.00~ 0.00	0.0005	
Corticosteroid Hormones	11	-6.45± 6.35	-5.00	-19.00~ 0.00	0.0071	
Oestrogens & Progesterones & Related Synthetic Drugs	3	-7.67± 6.11	-9.00	-13.00~ -1.00	0.1618	
Other Drugs Affecting Hormonal Regulation	1	-11.00	-11.00	-11.00~ -11.00		
Trophic Hormones & Related Synthetic Drugs	1	-12.00	-12.00	-12.00~ -12.00		
Nutrition	9	-7.89± 9.18	-7.00	-21.00~ 7.00	0.0328	
Parenteral Nutritional Products	5	-11.60± 9.42	-11.00	-21.00~ 0.00	0.0512	
Electrolytes	2	-1.50± 12.02	-1.50	-10.00~ 7.00	0.8888	
Appetite Enhancers	2	-12.00± 12.73	-12.00	-21.00~ -3.00	0.4097	
Enteral / Nutritional Products	1	-7.00	-7.00	-7.00~ -7.00		
Eye	9	-6.78± 6.22	-8.00	-18.00~ 1.00	0.0114	
Ophthalmic Lubricants	3	-5.00± 4.36	-7.00	-8.00~ 0.00	0.1853	
Eye Anti-infectives & Antiseptics	2	-4.00± 5.66	-4.00	-8.00~ 0.00	0.5000	
Eye Corticosteroids	2	-13.00± 7.07	-13.00	-18.00~ -8.00	0.2338	

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2	-9.00± 12.73	-9.00	-18.00~ 0.00	0.5000	
Other Eye Preparations	2	-4.50± 7.78	-4.50	-10.00~ 1.00	0.5635	
Antiglaucoma Preparations	1	-11.00	-11.00	-11.00~ -11.00		
Mydriatic Drugs	1	-8.00	-8.00	-8.00~ -8.00		
Dermatologicals	9	-7.00± 5.70	-7.00	-16.00~ 2.00	0.0062	
Topical Corticosteroids	4	-7.00± 6.38	-5.00	-16.00~ -2.00	0.1157	
Other Dermatologicals	2	-6.50± 2.12	-6.50	-8.00~ -5.00	0.1444	
Topical Antibiotics	2	-0.50± 3.54	-0.50	-3.00~ 2.00	0.8743	
Topical Antifungals & Antiparasites	1	-8.00	-8.00	-8.00~ -8.00		
Emollients & Skin Protectives	1	-2.00	-2.00	-2.00~ -2.00		
Psoriasis, Seborrhea & Ichthyosis Preparations	1	-2.00	-2.00	-2.00~ -2.00		
Skin Antiseptics & Disinfectants	1	-11.00	-11.00	-11.00~ -11.00		
Topical Anti-infectives with Corticosteroids	1	-13.00	-13.00	-13.00~ -13.00		
Ear & Mouth / Throat	1	-8.00	-8.00	-8.00~ -8.00		
Mouth / Throat Preparations	1	-8.00	-8.00	-8.00~ -8.00		
Miscellaneous	8	-1.25± 4.98	-0.50	-8.00~ 7.00	0.5006	
Miscellaneous	8	-1.25± 4.98	-0.50	-8.00~ 7.00	0.5006	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.
Dictionary: KIMS

E. Special population

Subjects of '65 or/and over' were classified into elderly group. When analyzing ICIQ score change before/after the study drug administration in elderly and non-elderly groups, the mean decrease of 5.88±6.50 was found in the group of '65 or/and over', which was statistically significant (p<0.0001). The mean decrease of 6.15±6.32 was found in the group of 'below 65 years', which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.6471) (Table 117).

When analyzing ICIQ score change before/after the study drug administration by renal impairment, the mean decrease of 0.50±3.70 was found in subjects with renal impairment, which was not statistically significant (p=0.8043). Subjects without renal impairment showed the mean decrease of 6.05±6.41, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.0847) (Table 117).

When analyzing ICIQ score change before/after the study drug administration by hepatic impairment, the mean decrease of 5.33±6.19 was found in subjects with hepatic impairment, which was not statistically significant (p=0.0884). Subjects without hepatic impairment showed the mean decrease of 6.01±6.42, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.7968) (Table 117).

Table 117. Effectiveness evaluation in the special population (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Elderly	below 65 years	223	-6.15± 6.32	-5.00	-21.00~ 7.00	<0.0001	0.6471
	65 or/and over	255	-5.88± 6.50	-5.00	-21.00~ 13.00	<0.0001	
Renal impairment	Yes	4	-0.50± 3.70	-0.50	-5.00~ 4.00	0.8043	0.0847
	No	474	-6.05± 6.41	-5.00	-21.00~ 13.00	<0.0001	
Hepatic impairment	Yes	6	-5.33± 6.19	-3.50	-16.00~ 0.00	0.0884	0.7968
	No	472	-6.01± 6.42	-5.00	-21.00~ 13.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

F. Information of the study drug administration

When analyzing ICIQ score change before/after the study drug administration by the number of injection sites and total injection dose, all subjects in the effectiveness population received total 100 U in 20 sites and their ICIQ score change before/after the study drug administration was the same as that of the effectiveness population (Table 118).

When analyzing ICIQ score change before/after the study drug administration by use of anesthesia at the study drug administration, the mean decrease of 4.50±6.30 was found in 'None' anesthesia group, which was statistically significant (p<0.0001). The mean decrease of 6.23±6.32 was found in 'Local', which was statistically significant (p<0.0001). The mean decrease of 6.08±6.64 was found in 'General', which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1963) (Table 118).

When analyzing the ICIQ score change by use of prophylactic antibiotics before, during, and after the study drug administration, the mean decrease of 6.06±6.41 was found in subjects with antibiotics, which was statistically significant (p<0.0001). Subjects without antibiotics showed the mean decrease of 5.52±6.52, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.5732) (Table 118).

Table 118. Effectiveness evaluation by the information of study drug administration (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Number of Injection Sites	20	478	-6.00± 6.41	-5.00	-21.00~ 13.00	<0.0001	
	30	0					
Total Units Injected	100	478	-6.00± 6.41	-5.00	-21.00~ 13.00	<0.0001	
	200	0					
Anesthesia	None	52	-4.50± 6.30	-2.00	-18.00~ 9.00	<0.0001	0.1963
	Local	302	-6.23± 6.32	-6.00	-21.00~ 13.00	<0.0001	
	General	124	-6.08± 6.64	-4.00	-21.00~ 7.00	<0.0001	
Prophylactic Antibiotic Use	Yes	428	-6.06± 6.41	-5.00	-21.00~ 13.00	<0.0001	0.5732
	No	50	-5.52± 6.52	-4.00	-21.00~ 8.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.

		n	mean± std	median	min~ max	p-value (a)	p-value (b)

The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

G. Clean intermittent catheterization

When analyzing ICIQ score change before/after the study drug administration by use of clean intermittent catheterization before the study drug administration, the mean decrease of 5.43±6.50 was found in subjects with clean intermittent catheterization, which was statistically significant (p<0.0001). Subjects without clean intermittent catheterization showed the mean decrease of 6.16±6.39, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.3030) (Table 119).

When analyzing ICIQ score change before/after the study drug administration by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, the mean decrease of 6.22±6.45 was found in subjects with urinary catheterization, which was statistically significant (p<0.0001). Subjects without urinary catheterization showed the mean decrease of 6.14±6.38, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.9193). Among the subjects with urinary catheterization, the mean decrease of 8.36±6.51 was found in subjects who initiated catheterization due to urinary retention (p=0.0003) and the mean decrease of 5.84±6.38 was found in subjects who initiated catheterization due to other reason (p<0.0001) (Table 119).

Table 119. Effectiveness evaluation by use of clean intermittent catheterization (Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Routine Urinary Catheterization(before BOTOX)	Yes	103	-±5.436.50	-4.00	-21.00~ 8.00	<0.0001	0.3030
	No	375	-±6.166.39	-5.00	-21.00~13.00	<0.0001	
Initiation of CIC after BOTOX injection§	Yes	101	-±6.226.45	-5.00	-20.00~13.00	<0.0001	0.9193**
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	14	-±8.366.51	-9.00	-18.00~ 0.00	0.0003	
	initiated CIC due to "Other Reason"	88	-±5.846.38	-4.00	-20.00~13.00	<0.0001	
	No	274	-±6.146.38	-5.00	-21.00~ 9.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
**The p-value is about that relation between Yes/No and the amount of ICIQ Score Change.
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

H. Factors that may affect effectiveness

For the effectiveness evaluation in this PMS, analysis was conducted by age, sex, treatment setting, pregnancy status, symptoms, past treatment history, medical history, concomitant medications, and the information of the study drug administration as well as in special population such as the elderly and subjects with renal or hepatic impairment.

The analysis results showed statistically significant difference in effectiveness rate by sex (p=0.0090).

When analyzing ICIQ score change before/after the study drug administration by sex, 'males' showed the mean decrease of 4.58±5.83and 'females' showed the mean decrease of 6.42±6.52, and both were statistically significant (each p<0.0001). Although the difference in ICIQ score change between the groups was statistically significant (p=0.0090), its relevance is unclear since both groups showed a statistically significant reduction in ICIQ score.

Ⅳ. Discussion on Results and Further Measures (Overactive Bladder)

4. Discussion on Results and Further Measures (Overactive Bladder)

During the re-examination period, CRFs were collected from a total of 564 subjects. Among the subjects whose CRFs were retrieved, a total of 525 subjects were included in the safety evaluation except 28 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 2 subjects of follow-up failure, and 9 subjects who violate the dosage (ie, subject received an unapproved dosage). Among the safety population, 478 subjects were included in the effectiveness evaluation, except 47 subjects whose ICIQ Scores at the baseline or follow-up on the CRF are not recorded.

During the study period, 51 AEs occurred in 40 out of 525 subjects in the safety population, which indicated that incidence of AEs was 7.62%. Examining the AEs by PT, 'URINARY RETENTION' occurred in 1.52% (8/525 subjects), followed by 'DYSURIA' in 0.57% (3/525 subjects) and 'HAEMATURIA', 'URODYNIA' ', 'NAUSEA', 'INFECTION', 'CYSTITIS', and 'DIZZINESS' each in 0.38% (2/525 subjects). Among them, 20 events occurred in 17 subjects (3.24%) were ADRs which cannot rule out the relationship to the study drug. Examining the ADRs by PT, 'URINARY RETENTION' occurred in 1.52% (8/525 subjects), followed by 'DYSURIA' in 0.57% (3/525 subjects) and others in 0.19% (1/525 subjects).

During the PMS period, 21 cases of unexpected AE were reported from 18 subjects in the safety population (3.43%). Examining the unexpected AEs by PT, 'URINARY HESITATION' and others occurred in 0.19% (1/525 subjects) each. Among them, 2 events occurred in 2 subjects (0.38%) were unexpected ADRs which cannot rule out the relationship to the study drug. Examining the unexpected ADRs by PT, 'URINARY HESITATION' and 'PERINEAL PAIN MALE' occurred in 0.19% (1/525 subjects) each.

During the study period, 9 SAEs were reported from 8 subjects (1.52%) in the safety population. Examining the SAEs by PT, 'ANAL PAIN', 'CYSTITIS', 'PYELONEPHRITIS', 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', 'ARTHRALGIA', 'ARTHRITIS', 'HYPONATRAEMIA', and 'ALCOHOL PROBLEM' occurred in 0.19% (1/525 subjects) each. Among them, 1 event of 'PYELONEPHRITIS' occurred in 1 subject (0.19%), and it was ADR which cannot rule out the relationship to the study drug.

When classifying and evaluating the expectedness of AEs, 'Expected AE' accounted for 58.82% (30/51 events) and 'Unexpected AE' accounted for 41.18% (21/51 events).

When classifying and evaluating the seriousness of AEs into 'Yes' and 'No', 'No' accounted for 82.35% (42/51 events) and 'Yes' accounted for 17.65% (9/51 events).

When classifying and evaluating the severity of AEs, 'Mild' occurred in 62.75% (32/3 events), 'Moderate' in 37.25% (19/3 event) and none were severe.

When classifying and evaluating the outcome of AEs, 'Resolved' was reported in 58.82% (30/51 events), followed by 'Ongoing' in 37.25% (19/51 events) and 'Resolved without sequelae' in 3.92% (2/51 events). No fatal outcome has been reported.

When classifying and evaluating the causal relationship of AEs to the study drug, 'Unlikely' was reported in 60.78% (31/51 events), followed by 'Possible' in 17.65% (9/51 events), 'Certain' and 'Probable/Likely' in 9.80% (5/51 events) each, and 'Conditional/Unclassified' in 1.91% (1/51 event).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure, 'Unlikely' was reported in 72.55% (37/51 events), 'Possible' in 13.73% (7/51 events), 'Probable/Likely' 9.80% (5/51 events), and 'Certain' and 'Conditional/Unclassified' was reported in 1.96% (1/51 events) each.

When comparing and analyzing the ICIQ score charge in 478 subjects of the effectiveness population, the mean score decreased by 6.00±6.41 from 12.20±6.56 before the study drug administration to 6.19±6.27 after the study drug administration. The mean change in ICIQ from baseline was statistically significant ($p<0.0001$).

In conclusion, the PMS study results showed no specific trend comparing to previously reported AE incidence and no specific matter that may affect the safety and effectiveness. There were no AEs due to distant spread of toxin. Therefore, we will continuously monitor the use of BOTOX through routine pharmacovigilence activities.

C. Neurogenic Detrusor Overactivity and Overactive Bladder

Ⅰ. General Matters of Investigation (Neurogenic Detrusor Overactivity and Overactive Bladder)

1. General Matters of Investigation (Neurogenic Detrusor Overactivity and Overactive Bladder)

1.1 Re-examination period (Neurogenic Detrusor Overactivity and Overactive Bladder)

31 Aug 2012 ~ 30 Aug 2016

1.2 Number of subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

During this re-examination period, CRFs were collected from a total of 739 subjects. Among the subjects whose CRFs were retrieved, a total of 686 subjects were included in the safety evaluation except 35 subjects who didn't receive Botox for this study due to consent withdrawal or other reasons, 2 subjects lost to follow-up, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescibed Information), and 10 subjects who violate the dosage (ie, subjects received an unapproved). Among the safety population, 612 subjects were included in the effectiveness evaluation, except 74 subjects whose record ICIQ Score at baseline or follow-up on the CRF are not completed.

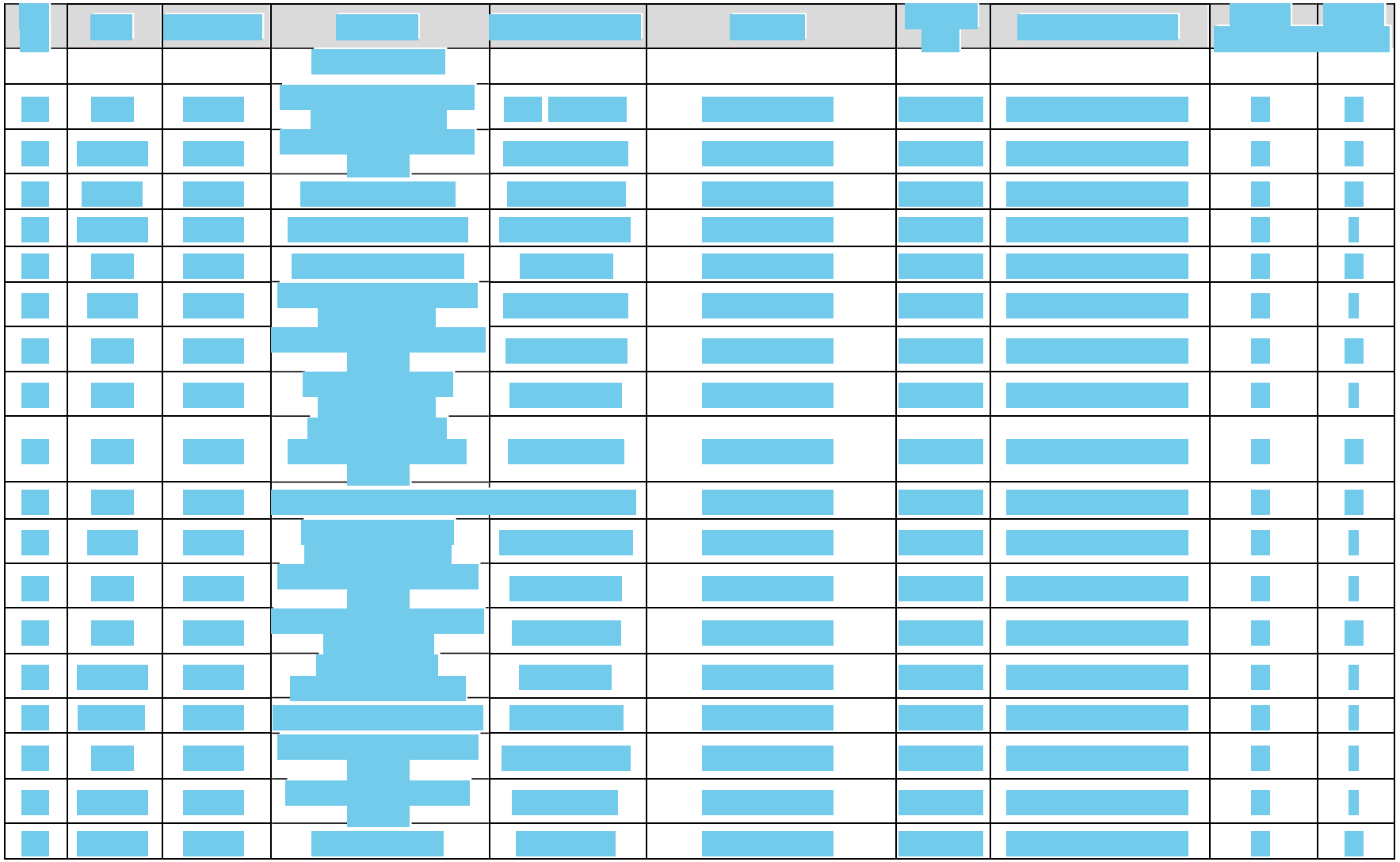
Number of subjects whose CRFs were retrieved	739
Number of subjects included in safety evaluation	686
Number of subjects included in effectiveness evaluation	612

Number of sites	From 31 Aug 2012 to 30 Aug 2016, CRFs were collected from 739 subjects by 45 investigators in 43 hospitals.
Method of investigation	This PMS was done in a manner that subjects who received Botox Inj. following the signed date were asked to successively participate in the PMS, up to the requested number of subjects, and it was pooled with post-marketing clinical tiral (Phase 4) data for analysis.
CRF format	Appendix 2
Point to be investigated with priority	There was no specific focus in this surveillance since no specific issues had been identified in clinical study results during the development phase as well as in post-marketing experiences in other countries. During this re-examination period, very rarely occurring AEs and unexpected AEs of which causal relationship to the study drug had not been established were to be monitored and

	investigated with particular interest.

1.3 PMS management chart (Neurogenic Detrusor Overactivity and Overactive Bladder)

Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled
[redacted]									



Site No.	Area	Department	Site Name	Investigator Name	Case No.	Contract Date	Surveillance Period	Subject Contracted	Subject Enrolled
[redacted]									
Total								1,210	739

* CRFs of subjects in the sites were collected through post-marketing clinical trial (Phase 4).

Ⅱ. Overview of PMS Results (Neurogenic Detrusor Overactivity and Overactive Bladder)

2. Overview of PMS Results (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.1 Overview and purpose of PMS (Neurogenic Detrusor Overactivity and Overactive Bladder)

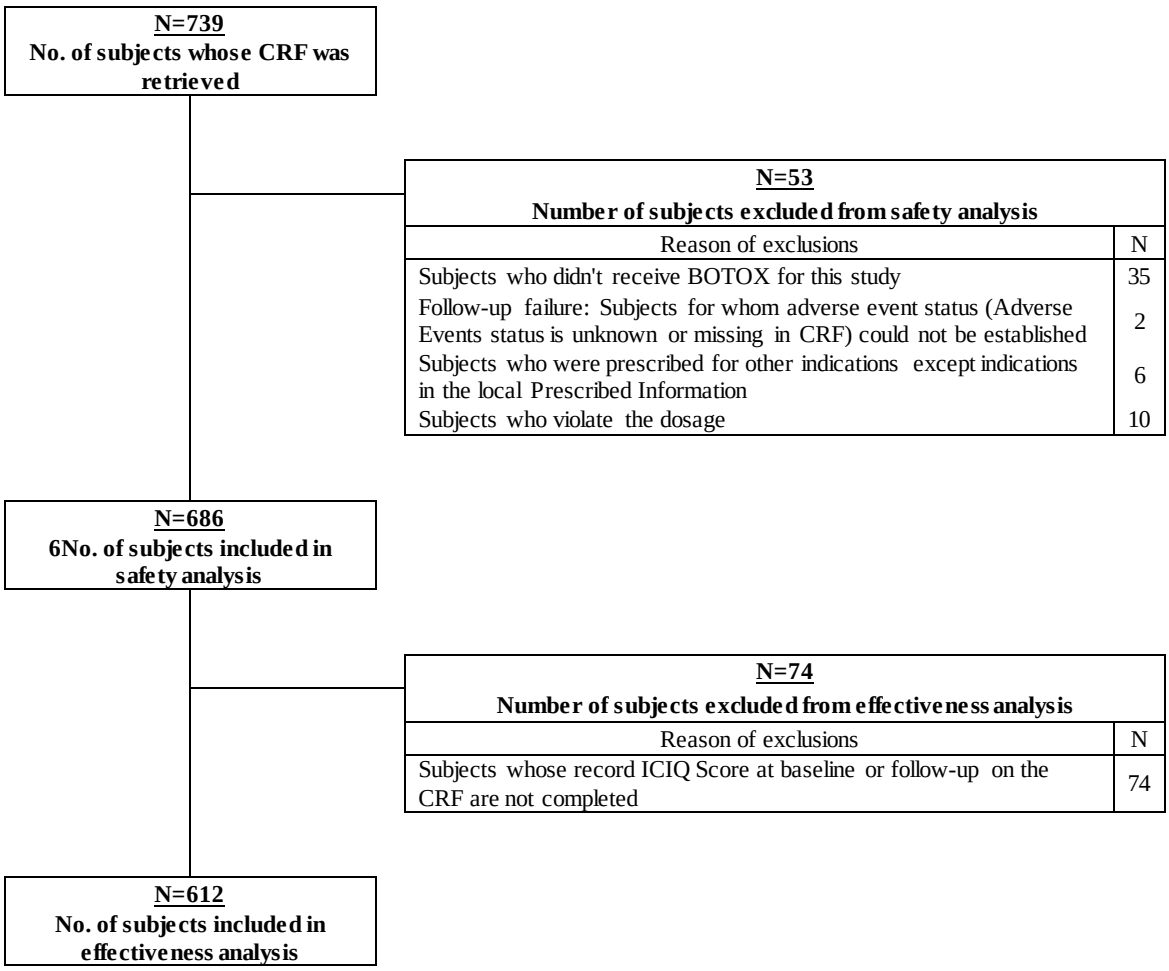
This PMS was conducted to examine whether AEs and SAEs occurred, frequency of AEs and the variations, and factors likely to influence the safety and effectiveness under the post-marketing uses of BOTOX in subjects of 'Treatment of urinary incontinence caused by Neurogenic Detrusor Overactivity (e.g. spinal cord injury, multiple sclerosis) in adults aged 18 years or over who have an inadequate response to or are intolerant of an anticholinergic therapy' and in subjects of 'Treatment of Overactive Bladder with urge urinary incontinence, urgency, and frequency in adults aged 18 years or over who have an inadequate response to or are intolerant of an anticholinergic therapy (hereafter 'Neurogenic Detrusor Overactivity and Overactive Bladder')' who received Botox Inj. (hereafter the 'study drug').

This PMS investigated subjects' fundamental demographic data, follow-up duration, past treatment history, medical history, special population, information of study drug administration, use of clean intermittent catheterization, safety, and effectiveness. This PMS was planned to investigate all types of AEs, which were incurred during the investigation period including AEs whose causal relationship to BOTOX Inj. has not been established yet and unexpected AEs/ADRs. The purpose of this study was to evaluate the safety and effectiveness of BOTOX for the treatment of NDO or OAB through active surveillance under routine clinical practice after the launch of BOTOX in Korea.□

2.2 Analysis set of PMS (Neurogenic Detrusor Overactivity and Overactive Bladder)

During this PMS, CRFs were collected from 739 subjects. Among the subjects, 686 subjects were included in the safety evaluation except 35 subjects who didn’t received Botox for this study due to consent withdrawal or other reasons, 2 subjects of follow-up failure, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescibed Information), and 10 subjects who violate the dosage (ie, subjects received an unapproved dosage). Among the safety population, 612 subjects were included in the effectiveness evaluation, except 74 subjects whose record ICIQ Score at baseline or follow-up on the CRF are not completed (Figure 3).

Figure 3. Analysis set of PMS (Neurogenic Detrusor Overactivity and Overactive Bladder)



2.3 Fundamental demographic data of subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.3.1 All subjects

Of 739 subjects with CRFs collected, age information was identified from 737 subejects and the mean age was 60.00±15.16 years, ranged from 18 to 89 years of age. The largest subject age group was '≥ 70 years' in 31.75% (234/737 subjects), followed by '< 50 years' in 23.61% (174/737 subjects), '≥ 60 years to < 70 years' in 22.93% (169/737 subjects), and '≥ 50 years to < 60 years' in 21.71% (160/737 subjects) (Table 120).

In all subjects, 'Male' accounted for 33.51% (247/737 subjects) and 'Female' accounted for 66.49% (490/737 subjects) (Table 120).

In all subjects, the mean height was 159.94±9.19 cm, ranged from 133.00 to 185.00 cm (Table 120).

In all subjects, the mean body weight was 61.50±10.53 kg, ranged from 32.50 to 100.00 kg (Table 120).

When classifying all subjects by treatment setting, 'Outpatient' was 46.54% (343/737 subjects) and 'Inpatient' was 53.46% (394/737 subjects) (Table 120).

Indications that the subjects were diagnosed with included 'Neurogenic Detrusor Overactivity' in 23.47% (173/737 subjects) and 'Overactive Bladder' in 76.53% (564/737 subjects) (Table 120).

The mean duration after diagnosed with 'Neurogenic Detrusor Overactivity (NDO)' in all subjects was 11.16±10.86 years and the most common underlying neurologic condition (multiple counting allowed) was 'Spinal Cord Injury' in 92.49% (160/173 subjects), followed by 'Other' in 4.62% (8/173 subjects) and 'Multiple Sclerosis' in 3.47% (6/173 subjects). Underlying conditions belonging to 'Other' included 'Cerebral infarction' and 'Stroke' (Table 120).

The mean duration after diagnosed with 'Overactive Bladder (OAB)' in all subjects was 4.82±5.27 years and the most common symptom (multiple counting allowed) was 'Frequency' in 72.52% (409/564 subjects), followed by 'Urge urinary incontinence' in 70.74% (399/564 subjects), 'Urgency' in 66.49% (375/564 subjects), and 'Other' in 17.73% (100/564 subjects). Symptoms belonging to 'Other' included 'Nocturia' and 'Stress urinary incontinence' (Table 120).

Among female subjects, there was no pregnant subject (Table 120).

Table 120. Demographic data in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Age	mean±std (years)	60.00± 15.16
	median	61.00
	min ~ max	18.00~ 89.00
	< 50 years	174(23.61)
	≥ 50 years to < 60 years	160(21.71)
	≥ 60 years to < 70 years	169(22.93)
	≥ 70 years	234(31.75)
	Total	737(100.00)
Sex	Male	247(33.51)
	Female	490(66.49)
	Total	737(100.00)
Height	n	730
	mean±std (cm)	159.94± 9.19
	median	159.70
	min ~ max	133.00~185.00
Weight	n	732
	mean±std (kg)	61.50± 10.53
	median	61.00
	min ~ max	32.50~ 100.00
Treatment Setting	Outpatient	343(46.54)
	Inpatient	394(53.46)
	Total	737(100.00)
Currently pregnant	Yes	0(0.00)
* for female	No	490(100.00)

		Total n(%)
	Total	490(100.00)
Diagnosis	NDO	173(23.47)
	OAB	564(76.53)
	Total	737(100.00)
Duration since NDO diagnosis	n	173
	mean±std (years)	11.16± 10.86
	median	7.00
	min ~ max	0.00~ 73.00
Duration since OAB diagnosis	n	542
	mean±std (years)	4.82± 5.27
	median	3.00
	min ~ max	0.00~ 40.00
Underlying neurologic condition§	Multiple Sclerosis	6(3.47)
* for patients with NDO	Spinal Cord Injury	160(92.49)
Overlapped¶	Other	8(4.62)
	Total	173(100.00)
Symptoms	Urge urinary incontinence	399(70.74)
* for patients with OAB	Urgency	375(66.49)
Overlapped¶	Frequency	409(72.52)
	Other	100(17.73)
	Total	564(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).
Missing: 2 (Age), 2 (Sex), 2 (Height), 2 (Weight), 2 (Treatment Setting), 2 (Diagnosis), 2 (Duration since OAB diagnosis)
Unkown: 7 (Height), 5 (Weight), 22 (Duration since OAB diagnosis)

2.3.2 Safety population

Of 686 subjects in the safety population, the mean age was 59.95±15.21 years, ranged from 18 to 89 years of age. The largest subject age group was '≥ 70 years' in 31.92% (219/686 subjects), followed by '< 50 years' in 23.62% (162/686 subjects), '≥ 60 years to < 70 years' in 22.74% (156/686 subjects), and '≥ 50 years to < 60 years' in 21.72% (149/686 subjects) (Table 121).

In the safety population, 'Male' accounted for 34.40% (236/686 subjects) and 'Female' accounted for 65.60% (450/686 subjects) (Table 121).

In the safety population, the mean height was 160.00±9.25 cm, ranged from 133.00 to 185.00 cm (Table 121).

In the safety population, the mean body weight was 61.48±10.52 kg, ranged from 32.50 to 100.00 kg (Table 121).

When classifying the safety population by treatment setting, 'Outpatient' was 47.81% (328/686 subjects) and 'Inpatient' was 52.19% (358/686 subjects) (Table 121).

Indications that the subjects were diagnosed with included 'NDO' in 23.47% (161/686 subjects) and 'OAB' in 76.53% (525/686 subjects) (Table 121).

The mean duration after diagnosed with NDO in the safety population was 11.32±10.91 years and the most common underlying neurologic condition (multiple counting allowed) was 'Spinal Cord Injury' in 96.89% (156/161 subjects), followed by 'Multiple Sclerosis' in 3.11% (5/161 subjects) and 'Others' in 0.62% (1/161 subjects) (Table 121).

The mean duration after diagnosed with OAB in the safety population was 4.84±5.35 years and the most common symptom (multiple counting allowed) was 'Frequency' in 73.33% (385/525 subjects), followed by 'Urge urinary incontinence' in 71.62% (376/525 subjects), 'Urgency' in 66.29% (348/525 subjects), and 'Other' in 18.86% (99/525 subjects) (Table 121).

Among female subjects, there was no pregnant subject (Table 121).

Table 121. Demographic data in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Age	mean±std (years)	59.95± 15.21
	median	61.00
	min ~ max	18.00~ 89.00
	< 50 years	162(23.62)
	≥ 50 years to < 60 years	149(21.72)
	≥ 60 years to < 70 years	156(22.74)
	≥ 70 years	219(31.92)
	Total	686(100.00)
Sex	Male	236(34.40)
	Female	450(65.60)
	Total	686(100.00)
Height	n	683
	mean±std (cm)	160.00± 9.25
	median	159.80
	min ~ max	133.00~ 185.00
Weight	n	685
	mean±std (kg)	61.48± 10.52
	median	61.00
	min ~ max	32.50~ 100.00
Treatment Setting	Outpatient	328(47.81)
	Inpatient	358(52.19)
	Total	686(100.00)
Currently pregnant * for female	Yes	0(0.00)
	No	450(100.00)
	Total	450(100.00)
Diagnosis	NDO	161(23.47)
	OAB	525(76.53)
	Total	686(100.00)
Duration since NDO diagnosis	n	161
	mean±std (years)	11.32± 10.91
	median	7.00
	min ~ max	0.00~ 73.00
Duration since OAB diagnosis	n	505
	mean±std (years)	4.84± 5.35
	median	3.00

		Total n(%)
	min ~ max	0.00~ 40.00
Underlying neurologic condition§	Multiple Sclerosis	5(3.11)
* for patients with NDO	Spinal Cord Injury	156(96.89)
Overlapped¶	Other	1(0.62)
	Total	161(100.00)
Symptoms	Urge urinary incontinence	376(71.62)
* for patients with OAB	Urgency	348(66.29)
Overlapped¶	Frequency	385(73.33)
	Other	99(18.86)
	Total	525(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).
Unkown: 3 (Height), 1 (Weight), 20 (Duration since OAB diagnosis)

51 subjects were excluded in the safety evaluation for the following reasons: 35 subjects who didn't received Botox for this study due to consent withdrawal or other reasons, 2 subjects of follow-up failure, 6 subjects who were prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescibed Information), and 10 subjects who violate the dosage (ie, subjects received an unapproved dosage).

2.4 Follow-up duration (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.4.1 All subjects

During the PMS period, the mean follow-up duration in all subjects was 59.88±36.72 days (Table 122).

Table 122. Follow-up duration in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total (N=739)
n	702
mean±std (days)	59.88± 36.72
median	49.00
min ~ max	17.00~ 485.00

Length of follow-up = Date of follow-up - Date of initial visit + 1
Missing: 37

2.4.2 Safety population

During the PMS period, the mean follow-up duration in the safety population was 60.05±37.00 days (Table 123).

Table 123. Follow-up duration in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total (N=686)
n	686
mean±std (days)	60.05± 37.00
median	49.00
min ~ max	17.00~ 485.00

Length of follow-up = Date of follow-up - Date of initial visit + 1

2.5 Past treatment history (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.5.1 All subjects

In all subjects, 98.19% (706/719 subjects) had received anticholinergic therapy. In subjects diagnosed with 'OAB', 56.02% (307/548 subjects) had used other OAB drugs after anticholinergic therapy (Table 124).

Proportion of subjects who had received sacral neuromodulation therapy was 1.67% (12/720 subjects) and proportion of subjects who had used the study drug or other botulinum toxin was 5.00% (36/720 subjects) (Table 124).

Table 124. Past treatment history in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Previous Anticholinergic Therapy	Yes	706(98.19)
	No	13(1.81)
	Total	719(100.00)
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	307(56.02)
	No	241(43.98)
	Total	548(100.00)
Previous Use of Sacral Neuromodulation Therapy	Yes	12(1.67)
	No	708(98.33)
	Total	720(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	36(5.00)
	None	684(95.00)
	Total	720(100.00)

The denominator is number of total subjects.
Missing: 20 (Previous Anticholinergic Therapy), 16 (Another OAB drug also used after anticholinergic therapy), 19 (Previous Use of Sacral Neuromodulation Therapy), 19 (Previous BOTOX or Other Botulinum Toxin Treatment)

2.5.2 Safety population

In the safety population, 98.40% (675/686 subjects) had received anticholinergic therapy. In subjects diagnosed with OAB, 56.00% (294/525 subjects) had used other OAB drugs after anticholinergic therapy (Table 125).

Proportion of subjects who had received sacral neuromodulation therapy was 1.46% (10/686 subjects) and proportion of subjects who had used the study drug or other botulinum toxin was 4.66% (32/686 subjects) (Table 125).

Table 125. Past treatment history in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Previous Anticholinergic Therapy	Yes	675(98.40)
	No	11(1.60)
	Total	686(100.00)
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	294(56.00)
	No	231(44.00)
	Total	525(100.00)
Previous Use of Sacral Neuromodulation Therapy	Yes	10(1.46)
	No	676(98.54)
	Total	686(100.00)
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	32(4.66)
	None	654(95.34)
	Total	686(100.00)

The denominator is number of total subjects.

2.6 Medical history (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.6.1 All subjects

In all subjects, 83.15% (597/718 subjects) had medical history including surgeries and complications of underlying diseases (Table 126).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 51.42% (307/597 subjects), followed by 'Factors influencing health status and contact with health services' in 42.38% (253/597 subjects) and 'Endocrine, nutritional and metabolic diseases' in 34.84% (208/597 subjects) (Table 126).

In total, 5.16% (38/737 subjects) of subjects had allergy history (Table 126).

When analyzing the type of allergy history by allowing multiple counting, 'Factors influencing health status and contact with health services' accounted for 52.63% (20/38 subjects), followed by 'Injury, poisoning and certain other consequences of external causes' in 47.37% (18/38 subjects) and allergens included 'contrast media' and 'levofloxacin' (Table 126).

Table 126. Medical history in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	597(83.15)
	None	121(16.85)
	Total	718(100.00)
	Details for Medical History by dictionary (Overlapped¶)	
	Diseases of the circulatory system	307(51.42)
	Factors influencing health status and contact with health services	253(42.38)
	Endocrine, nutritional and metabolic diseases	208(34.84)
	Diseases of the genitourinary system	156(26.13)
	Diseases of the digestive system	146(24.46)
	Diseases of the musculoskeletal system and connective tissue	146(24.46)
	Neoplasms	107(17.92)
	Mental and behavioural disorders	105(17.59)
	Diseases of the nervous system	95(15.91)
	Diseases of the respiratory system	56(9.38)
	Diseases of the eye and adnexa	50(8.38)
	Injury, poisoning and certain other consequences of external causes	47(7.87)
	Certain infectious and parasitic diseases	39(6.53)
	Diseases of the skin and subcutaneous tissue	31(5.19)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	14(2.35)
	Diseases of the ear and mastoid process	11(1.84)
	Congenital malformations, deformations and chromosomal abnormalities	6(1.01)
	Pregnancy, childbirth and the puerperium	1(0.17)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	70(11.73)
History of Allergies	Yes	38(5.16)
	None	699(94.84)
	Total	737(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	20(52.63)
	Injury, poisoning and certain other consequences of external causes	18(47.37)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Missing: 17 (Medical History, Including Surgeries and Complications of Underlying Diseases), 2 (History of Allergies)
Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

2.6.2 Safety population

In the safety population, 83.14% (567/682 subjects) had medical history including surgeries and complications of underlying diseases (Table 127).

When analyzing the type of medical history by allowing multiple counting, the most common medical history was 'Diseases of the circulatory system' in 50.97% (289/567 subjects), followed by 'Factors influencing health status and contact with health services' in 42.15% (239/567

subjects) and 'Endocrine, nutritional and metabolic diseases' in 34.39% (195/567 subjects) (Table 127).

In total, 5.25% (36/686 subjects) of subjects had allergy history (Table 127).

When analyzing the type of allergy history, 'Factors influencing health status and contact with health services' and 'Injury, poisoning and certain other consequences of external causes' accounted for 50.00% (18/36 subjects) each (Table 127).

Table 127. Medical history in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	567(83.14)
	None	115(16.86)
	Total	682(100.00)
	Details for Medical History by dictionary (Overlapped¶)	
	Diseases of the circulatory system	289(50.97)
	Factors influencing health status and contact with health services	239(42.15)
	Endocrine, nutritional and metabolic diseases	195(34.39)
	Diseases of the genitourinary system	145(25.57)
	Diseases of the digestive system	141(24.87)
	Diseases of the musculoskeletal system and connective tissue	136(23.99)
	Neoplasms	100(17.64)
	Mental and behavioural disorders	99(17.46)
	Diseases of the nervous system	91(16.05)
	Diseases of the respiratory system	55(9.70)
	Diseases of the eye and adnexa	42(7.41)
	Injury, poisoning and certain other consequences of external causes	46(8.11)
	Certain infectious and parasitic diseases	37(6.53)
	Diseases of the skin and subcutaneous tissue	30(5.29)
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	14(2.47)
	Diseases of the ear and mastoid process	11(1.94)
	Congenital malformations, deformations and chromosomal abnormalities	5(0.88)
	Pregnancy, childbirth and the puerperium	1(0.18)
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	66(11.64)
History of Allergies	Yes	36(5.25)
	None	650(94.75)
	Total	686(100.00)
	Details for History of Allergies by dictionary	
	Factors influencing health status and contact with health services	18(50.00)
	Injury, poisoning and certain other consequences of external causes	18(50.00)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

2.7 Concomitant medication (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.7.1 All subjects

Subjects who received concomitant medications accounted for 94.14% (675/717 subjects) (Table 128).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 87.70% (592/675 subjects), followed by 'Central Nervous System' in 69.63% (470/675 subjects) and 'Gastrointestinal & Hepatobiliary System' in 58.37% (394/675 subjects) (Table 128).

Table 128. Concomitant medications in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total n(%)
Yes	675(94.14)
No	42(5.86)
Total	717(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	592(87.70)
Anaesthetics - Local & General	592(87.70)
Central Nervous System	470(69.63)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	214(31.70)
Analgesics (Non-Opioid) & Antipyretics	180(26.67)
Analgesics (Opioid)	118(17.48)
Hypnotics & Sedatives	85(12.59)
Antidepressants	84(12.44)
Drugs For Neuropathic Pain	64(9.48)
Anxiolytics	55(8.15)
Anticonvulsants	53(7.85)
Nootropics & Neurotonics	35(5.19)
Neurodegenerative Disease Drugs	25(3.70)
Antiparkinsonian Drugs	19(2.81)
Antipsychotics	15(2.22)
Antivertigo Drugs	5(0.74)
Antimigraine Preparations	2(0.30)
Other CNS Drugs & Agents for ADHD	1(0.15)
Gastrointestinal & Hepatobiliary System	394(58.37)
Antacids, Antireflux Agents & Antiulcerants	254(37.63)
GIT Regulators, Antiflatulents & Anti-inflammatories	132(19.56)
Digestives	92(13.63)
Laxatives, Purgatives	84(12.44)
Antiemetics	36(5.33)
Antispasmodics	28(4.15)
Antidiarrheals	12(1.78)
Cholagogues, Cholelitholytics & Hepatic Protectors	10(1.48)
Other Gastrointestinal Agents	1(0.15)
Miscellaneous	4(0.59)
Cardiovascular & Hematopoietic System	272(40.30)

	Total n(%)
Dyslipidaemic Agents	99(14.67)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	96(14.22)
Calcium Antagonists	73(10.81)
Angiotensin II Antagonists	60(8.89)
Other Antihypertensives	43(6.37)
Haemostatics	38(5.63)
Beta-Blockers	37(5.48)
Peripheral Vasodilators & Cerebral Activators	24(3.56)
Diuretics	17(2.52)
Anti-Anginal Drugs	16(2.37)
Other Cardiovascular Drugs	13(1.93)
Vasoconstrictors	10(1.48)
Cardiac Drugs	6(0.89)
Phlebitis & Varicose Preparations	4(0.59)
Antidiuretics	3(0.44)
Haematopoietic Agents	2(0.30)
ACE Inhibitors/Direct Renin Inhibitors	1(0.15)
Miscellaneous	7(1.04)
Musculo-Skeletal System	115(17.04)
Muscle Relaxants	75(11.11)
Neuromuscular Disorder Drugs	38(5.63)
Other Drugs Acting on the Musculo-Skeletal System	19(2.81)
Anti-Inflammatory Enzymes	13(1.93)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	5(0.74)
Hyperuricemia & Gout Preparations	1(0.15)
Endocrine & Metabolic System	113(16.74)
Antidiabetic Agents	77(11.41)
Other Agents Affecting Metabolism	23(3.41)
Thyroid Hormones	13(1.93)
Agents Affecting Bone Metabolism	10(1.48)
Insulin Preparations	6(0.89)
Antithyroid Agents	1(0.15)
Miscellaneous	1(0.15)
Intravenous & Other Sterile Solutions	90(13.33)
Intravenous & other sterile solutions	90(13.33)
Genito-Urinary System	85(12.59)
Drugs for Bladder & Prostate Disorders	82(12.15)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	6(0.89)
Other Drugs Acting on the Genito-Urinary System	1(0.15)
Respiratory System	60(8.89)
Antiasthmatic & COPD Preparations	38(5.63)
Cough & Cold Preparations	34(5.04)
Nasal Decongestant & Other Nasal Preparations	5(0.74)
Oncology	57(8.44)
Supportive Care Therapy	50(7.41)
Hormonal Chemotherapy	5(0.74)
Cytotoxic Chemotherapy	2(0.30)
Vitamins & Minerals	53(7.85)
Calcium / with Vitamins	30(4.44)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	11(1.63)
Vitamin B-complex / with C	10(1.48)
Vitamins &/or Minerals	8(1.19)

	Total n(%)
Vitamin C	1(0.15)
Vitamins & Minerals (Geriatric)	1(0.15)
Vitamins A, D & E	1(0.15)
Miscellaneous	1(0.15)
Anti-infectives (systemic)	32(4.74)
Cephalosporins	14(2.07)
Quinolones	9(1.33)
Antivirals	6(0.89)
Antifungals	5(0.74)
Antiamoebics	2(0.30)
Macrolides	2(0.30)
Aminoglycosides	1(0.15)
Anti-TB Agents	1(0.15)
Antibacterial Combinations	1(0.15)
Other Antibiotics	1(0.15)
Tetracyclines	1(0.15)
Allergy & Immune System	28(4.15)
Antihistamines & Antiallergics	22(3.26)
Immunosuppressants	5(0.74)
Vaccines, Antisera & Immunologicals	1(0.15)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	23(3.41)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	23(3.41)
Hormones	21(3.11)
Corticosteroid Hormones	15(2.22)
Oestrogens & Progesterones & Related Synthetic Drugs	4(0.59)
Other Drugs Affecting Hormonal Regulation	2(0.30)
Trophic Hormones & Related Synthetic Drugs	1(0.15)
Nutrition	20(2.96)
Parenteral Nutritional Products	14(2.07)
Electrolytes	8(1.19)
Appetite Enhancers	3(0.44)
Enteral / Nutritional Products	1(0.15)
Supplements & Adjuvant Therapy	1(0.15)
Eye	12(1.78)
Ophthalmic Lubricants	5(0.74)
Eye Anti-infectives & Antiseptics	3(0.44)
Eye Corticosteroids	2(0.30)
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2(0.30)
Other Eye Preparations	2(0.30)
Antiglaucoma Preparations	1(0.15)
Mydriatic Drugs	1(0.15)
Dermatologicals	11(1.63)
Topical Corticosteroids	5(0.74)
Other Dermatologicals	2(0.30)
Topical Antibiotics	2(0.30)
Topical Antifungals & Antiparasites	2(0.30)
Emollients & Skin Protectives	1(0.15)
Psoriasis, Seborrhea & Ichthyosis Preparations	1(0.15)
Skin Antiseptics & Disinfectants	1(0.15)
Topical Anti-infectives with Corticosteroids	1(0.15)
Ear & Mouth / Throat	1(0.15)
Mouth / Throat Preparations	1(0.15)

	Total n(%)
Miscellaneous	8(1.19)
Miscellaneous	8(1.19)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS
Missing: 22

2.7.2 Safety population

In the safety population, subjects who received concomitant medications accounted for 94.61% (649/686 subjects) (Table 129).

When analyzing the type of concomitant medications by allowing multiple counting, the most common concomitant medication was 'Anaesthetics - Local & General' in 88.75% (576/649 subjects), followed by 'Central Nervous System' in 69.95% (454/649 subjects) and 'Gastrointestinal & Hepatobiliary System' in 58.86% (382/649 subjects) (Table 129).

Table 129. Concomitant medication in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total n(%)
Yes	649(94.61)
None	37(5.39)
Total	686(100.00)
Details for Concomitant Medication by dictionary (Overlapped¶)	
Anaesthetics- Local & General	576(88.75)
Anaesthetics - Local & General	576(88.75)
Central Nervous System	454(69.95)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	205(31.59)
Analgesics (Non-Opioid) & Antipyretics	177(27.27)
Analgesics (Opioid)	116(17.87)
Hypnotics & Sedatives	83(12.79)
Antidepressants	80(12.33)
Drugs For Neuropathic Pain	63(9.71)
Anxiolytics	54(8.32)
Anticonvulsants	49(7.55)
Nootropics & Neurotonics	33(5.08)
Neurodegenerative Disease Drugs	22(3.39)
Antiparkinsonian Drugs	19(2.93)
Antipsychotics	14(2.16)
Antivertigo Drugs	5(0.77)
Antimigraine Preparations	2(0.31)
Other CNS Drugs & Agents for ADHD	1(0.15)
Gastrointestinal & Hepatobiliary System	382(58.86)
Antacids, Antireflux Agents & Antiulcerants	247(38.06)
GIT Regulators, Antiflatulents & Anti-inflammatories	132(20.34)
Digestives	89(13.71)

	Total n(%)
Laxatives, Purgatives	81(12.48)
Antiemetics	34(5.24)
Antispasmodics	26(4.01)
Antidiarrheals	12(1.85)
Cholagogues, Cholelitholytics & Hepatic Protectors	9(1.39)
Other Gastrointestinal Agents	1(0.15)
Miscellaneous	4(0.62)
Cardiovascular & Hematopoietic System	258(39.75)
Dyslipidaemic Agents	91(14.02)
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	89(13.71)
Calcium Antagonists	68(10.48)
Angiotensin II Antagonists	55(8.47)
Other Antihypertensives	40(6.16)
Haemostatics	38(5.86)
Beta-Blockers	36(5.55)
Peripheral Vasodilators & Cerebral Activators	23(3.54)
Diuretics	15(2.31)
Anti-Anginal Drugs	16(2.47)
Other Cardiovascular Drugs	13(2.00)
Vasoconstrictors	10(1.54)
Cardiac Drugs	6(0.92)
Phlebitis & Varicose Preparations	4(0.62)
Antidiuretics	3(0.46)
Haematopoietic Agents	2(0.31)
ACE Inhibitors/Direct Renin Inhibitors	1(0.15)
Miscellaneous	7(1.08)
Musculo-Skeletal System	110(16.95)
Muscle Relaxants	71(10.94)
Neuromuscular Disorder Drugs	37(5.70)
Other Drugs Acting on the Musculo-Skeletal System	18(2.77)
Anti-Inflammatory Enzymes	13(2.00)
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	5(0.77)
Hyperuricemia & Gout Preparations	1(0.15)
Endocrine & Metabolic System	108(16.64)
Antidiabetic Agents	74(11.40)
Other Agents Affecting Metabolism	21(3.24)
Thyroid Hormones	13(2.00)
Agents Affecting Bone Metabolism	10(1.54)
Insulin Preparations	5(0.77)
Antithyroid Agents	1(0.15)
Miscellaneous	1(0.15)
Intravenous & Other Sterile Solutions	88(13.56)
Intravenous & other sterile solutions	88(13.56)
Genito-Urinary System	82(12.63)
Drugs for Bladder & Prostate Disorders	79(12.17)
Drugs for Erectile Dysfunction and Ejaculatory Disorders	6(0.92)
Other Drugs Acting on the Genito-Urinary System	1(0.15)
Respiratory System	57(8.78)
Antiasthmatic & COPD Preparations	37(5.70)
Cough & Cold Preparations	32(4.93)
Nasal Decongestant & Other Nasal Preparations	5(0.77)
Oncology	53(8.17)

	Total n(%)
Supportive Care Therapy	47(7.24)
Hormonal Chemotherapy	4(0.62)
Cytotoxic Chemotherapy	2(0.31)
Vitamins & Minerals	48(7.40)
Calcium / with Vitamins	26(4.01)
Vitamins & Minerals (Pre & Post Natal) / Antianemics	11(1.69)
Vitamin B-complex / with C	9(1.39)
Vitamins &/or Minerals	8(1.23)
Vitamin C	1(0.15)
Vitamins & Minerals (Geriatric)	1(0.15)
Vitamins A, D & E	1(0.15)
Miscellaneous	1(0.15)
Anti-infectives (systemic)	31(4.78)
Cephalosporins	13(2.00)
Quinolones	9(1.39)
Antivirals	6(0.92)
Antifungals	5(0.77)
Antiamoebics	1(0.15)
Macrolides	2(0.31)
Aminoglycosides	1(0.15)
Anti-TB Agents	1(0.15)
Antibacterial Combinations	1(0.15)
Other Antibiotics	1(0.15)
Tetracyclines	1(0.15)
Allergy & Immune System	27(4.16)
Antihistamines & Antiallergics	22(3.39)
Immunosuppressants	4(0.62)
Vaccines, Antisera & Immunologicals	1(0.15)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	21(3.24)
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	21(3.24)
Hormones	19(2.93)
Corticosteroid Hormones	14(2.16)
Oestrogens & Progesterones & Related Synthetic Drugs	3(0.46)
Other Drugs Affecting Hormonal Regulation	2(0.31)
Trophic Hormones & Related Synthetic Drugs	1(0.15)
Nutrition	19(2.93)
Parenteral Nutritional Products	13(2.00)
Electrolytes	8(1.23)
Appetite Enhancers	3(0.46)
Enteral / Nutritional Products	1(0.15)
Supplements & Adjuvant Therapy	1(0.15)
Eye	12(1.85)
Ophthalmic Lubricants	5(0.77)
Eye Anti-infectives & Antiseptics	3(0.46)
Eye Corticosteroids	2(0.31)
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2(0.31)
Other Eye Preparations	2(0.31)
Antiglaucoma Preparations	1(0.15)
Mydriatic Drugs	1(0.15)
Dermatologicals	11(1.69)
Topical Corticosteroids	5(0.77)
Other Dermatologicals	2(0.31)

	Total n(%)
Topical Antibiotics	2(0.31)
Topical Antifungals & Antiparasites	2(0.31)
Emollients & Skin Protectives	1(0.15)
Psoriasis, Seborrhea & Ichthyosis Preparations	1(0.15)
Skin Antiseptics & Disinfectants	1(0.15)
Topical Anti-infectives with Corticosteroids	1(0.15)
Ear & Mouth / Throat	1(0.15)
Mouth / Throat Preparations	1(0.15)
Miscellaneous	8(1.23)
Miscellaneous	8(1.23)

The denominator for 'Yes/None' is number of total subjects.
The denominator for details is number of subjects in 'Yes'.
¶ The same subject may appear in different categories.
Dictionary: KIMS

2.8 Special population (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.8.1 All subjects

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 43.42% (320/737 subjects) were included in elderly group (Table 130).

In total, 1.22% (9/737 subjects) had renal impairment and the renal impairment included 'chronic kidney disease' and 'hydronephrosis' (Table 130).

In total, 1.63% (12/737 subjects) had hepatic impairment and the hepatic impairment included 'liver cirrhosis', 'fatty liver', and 'hepatitis B' (Table 130).

Table 130. Special population in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Elderly	below 65 years	417(56.58)
	65 or/and over	320(43.42)
	Total	737(100.00)
Renal impairment	Yes	9(1.22)
	No	728(98.78)
	Total	737(100.00)
Hepatic impairment	Yes	12(1.63)
	No	725(98.37)
	Total	737(100.00)

The denominator is number of total subjects.
Missing: 2

2.8.2 Safety population

During the PMS period, subjects of '65 or/and over' were classified into elderly group, and 43.59% (299/686 subjects) in the safety population were included in elderly group. Subjects with renal impairment accounted for 1.17% (8/686 subjects) and subjects with hepatic impairment accounted for 1.46% (10/686 subjects) (Table 131).

Table 131. Special population in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Elderly	below 65 years	387(56.41)
	65 or/and over	299(43.59)
	Total	686(100.00)
Renal impairment	Yes	8(1.17)
	No	678(98.83)
	Total	686(100.00)
Hepatic impairment	Yes	10(1.46)
	No	676(98.54)
	Total	686(100.00)

The denominator is number of total subjects.

2.9 Information of study drug administration (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.9.1 All subjects

When analyzing the number of injection sites of study drug in all subjects, 20 sites accounted for 75.00% (528/704 subjects), followed by 30 sites in 24.43% (172/704 subjects) and others in 0.57% (4/704 subjects) (Table 132).

When analyzing the total units injected, 100 U accounted for 75.14% (529/704 subjects), followed by 200 U in 24.72% (174/704 subjects) and 50 U in 0.14% (1/704 subjects) (Table 132).

When investigating anesthesia upon study drug administration, 'Local' accounted for 63.21% (445/704 subjects), 'General' 24.86% (175/704 subjects), and 'None' 11.93% (84/704 subjects) (Table 132).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 91.65% (648/707 subjects) (Table 132).

Table 132. Information of the study drug administration in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Number of Injection Sites	20	528(75.00)

		Total n(%)
	30	172(24.43)
	Other	4(0.57)
	Total	704(100.00)
Total Units Injected	50	1(0.14)
	100	529(75.14)
	200	174(24.72)
	Total	704(100.00)
Anesthesia	None	84(11.93)
	Local	445(63.21)
	General	175(24.86)
	Total	704(100.00)
Prophylactic Antibiotic Use	Yes	648(91.65)
	No	59(8.35)
	Total	707(100.00)

The denominator is number of total subjects.
Missing: 35 (Number of Injection Sites), 35 (Total Units Injected), 35 (Anesthesia), 32 (Prophylactic Antibiotic Use)

2.9.2 Safety population

All subjects diagnosed with NDO in the safety population received total 200 U in 30 sites, while all subjects diagnosed with OAB in the safety population received total 100 U in 20 sites. Thus, all subjects were determined to observe the dose/dosage for the applicable indications (Table 133).

When investigating anesthesia upon the study drug administration, 'Local' accounted for 63.41% (435/686 subjects), 'General' 24.49% (168/686 subjects), and 'None' 12.10% (83/686 subjects) (Table 133).

Subjects who used prophylactic antibiotics before, during, or after the study drug administration accounted for 91.98% (631/686 subjects) (Table 133).

Table 133. Information of study drug administration in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Number of Injection Sites	20	525(76.53)
	30	161(23.47)
	Total	686(100.00)
Total Units Injected	100	525(76.53)
	200	161(23.47)
	Total	686(100.00)
Anesthesia	None	83(12.10)
	Local	435(63.41)
	General	168(24.49)
	Total	686(100.00)
Prophylactic Antibiotic Use	Yes	631(91.98)
	No	55(8.02)

		Total n(%)
	Total	686(100.00)

The denominator is number of total subjects.

2.10 Clean intermittent catheterization (Neurogenic Detrusor Overactivity and Overactive Bladder)

2.10.1 All subjects

In all subjects, 36.50% (269/737 subjects) received clean intermittent catheterization before the study drug administration and 63.50% (468/737 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean PVR urine volume prior to BOTOX treatment was 34.58±54.91 mL (Table 134).

Among the subjects not performing clean intermittent catheterization beforethe study drug administration, 25.55% (116/454 subjects) received urinary catheterization after the study drug administration including 4.41% (20/454 subjects) who initiated catheterization due to urinary retention and 21.59% (98/454 subjects) who initiated catheterization due to other reason (Table 134).

Table 134. Clean intermittent catheterization in all subjects (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	269(36.50)
	No	468(63.50)
	Total	737(100.00)
Post-Void Residual Urine Volume(before BOTOX)*	n	448
* In subjects not performing CIC before BOTOX	mean±std (mL)	34.58± 54.91
	median	17.00
	min ~ max	0.00~ 430.00
Initiation of CIC after BOTOX injection§	Yes	116(25.55)
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	20(4.41)
	initiated CIC due to "Other Reason"	98(21.59)
	No	338(74.45)
	Total	454(100.00)

The denominator is number of total subjects.
Missing: 271(Post-Void Residual Urine Volume(before BOTOX)), 32(Catheterization after BOTOX injection)
Not Done: 5(Post-Void Residual Urine Volume(before BOTOX))
Unknown: 15(Post-Void Residual Urine Volume(before BOTOX))
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

2.10.2 Safety population

In the safety population, 36.44% (250/686 subjects) received clean intermittent catheterization before the study drug administration and 63.56% (436/686 subjects) did not. In the subjects not performing clean intermittent catheterization before the study drug administration, the mean PVR urine volume prior to BOTOX treatment was 33.96±52.73 mL (Table 135).

Among the subjects not performing clean intermittent catheterization before the study drug administration, 25.69% (112/436 subjects) received urinary catheterization after the study drug administration including 4.13% (18/436 subjects) who initiated catheterization due to urinary retention and 21.79% (95/436 subjects) who initiated catheterization due to other reason (Table 135).

Table 135. Clean intermittent catheterization in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Routine Urinary Catheterization(before BOTOX)	Yes	250(36.44)
	No	436(63.56)
	Total	686(100.00)
Post-Void Residual Urine Volume(before BOTOX)*	n	417
* In subjects not performing CIC before BOTOX	mean±std (mL)	33.96± 52.73
	median	17.00
	min ~ max	0.00~ 430.00
Initiation of CIC after BOTOX injection§	Yes	112(25.69)
§ In subjects not performing CIC before BOTOX	initiated CIC due to “Urinary Retention”	18(4.13)
	initiated CIC due to “Other Reason”	95(21.79)
	No	324(74.31)
	Total	436(100.00)

The denominator is number of total subjects.
Not Done: 5(Post-Void Residual Urine Volume(before BOTOX))
Unknown: 14(Post-Void Residual Urine Volume(before BOTOX))
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

Ⅲ. Results of PMS (Neurogenic Detrusor Overactivity and Overactive Bladder)

3. Results of PMS (Neurogenic Detrusor Overactivity and Overactive Bladder)

3.1 Incidence of Adverse Events (Neurogenic Detrusor Overactivity and Overactive Bladder)

Source: Post-marketing Surveillance
Events to be reported: All AEs occurring to subjects during the entire surveillance period were to be included in the report, regardless of their causal relationship to the study drug.

It was specified that any AEs, which occurred during the PMS period, should be reported by the physician (investigator) to Allergan Korea Ltd. irrespective of their causal relationship to the study drug, and of these, any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to a series of procedure as soon as they are reported.

In this report, classification of AEs was presented in accordance with the WHO-ART 092 classification criteria.

During the PMS period, 78 AEs occurred in 59 out of 686 subjects in the safety population, which indicated that incidence of AEs was 8.60% (Table 136).

Table 136. Incidence of AEs (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)
Total	59(8.60)	(6.50, 10.70)	78	686(100.00)

† The percentage of 'Incidence rate of AE' = (No. subjects of AE / No. subjects of safety analysis sets) * 100%
‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.

3.1.1 Serious AEs/ADRs

It was specified that any SAEs, which occurred during the PMS period, should be reported irrespective of their causal relationship to the study drug, and any SAEs should be reported to Korea Institute of Drug Safety & Risk Management according to the procedure as soon as they are reported.

During the PMS period, a total of 11 SAEs were reported in 9 of all 702 subjects (1.28%) except those who didn't receive the study drug or those of follow-up failure (Table 137).

Examining the SAEs by SOC, the most common SAEs were 'Musculo-skeletal system disorders' and 'Resistance mechanism disorders' in 0.28% (2/702 subjectss) each, followed by 'Urinary system disorders', 'Gastro-intestinal system disorders', 'Central & peripheral nervous system disorders', 'Metabolic and nutritional disorders', and 'Secondary terms - events' in 0.14% (1/702 subjects) each. Examining the SAEs by PT, 'HAEMATURIA', 'ANAL PAIN', 'CYSTITIS', 'PYELONEPHRITIS', 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', 'ARTHRALGIA', 'ARTHRITIS', 'HYPONATRAEMIA', and 'ALCOHOL PROBLEM' occurred in 0.14% (1/702 subjects) each (Table 137).

The subject who was occurred 2 SAEs of 'HAEMATURIA' was prescribed BOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescribed Information), so that excluded from the safety population.

Among them, 1 event occurred in 1 subject (0.14%) was an SADR which cannot rule out the relationship to the study drug: "Gastro-intestinal system disorders"- 'PYELONEPHRITIS' (Table 137).

Individual SAEs are presented in following table (Table 138).

Table 137. SAEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.14)	(0.00, 0.42)	2	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.14)	(0.00, 0.42)	2	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.28)	(0.00, 0.68)	2	1(0.14)	(0.00, 0.42)	1
CYSTITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Central & peripheral nervous system disorders	1(0.14)	(0.00, 0.42)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Total	9(1.28)	(0.45, 2.11)	11	1(0.14)	(0.00, 0.42)	1

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of SAE' = (No. subjects of SAE/No. subjects who enrolled this study and received BOTOX)*100%
The percentage of 'Incidence rate of SADR' = (No. subjects of SADR/No. subjects who enrolled this study and received BOTOX)*100%
95% Confidence Interval for SAE/SADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

Table 138. Details of SAEs in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
	Urinary system disorders	HAEMATURIA	2015-11-09	2015-11-11	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
	Urinary system disorders	HAEMATURIA	2015-11-20	2015-11-25	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).

During the PMS period, 9 SAEs were reported from 8 subjects (1.17%) in the safety population (Table 139).

Examining the SAEs by SOC, the highest incidence was found in 'Resistance mechanism disorders' and 'Musculo-skeletal system disorders' in 0.29% (2/686 subjects) each, followed by 'Gastro-intestinal system disorders', 'Central & peripheral nervous system disorders', 'Metabolic and nutritional disorders', and 'Secondary terms - events' in 0.15% (1/686 subjects) each. Examining the SAEs by PT, 'ANAL PAIN', 'CYSTITIS', 'PYELONEPHRITIS', 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', 'ARTHRALGIA', 'ARTHRITIS', 'HYPONATRAEMIA', and 'ALCOHOL PROBLEM' occurred in 0.15% (1/686 subjects) each (Table 139).

Among them, 1 event occurred in 1 subject (0.15%) was an SADR which cannot rule out the relationship to the study drug: "Resistance mechanism disorders"- 'PYELONEPHRITIS' (Table 139).

Individual SAEs are presented in following table (Table 140).

Table 139. SAEs onset status in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Serious AE			Serious ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Gastro-intestinal system disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	2(0.29)	(0.00, 0.70)	2	1(0.15)	(0.00, 0.43)	1
CYSTITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Central & peripheral nervous system disorders	1(0.15)	(0.00, 0.43)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Total	8(1.17)	(0.36, 1.97)	9	1(0.15)	(0.00, 0.43)	1

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of SAE' = (No. subjects of SAE/No. subjects of safety analysis sets)*100%
The percentage of 'Incidence rate of SADR' = (No. subjects of SADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for SAE/SADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 140. Details of SAEs in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]-	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]-	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]-	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE

During the PMS period, 2 SAEs of "Urinary system disorders"- 'HAEMATURIA' were reported from 1 subject (6.25%). They were not SADRs which cannot rule out the relationship to the study drug (Table 141).

Individual SAEs are presented in following table (Table 142).

Table 141. SAEs onset status in the subjects excluded from the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Serious AE			Serious ADR		
	Incidence proportion n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence proportion n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(6.25)	(0.00, 18.11)	2	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(6.25)	(0.00, 18.11)	2	0(0.00)	(0.00, 0.00)	0
Total	1(6.25)	(0.00, 18.11)	2	0(0.00)	(0.00, 0.00)	0

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence proportion of SAE' = (No. subjects of SAE / No. subjects of excluded from safety analysis sets) * 100%
The percentage of 'Incidence proportion of SADR' = (No. subjects of SADR / No. subjects of excluded from safety analysis sets) * 100%
95% Confidence Interval for SAE/SADR incidence proportion was calculated using the normal approximation method.
† Excluded from safety analysis set: "Subjects who didn't receive BOTOX for this study", "Subjects for whom adverse event status (Adverse Events status is unknown or missing in CRF) could not be established" of subjects excluded from safety analysis set were excluded.
Dictionary: WHO-ART 092

Table 142. Details of SAEs incurred in the subjects excluded from the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-09	2015-11-11	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-20	2015-11-25	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE

† Excluded from safety analysis set: "Subjects who didn't receive BOTOX for this study" of subjects excluded from safety analysis set were excluded.

3.1.2 Unexpected AEs/ADRs

During the study period, a total of 30 unexpected AEs were reported in 26 of all 702 subjects (3.70%) except those who didn't receive the study drug or those of follow-up failure (Table 143).

Examining the unexpected AEs by SOC, the highest incidence was found in 'Gastro-intestinal system disorders' and 'Body as a whole - general disorders' in 0.71% (5/702 subjects) each, followed by 'Central & peripheral nervous system disorders' in 0.57% (4/702 subjects) and 'Musculo-skeletal system disorders' in 0.43% (3/702 subjects). Examining the unexpected AEs by PT, 'PELVIC PAIN' and 'HEADACHE' occurred in 0.28% (2/702 subjects) each, and others in 0.14% (1/702 subjects) each (Table 143).

Among them, 5 events occurred in 5 subjects (0.71%) were unexpected ADRs which cannot rule out the relationship to the study drug: "Urinary system disorders" - 'URINARY HESITATION' and "Reproductive disorders, male"- 'PERINEAL PAIN MALE', 'TESTIS DISORDER' accounted for 0.14% (1/702 subjects) each (Table 143).

Individual unexpected AEs are presented in the table below (Table 144).

Table 143. Unexpected AEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
URINARY HESITATION	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Gastro-intestinal system disorders	5(0.71)	(0.09, 1.33)	5	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	5(0.71)	(0.09, 1.33)	5	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous	4(0.57)	(0.01, 1.13)	5	0(0.00)	(0.00, 0.00)	0

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
system disorders						
HEADACHE	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.43)	(0.00, 0.91)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	2(0.28)	(0.00, 0.68)	2	2(0.28)	(0.00, 0.68)	2
PERINEAL PAIN MALE	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
TESTIS DISORDER	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Endocrine disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Total	26(3.70)	(2.31, 5.10)	30	3(0.43)	(0.00, 0.91)	3

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE / No. subjects who enrolled this study and received BOTOX) * 100%
The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR / No. subjects who enrolled this study and received BOTOX) * 100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

Table 144. Details of unexpected AEs incurred in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).

During the PMS period, a total of 30 unexpected AEs were reported from 30 subjects (4.37%) in the safety population (Table 145).

Examining unexpected AEs by SOC, the highest incidence was found in 'Gastro-intestinal system disorders' and ‘Body as a whole - general disorders’ in 0.73% (5/686 subjects) each, followed by 'Central & peripheral nervous system disorders' in 0.58% (4/686 subjects) and 'Musculo-skeletal system disorders ' in 0.44% (3/686 subjects). Examining the unexpected AEs by PT, 'PELVIC PAIN' and 'HEADACHE' occurred in 0.29% (2/686 subjects) each and others in 0.15% (1/686 subjects) each (Table 145).

Among them, 3 events occurred in 3 subjects (0.44%) were unexpected ADRs which cannot rule out the relationship to the study drug: "Urinary system disorders"- 'URINARY HESITATION' and "Reproductive disorders, male"- 'PERINEAL PAIN MALE', 'TESTIS DISORDER' accounted for 0.15% (1/686 subjects) each (Table 145).

Individual unexpected AEs are presented in the table below (Table 146).

Table 145. Unexpected AEs onset status in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Unexpected AE			Unexpected ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
URINARY HESITATION	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Gastro-intestinal system disorders	5(0.73)	(0.09, 1.37)	5	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	5(0.73)	(0.09, 1.37)	5	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	4(0.58)	(0.01, 1.15)	5	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.44)	(0.00, 0.93)	3	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	2(0.29)	(0.00, 0.70)	2	2(0.29)	(0.00, 0.70)	2
PERINEAL PAIN MALE	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
TESTIS DISORDER	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Endocrine disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Total	26(3.79)	(2.36, 5.22)	30	3(0.44)	(0.00, 0.93)	3

ADR (Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'.
The percentage of 'Incidence rate of Unexpected AE' = (No. subjects of Unexpected AE / No. subjects of safety analysis sets) * 100%

The percentage of 'Incidence rate of Unexpected ADR' = (No. subjects of Unexpected ADR / No. subjects of safety analysis sets) * 100%
95% Confidence Interval for Unexpected AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 146. Details of unexpected AEs incurred in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes
	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes
	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No
	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No
	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No
	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes
	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes
	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No
	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes
	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes

During the PMS period, no unexpected AE was reported in the subjects excluded from the safety population.

3.1.3 AEs/ADRs

During the study period, a total of 81 AEs were reported in 61 of all 702 subjects (8.69%) except those who didn't receive the study drug or those of follow-up failure (Table 147).

Examining the AEs by SOC, the highest incidence was found in 'Urinary system disorders' in 3.28% (23/702 subjects), followed by 'Gastro-intestinal system disorders' in 1.57% (11/702 subjects) and 'Resistance mechanism disorders' in 1.42% (10/702 subjects). Examining the AEs by PT, 'URINARY RETENTION' occurred in 1.42% (10/702 subjects), 'URINARY TRACT INFECTION' in 1.00% (7/702 subjects) and 'DYSURIA' in 0.71% (5/702 subjects) (Table 147).

Among them, 31 events occurred in 27 subjects (3.85%) were ADRs which cannot rule out the relationship to the study drug (Table 147).

Examining the ADRs by SOC, 'Urinary system disorders' occurred in 2.56% (18/702 subjects), followed by 'Resistance mechanism disorders' in 0.57% (4/702 subjects) and 'Gastro-intestinal system disorders', 'Musculo-skeletal system disorders', and 'Reproductive disorders, male' in 0.28% (2/702 subjects) each. Examining the ADRs by PT, 'URINARY RETENTION' occurred in 1.42% (10/702 subjects), 'DYSURIA' in 0.71% (5/702 subjects) and 'URINARY TRACT INFECTION' and 'MYALGIA' in 0.28% (2/702 subjects) each (Table 147).

Individual AEs are presented in the table below (Table 148).

Table 147. AEs onset status in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	23(3.28)	(1.96, 4.59)	27	18(2.56)	(1.39, 3.73)	21
URINARY RETENTION	10(1.42)	(0.55, 2.30)	10	10(1.42)	(0.55, 2.30)	10
DYSURIA	5(0.71)	(0.09, 1.33)	5	5(0.71)	(0.09, 1.33)	5
HAEMATURIA	3(0.43)	(0.00, 0.91)	4	1(0.14)	(0.00, 0.42)	1
PYURIA	2(0.28)	(0.00, 0.68)	2	1(0.14)	(0.00, 0.42)	1
URODYNIA	2(0.28)	(0.00, 0.68)	2	1(0.14)	(0.00, 0.42)	1
DIFFICULTY IN MICTURITION	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
URETHRAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
URINARY HESITATION	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Gastro-intestinal system disorders	11(1.57)	(0.65, 2.49)	11	2(0.28)	(0.00, 0.68)	2
NAUSEA	3(0.43)	(0.00, 0.91)	3	1(0.14)	(0.00, 0.42)	1
ABDOMINAL DISCOMFORT	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
DYSPEPSIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	10(1.42)	(0.55, 2.30)	10	4(0.57)	(0.01, 1.13)	4
URINARY TRACT INFECTION	7(1.00)	(0.26, 1.73)	7	2(0.28)	(0.00, 0.68)	2
CYSTITIS	2(0.28)	(0.00, 0.68)	2	1(0.14)	(0.00, 0.42)	1
PYELONEPHRITIS	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Body as a whole - general disorders	7(1.00)	(0.26, 1.73)	8	0(0.00)	(0.00, 0.00)	0
FEVER	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	6(0.85)	(0.17, 1.54)	8	0(0.00)	(0.00, 0.00)	0
DIZZINESS	3(0.43)	(0.00, 0.91)	3	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0

	AE			ADR		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
GAIT DISTURBANCE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	5(0.71)	(0.09, 1.33)	5	2(0.28)	(0.00, 0.68)	2
MYALGIA	2(0.28)	(0.00, 0.68)	2	2(0.28)	(0.00, 0.68)	2
ARTHRALGIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	2(0.28)	(0.00, 0.68)	2	2(0.28)	(0.00, 0.68)	2
PERINEAL PAIN MALE	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
TESTIS DISORDER	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1
Endocrine disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.28)	(0.00, 0.68)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Total	61(8.69)	(6.61, 10.77)	81	27(3.85)	(2.42, 5.27)	31

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects who enrolled this study and received BOTOX)*100%
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects who enrolled this study and received BOTOX)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

Table 148. Details of AEs in all subjects except those who didn't received the study drug or those of follow-up failure (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-04-16		Mild	None	Ongoing	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-05-05	2015-05-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Conditional/unclassified	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	CONSTIPATION	2015-12-21	2015-12-25	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Expected AE
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	DIFFICULTY IN MICTURITION	2015-01-29	2015-01-29	Mild	Not applicable	Resolved without sequelae	Certain	Unassessable/unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2015-03-03	2015-03-03	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unassessable/unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-03-21	2016-04-01	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2014-04-07		Moderate	None	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2014-10-27		Moderate	Not applicable	Ongoing	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	PYURIA	2014-10-27		Moderate	Not applicable	Ongoing	Certain	Certain	Yes	Expected AE
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2014-09-22	2014-10-05	Moderate	Not applicable	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY FREQUENCY	2014-11-11		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2016-02-04	2016-02-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Possible	No	Expected AE
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2014-06-08	2014-06-08	Mild	Not applicable	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Urinary system disorders	URINARY RETENTION	2015-07-23	2015-08-20	Mild	Not applicable	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-10-01	2015-10-04	Moderate	Not applicable	Resolved without sequelae	Unassessable/unclassifiable	Unassessable/unclassifiable	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-10-19		Moderate	Not applicable	Ongoing	Probable/likely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-19	2015-12-29	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-02-25	2015-02-25	Mild	Not applicable	Resolved without sequelae	Possible	Possible	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-04-01	2016-04-06	Mild	Not applicable	Resolved without sequelae	Possible	Probable/likely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-03-17		Mild	Not applicable	Ongoing	Possible	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-13	2015-11-14	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-09	2015-11-11	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-20	2015-11-25	Moderate	Not applicable	Resolved without sequelae	Unlikely	Certain	Yes	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Skin and appendages disorders	DRUG ERUPTION	2016-03-14	2016-04-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Body as a whole - general disorders	WEAKNESS GENERALIZED	2016-07-19	2016-07-19	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-25	2016-06-01	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-22	2016-01-31	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-29		Moderate	None	Ongoing	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-05	2016-05-09	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-03-21	2016-03-28	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URETHRAL PAIN	2016-04-12	2016-04-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2016-03-01	2016-03-01	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-06-02	2016-06-02	Moderate	None	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2015-12-21	2015-12-23	Mild	None	Resolved without sequelae	Probable/likely	Unlikely	No	Expected AE
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	PYURIA	2016-01-05	2016-01-10	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	MOUTH DRY	2016-02-02	2016-04-26	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ABDOMINAL DISCOMFORT	2016-01-11	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-20	2016-05-24	Moderate	None	Resolved without sequelae	Certain	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2016-03-10	2016-04-27	Mild	None	Resolved without sequelae	Possible	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-31	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Possible	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-31	2016-01-27	Mild	None	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-03	2016-05-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE

† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).

During the PMS period, a total of 78 AEs were reported from 59 subjects (8.60%) in the safety

population (Table 149).

Examining the AEs by SOC, the highest incidence was found in 'Urinary system disorders' in 3.06% (21/686 subjects), followed by 'Gastro-intestinal system disorders' in 1.60% (11/686 subjects) and 'Resistance mechanism disorders' in 1.46% (10/686 subjects). Examining the AEs by PT, 'URINARY RETENTION' occurred in 1.31% (9/686 subjects), 'URINARY TRACT INFECTION' in 1.02% (7/686 subjects), and 'DYSURIA' in 0.73% (5/686 subjects) (Table 149).

Among them, 30 events occurred in 26 subjects (3.79%) were ADRs which cannot rule out the relationship to the study drug (Table 149).

Examining the ADRs by SOC, the highest incidence was found in 'Urinary system disorders' in 2.48% (17/686 subjects), followed by "Resistance mechanism disorders' in 0.58% (4/686 subjects) and 'Gastro-intestinal system disorders', 'Musculo-skeletal system disorders', and 'Reproductive disorders, male' in 0.29% (2/686 subjects) each. Examining the ADRs by PT, 'URINARY RETENTION' occurred in 1.31% (9/686 subjects), 'DYSURIA' for 0.73% (5/686 subjects), and 'URINARY TRACT INFECTION' and 'MYALGIA' for 0.29% (2/686 subjects) each (Table 149).

Individual AEs are presented in the table below (Table 150).

Table 149. AEs onset status in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	AE			ADR		
	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	21(3.06)	(1.77, 4.35)	24	17(2.48)	(1.31, 3.64)	20
URINARY RETENTION	9(1.31)	(0.46, 2.16)	9	9(1.31)	(0.46, 2.16)	9
DYSURIA	5(0.73)	(0.09, 1.37)	5	5(0.73)	(0.09, 1.37)	5
HAEMATURIA	2(0.29)	(0.00, 0.70)	2	1(0.15)	(0.00, 0.43)	1
PYURIA	2(0.29)	(0.00, 0.70)	2	1(0.15)	(0.00, 0.43)	1
URODYNIA	2(0.29)	(0.00, 0.70)	2	1(0.15)	(0.00, 0.43)	1
DIFFICULTY IN MICTURITION	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
URETHRAL PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
URINARY HESITATION	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Gastro-intestinal system disorders	11(1.60)	(0.66, 2.54)	11	2(0.29)	(0.00, 0.70)	2
NAUSEA	3(0.44)	(0.00, 0.93)	3	1(0.15)	(0.00, 0.43)	1
ABDOMINAL DISCOMFORT	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
DYSPEPSIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	10(1.46)	(0.56, 2.35)	10	4(0.58)	(0.01, 1.15)	4
URINARY TRACT INFECTION	7(1.02)	(0.27, 1.77)	7	2(0.29)	(0.00, 0.70)	2
CYSTITIS	2(0.29)	(0.00, 0.70)	2	1(0.15)	(0.00, 0.43)	1

	AE			ADR		
	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
PYELONEPHRITIS	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Body as a whole - general disorders	7(1.02)	(0.27, 1.77)	8	0(0.00)	(0.00, 0.00)	0
FEVER	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	6(0.87)	(0.18, 1.57)	8	0(0.00)	(0.00, 0.00)	0
DIZZINESS	3(0.44)	(0.00, 0.93)	3	0(0.00)	(0.00, 0.00)	0
HEADACHE	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	5(0.73)	(0.09, 1.37)	5	2(0.29)	(0.00, 0.70)	2
MYALGIA	2(0.29)	(0.00, 0.70)	2	2(0.29)	(0.00, 0.70)	2
ARTHRALGIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	2(0.29)	(0.00, 0.70)	2	2(0.29)	(0.00, 0.70)	2
PERINEAL PAIN MALE	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
TESTIS DISORDER	1(0.15)	(0.00, 0.43)	1	1(0.15)	(0.00, 0.43)	1
Endocrine disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.29)	(0.00, 0.70)	2	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.15)	(0.00, 0.43)	1	0(0.00)	(0.00, 0.00)	0
Total	59(8.60)	(6.50, 10.70)	78	26(3.79)	(2.36, 5.22)	30

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects of safety analysis sets)*100%
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

Table 150. Details of AEs incurred in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Respiratory system disorders	THROAT PAIN	2014-04-16	2014-04-18	Moderate	Not applicable	Resolved without sequelae	Unlikely	Possible	Yes	Unexpected AE
[redacted]	Reproductive disorders, male	TESTIS DISORDER	2015-03-01	2015-03-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-04-16		Mild	None	Ongoing	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ANUS DISCOMFORT	2015-06-04		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	URODYNIA	2015-05-05	2015-05-15	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Conditional/unclassified	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	HEARTBURN	2015-05-15	2015-05-30	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Body as a whole - general disorders	UROGENITAL PROLAPSE	2016-05-18		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	FAECAL INCONTINENCE	2016-05-30		Mild	None	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	CONSTIPATION	2015-12-21	2015-12-25	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unlikely	Yes	Expected AE
[redacted]	Metabolic and nutritional disorders	DIABETES MELLITUS	2016-01-10		Moderate	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	DIFFICULTY IN MICTURITION	2015-01-29	2015-01-29	Mild	Not applicable	Resolved without sequelae	Certain	Unassessable/unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2015-03-03	2015-03-03	Mild	Not applicable	Resolved without sequelae	Conditional/ unclassified	Unassessable/unclassifiable	No	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-03-21	2016-04-01	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2014-04-07		Moderate	None	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	HAEMATURIA	2014-10-27		Moderate	Not applicable	Ongoing	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	PYURIA	2014-10-27		Moderate	Not applicable	Ongoing	Certain	Certain	Yes	Expected AE
[redacted]	Reproductive disorders, male	PERINEAL PAIN MALE	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Unexpected AE
[redacted]	Urinary system disorders	DYSURIA	2014-09-01		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2014-09-22	2014-10-05	Moderate	Not applicable	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY FREQUENCY	2014-11-11		Moderate	Not applicable	Ongoing	Possible	Possible	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2016-02-04	2016-02-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Possible	No	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Musculo-skeletal system disorders	ARTHRITIS	2016-05-30	2016-07-01	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2014-06-08	2014-06-08	Mild	Not applicable	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-07-23	2015-08-20	Mild	Not applicable	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-10-01	2015-10-04	Moderate	Not applicable	Resolved without sequelae	Unassessable/unclassifiable	Unassessable/unclassifiable	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-10-19		Moderate	Not applicable	Ongoing	Probable/likely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DEMENTIA	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	NORMAL PRESSURE HYDROCEPHALUS	2015-08-18		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Endocrine disorders	ADRENAL CORTICAL INSUFFICIENCY	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Metabolic and nutritional disorders	HYPONATRAEMIA	2015-12-17		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-19	2015-12-29	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-04-01	2016-04-06	Mild	Not applicable	Resolved without sequelae	Possible	Probable/likely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	ANAL PAIN	2015-06-11	2015-06-13	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Resistance mechanism disorders	CYSTITIS	2016-02-14	2016-02-26	Moderate	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-03-17		Mild	Not applicable	Ongoing	Possible	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-08-03		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Urinary system disorders	HAEMATURIA	2015-11-13	2015-11-14	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Secondary terms - events	ALCOHOL PROBLEM	2016-02-17	2016-03-04	Mild	Not applicable	Resolved with sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Reproductive disorders, female	VAGINITIS	2015-11-17	2015-12-08	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	ARTHRALGIA	2015-08-27	2015-08-31	Moderate	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Musculo-skeletal system disorders	BACK PAIN	2016-06-13		Mild	Not applicable	Ongoing	Unlikely	Unlikely	Yes	Unexpected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Skin and appendages disorders	DRUG ERUPTION	2016-03-14	2016-04-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	FEVER	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-11-04	2015-11-04	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Body as a whole - general disorders	PELVIC PAIN	2015-11-27	2015-11-27	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	GAIT DISTURBANCE	2016-06-22	2016-07-13	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Body as a whole - general disorders	WEAKNESS GENERALIZED	2016-07-19	2016-07-19	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-25	2016-06-01	Mild	Not applicable	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-22	2016-01-31	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-10	2016-01-14	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2015-12-29		Moderate	None	Ongoing	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-05	2016-05-09	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-03-21	2016-03-28	Moderate	None	Resolved without sequelae	Certain	Unlikely	No	Expected AE
[redacted]	Urinary system disorders	URETHRAL PAIN	2016-04-12	2016-04-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2016-03-01	2016-03-01	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	PYELONEPHRITIS	2016-05-04	2016-05-12	Moderate	None	Resolved without sequelae	Possible	Possible	Yes	Expected AE
[redacted]	Urinary system disorders	DYSURIA	2016-06-02	2016-06-02	Moderate	None	Resolved without sequelae	Probable/likely	Probable/likely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY HESITATION	2016-06-02	2016-07-27	Mild	None	Resolved without sequelae	Probable/likely	Probable/likely	No	Unexpected AE
[redacted]	Secondary terms - events	CLOSED HEAD INJURY	2016-06-09	2016-06-09	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	DIZZINESS	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE

caseno	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2015-12-21	2015-12-23	Mild	None	Resolved without sequelae	Probable/likely	Unlikely	No	Expected AE
[redacted]	Psychiatric disorders	INSOMNIA	2015-12-21	2016-01-04	Moderate	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE
[redacted]	Urinary system disorders	PYURIA	2016-01-05	2016-01-10	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	DYSPEPSIA	2016-02-11	2016-02-25	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Gastro-intestinal system disorders	MOUTH DRY	2016-02-02	2016-04-26	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Expected AE
[redacted]	Gastro-intestinal system disorders	ABDOMINAL DISCOMFORT	2016-01-11	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Urinary system disorders	URINARY RETENTION	2016-01-20	2016-05-24	Moderate	None	Resolved without sequelae	Certain	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN GROIN	2016-02-22	2016-02-24	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Central & peripheral nervous system disorders	HEADACHE	2016-03-03	2016-04-27	Mild	None	Resolved without sequelae	Unlikely	Unlikely	No	Unexpected AE
[redacted]	Musculo-skeletal system disorders	MYALGIA	2016-03-10	2016-04-27	Mild	None	Resolved without sequelae	Possible	Unlikely	No	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2015-12-31	2016-01-15	Mild	None	Resolved without sequelae	Unlikely	Possible	Yes	Expected AE
[redacted]	Gastro-intestinal system disorders	NAUSEA	2015-12-31	2016-01-27	Mild	None	Resolved without sequelae	Possible	Unlikely	Yes	Expected AE
[redacted]	Resistance mechanism disorders	URINARY TRACT INFECTION	2016-05-03	2016-05-19	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Expected AE
[redacted]	Body as a whole - general disorders	PAIN IN LIMB	2016-06-08	2016-06-13	Mild	None	Resolved without sequelae	Unlikely	Unlikely	Yes	Unexpected AE

3.1.4 Classification of AEs/ADRs by severity

A. Severity of AEs

When classifying and evaluating the severity of AEs reported in all 702 subjects except those who didn't receive the study drug or those of follow-up failure, 'Mild' occurred in 5.70%

(40/702 subjects), 'Moderate' in 3.28% (23/702 subjects) and none were severe (Table 151).

Table 151. Severity of AEs in all subjects except those who didn't received the study drug or those of follow-up failure by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	11(1.57)	(0.65, 2.49)	12	13(1.85)	(0.85, 2.85)	15	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	4(0.57)	(0.01, 1.13)	4	6(0.85)	(0.17, 1.53)	6	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.14)	(0.00, 0.42)	1	4(0.57)	(0.01, 1.13)	4	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.14)	(0.00, 0.42)	1	2(0.28)	(0.00, 0.67)	3	0(0.00)	(0.00, 0.00)	0
PYURIA	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URETHRAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	10(1.42)	(0.54, 2.30)	10	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
NAUSEA	2(0.28)	(0.00, 0.67)	2	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	6(0.85)	(0.17, 1.53)	6	4(0.57)	(0.01, 1.13)	4	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	6(0.85)	(0.17, 1.53)	6	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	6(0.85)	(0.17, 1.53)	7	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
FEVER	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	4(0.57)	(0.01, 1.13)	5	2(0.28)	(0.00, 0.67)	3	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.28)	(0.00, 0.67)	2	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
HYDROCEPHALUS									
Musculo-skeletal system disorders	3(0.43)	(0.00, 0.91)	3	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
ARTHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Endocrine disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	40(5.70)	(3.98, 7.42)	51	23(3.28)	(1.96, 4.60)	30	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects who enrolled this study and received BOTOX)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

When classifying and evaluating the severity of AEs reported in the safety population, 'Mild' occurred in 5.69% (39/686 subjects), 'Moderate' in 3.21% (22/686 subjects) and none were severe (Table 152).

Table 152. Severity of AEs in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	10(1.46)	(0.56, 2.36)	11	12(1.75)	(0.77, 2.73)	13	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.44)	(0.00, 0.94)	3	6(0.87)	(0.18, 1.56)	6	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.15)	(0.00, 0.44)	1	4(0.58)	(0.01, 1.15)	4	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URETHRAL PAIN	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	10(1.46)	(0.56, 2.36)	10	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
NAUSEA	2(0.29)	(0.00, 0.69)	2	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
ABDOMINAL DISCOMFORT	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANAL PAIN	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ANUS DISCOMFORT	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DYSPEPSIA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
FAECAL INCONTINENCE	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
HEARTBURN	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MOUTH DRY	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	6(0.87)	(0.18, 1.56)	6	4(0.58)	(0.01, 1.15)	4	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	6(0.87)	(0.18, 1.56)	6	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
Body as a whole - general disorders	6(0.87)	(0.18, 1.56)	7	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
FEVER	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PELVIC PAIN	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN GROIN	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
PAIN IN LIMB	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
UROGENITAL PROLAPSE	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
WEAKNESS GENERALIZED	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
Central & peripheral nervous system disorders	4(0.58)	(0.01, 1.15)	5	2(0.29)	(0.00, 0.69)	3	0(0.00)	(0.00, 0.00)	0
DIZZINESS	2(0.29)	(0.00, 0.69)	2	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
HEADACHE	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
DEMENTIA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
GAIT DISTURBANCE	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
NORMAL PRESSURE HYDROCEPHALUS	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	3(0.44)	(0.00, 0.94)	3	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ARTHRALGIA	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
ARTHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
BACK PAIN	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Metabolic and nutritional disorders	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
DIABETES MELLITUS	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
HYPONATRAEMIA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Endocrine disorders	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ADRENAL CORTICAL INSUFFICIENCY	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Neoplasms	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CERVICAL CARCINOMA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Psychiatric disorders	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
INSOMNIA	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, female	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
VAGINITIS	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Respiratory system disorders	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
THROAT PAIN	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
Skin and appendages disorders	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DRUG ERUPTION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Secondary terms - events	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
ALCOHOL PROBLEM	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CLOSED HEAD INJURY	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	39(5.69)	(3.96, 7.42)	50	22(3.21)	(1.89, 4.53)	28	0(0.00)	(0.00, 0.00)	0

The percentage of 'Incidence rate of AE' = (No. subjects of AE/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

B. Severity of ADRs

When classifying and evaluating the severity of ADRs reported in all 702 subjects except those who didn't receive the study drug or those of follow-up failur, 'Moderate' occurred in 2.14% (15/702 subjects), 'Mild' in 1.85% (13/702 subjects) and none were severe (Table 153).

Table 153. Severity of ADRs in all subjects except those who didn't received the study drug or those of follow-up failure by ADR type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	7(1.00)	(0.26, 1.74)	8	12(1.71)	(0.75, 2.67)	13	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
URINARY RETENTION	4(0.57)	(0.01, 1.13)	4	6(0.85)	(0.17, 1.53)	6	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.14)	(0.00, 0.42)	1	4(0.57)	(0.01, 1.13)	4	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
DIFFICULTY IN MICTURITION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	1(0.14)	(0.00, 0.42)	1	3(0.43)	(0.00, 0.91)	3	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(0.28)	(0.00, 0.67)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.14)	(0.00, 0.42)	1	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.14)	(0.00, 0.42)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	13(1.85)	(0.85, 2.85)	14	15(2.14)	(1.07, 3.21)	17	0(0.00)	(0.00, 0.00)	0

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects who enrolled this study and received BOTOX)*100%
† All subjects who enrolled this study and received BOTOX (ie, Subjects who didn't receive BOTOX for this study were not included).
Dictionary: WHO-ART 092

When classifying and evaluating the severity of ADRs reported in the safety population, 'Moderate' occurred in 2.19% (15/686 subjects), 'Mild' in 1.75% (12/686 subjects) and none were severe (Table 154).

Table 154. Severity of ADRs in the safety population by ADR type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
Urinary system disorders	6(0.87)	(0.18, 1.56)	7	12(1.75)	(0.77, 2.73)	13	0(0.00)	(0.00, 0.00)	0
URINARY RETENTION	3(0.44)	(0.00, 0.94)	3	6(0.87)	(0.18, 1.56)	6	0(0.00)	(0.00, 0.00)	0
DYSURIA	1(0.15)	(0.00, 0.44)	1	4(0.58)	(0.01, 1.15)	4	0(0.00)	(0.00, 0.00)	0
HAEMATURIA	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
PYURIA	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
URODYNIA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0

	Mild			Moderate			Severe		
	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n	Incidence rate n(%)	95% CI (Lower, Upper)	No. of AE n
DIFFICULTY IN MICTURITION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
URINARY FREQUENCY	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
URINARY HESITATION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Gastro-intestinal system disorders	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
NAUSEA	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
CONSTIPATION	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Resistance mechanism disorders	1(0.15)	(0.00, 0.44)	1	3(0.44)	(0.00, 0.94)	3	0(0.00)	(0.00, 0.00)	0
URINARY TRACT INFECTION	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
CYSTITIS	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
PYELONEPHRITIS	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
Musculo-skeletal system disorders	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
MYALGIA	2(0.29)	(0.00, 0.69)	2	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Reproductive disorders, male	1(0.15)	(0.00, 0.44)	1	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
PERINEAL PAIN MALE	0(0.00)	(0.00, 0.00)	0	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0
TESTIS DISORDER	1(0.15)	(0.00, 0.44)	1	0(0.00)	(0.00, 0.00)	0	0(0.00)	(0.00, 0.00)	0
Total	12(1.75)	(0.77, 2.73)	13	15(2.19)	(1.09, 3.29)	17	0(0.00)	(0.00, 0.00)	0

ADR(Adverse Drug Reaction): All AEs excluding the AEs whose causal relation with BOTOX is 'Unlikely'
The percentage of 'Incidence rate of ADR' = (No. subjects of ADR/No. subjects of safety analysis sets)*100%
95% Confidence Interval for AE/ADR Incidence rate was calculated using the normal approximation method.
Dictionary: WHO-ART 092

3.1.5 Classification of AEs in the safety population

The 78 AEs reported in the safety population were analyzed in detail.

When classifying and evaluating the expectedness of AEs into two of 'Expected AE' and 'Unexpected AE', 'Expected AE' accounted for 61.54% (48/78 events) and 'Unexpected AE' accounted for 38.46% (30/78 events) (Table 155).

When classifying and evaluating the seriousness of AEs into two of 'Serious' and 'Non-serious', 'Serious' accounted for 11.54% (9/78 events) and 'Non-serious' accounted for 88.46% (69/78 events) (Table 155).

When classifying and evaluating the severity of AEs into three of 'Mild', 'Moderate', and 'Severe', 'Mild' occurred in 64.10% (50/78 events) and 'Moderate' in 35.90% (28/78 events) (Table 155).

When classifying and evaluating the outcome of AEs incurred into four of 'Ongoing', 'Resolved without sequelae' 'Resolved with sequelae', and 'Death', 'Resolved without sequelae' was reported in 70.51% (55/78 events), 'Ongoing' in 26.92% (21/78 events), and 'Resolved with sequelae' in 2.56% (2/78 events) (Table 155).

When classifying and evaluating the causal relationship of AEs to the study drug into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and

'Unassessable/Unclassifiable', 'Unlikely' was reported in 61.54% (48/78 events), 'Possible' was reported in 15.38% (12/78 events), and 'Certain' was reported in 8.97% (7/78 events) (Table 155).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure into six of 'Certain', 'Probable/Likely', 'Possible', 'Unlikely', 'Conditional/Unclassified', and 'Unassessable/Unclassifiable', 'Unlikely' was reported in 74.36% (58/78 events), 'Possible' was reported in 12.82% (10/78 events), and 'Probable/Likely' was reported in 6.41% (5/78 events) (Table 155).

When classifying and evaluating the change in the study drug administration after AE into four of 'None', 'Regimen changed', 'Discontinued', and 'Not applicable', 'Not applicable' accounted for 51.28% (40/78 events) and 'None' accounted for 48.72% (38/78 events) (Table 155).

When classifying and evaluating use of AE treatment into two of 'Yes' and 'No', 'Yes' accounted for 62.82% (49/78 events) and 'No' accounted for 37.18% (29/78 events) (Table 155).

Table 155. Classification of AEs in the safety population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Total n(%)
Expected	Expected AE	48(61.54)
	Unexpected AE	30(38.46)
Seriousness	Serious	9(11.54)
	Non-serious	69(88.46)
Severity	Mild	50(64.10)
	Moderate	28(35.90)
	Severe	0(0.00)
Current Status	Ongoing	21(26.92)
	Resolved without sequelae	55(70.51)
	Resolved with sequelae	2(2.56)
	Death	0(0.00)
Causal Relationship	Certain	7(8.97)
	Probable/Likely	6(7.69)
	Possible	12(15.38)
	Unlikely	48(61.54)
	Conditional/Unclassified	4(5.13)
	Unassessable/Unclassifiable	1(1.28)
BOTOX Injection procedure	Certain	1(1.28)
	Probable/Likely	5(6.41)
	Possible	10(12.82)
	Unlikely	58(74.36)
	Conditional/Unclassified	1(1.28)
	Unassessable/Unclassifiable	3(3.85)
Change in BOTOX treatment after AE	None	38(48.72)
	Regimen changed	0(0.00)
	Discontinued	0(0.00)
	Not applicable	40(51.28)
Treatment received	Yes	49(62.82)
	No	29(37.18)
Total		78(100.00)

The denominator is number of total AE counts.

A. Expectedness

Incidence of AEs based on the expectedness is presented by AE type in the table below (Table 156).

Table 156. AEs onset status based on the expectedness by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Expected AE n(%)	Unexpected AE n(%)	Total n(%)
Urinary system disorders	23(95.83)	1(4.17)	24(30.77)
URINARY RETENTION	9(100.00)	0(0.00)	9(11.54)
DYSURIA	5(100.00)	0(0.00)	5(6.41)
HAEMATURIA	2(100.00)	0(0.00)	2(2.56)
PYURIA	2(100.00)	0(0.00)	2(2.56)
URODYNIA	2(100.00)	0(0.00)	2(2.56)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	1(1.28)
URETHRAL PAIN	1(100.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	1(100.00)	0(0.00)	1(1.28)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.28)
Gastro-intestinal system disorders	6(54.55)	5(45.45)	11(14.10)
NAUSEA	3(100.00)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	1(1.28)
ANAL PAIN	0(0.00)	1(100.00)	1(1.28)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.28)
CONSTIPATION	1(100.00)	0(0.00)	1(1.28)
DYSPEPSIA	0(0.00)	1(100.00)	1(1.28)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.28)
HEARTBURN	0(0.00)	1(100.00)	1(1.28)
MOUTH DRY	1(100.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	10(100.00)	0(0.00)	10(12.82)
URINARY TRACT INFECTION	7(100.00)	0(0.00)	7(8.97)
CYSTITIS	2(100.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	3(37.50)	5(62.50)	8(10.26)
FEVER	2(100.00)	0(0.00)	2(2.56)
PELVIC PAIN	0(0.00)	2(100.00)	2(2.56)
PAIN GROIN	0(0.00)	1(100.00)	1(1.28)
PAIN IN LIMB	0(0.00)	1(100.00)	1(1.28)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.28)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	3(37.50)	5(62.50)	8(10.26)
DIZZINESS	3(100.00)	0(0.00)	3(3.85)
HEADACHE	0(0.00)	2(100.00)	2(2.56)
DEMENTIA	0(0.00)	1(100.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	1(100.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	1(100.00)	1(1.28)
Musculo-skeletal system disorders	2(40.00)	3(60.00)	5(6.41)
MYALGIA	2(100.00)	0(0.00)	2(2.56)

	Expected AE n(%)	Unexpected AE n(%)	Total n(%)
ARTHRALGIA	0(0.00)	1(100.00)	1(1.28)
ARTHRITIS	0(0.00)	1(100.00)	1(1.28)
BACK PAIN	0(0.00)	1(100.00)	1(1.28)
Metabolic and nutritional disorders	0(0.00)	2(100.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	1(100.00)	1(1.28)
HYPONATRAEMIA	0(0.00)	1(100.00)	1(1.28)
Reproductive disorders, male	0(0.00)	2(100.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	1(1.28)
TESTIS DISORDER	0(0.00)	1(100.00)	1(1.28)
Endocrine disorders	0(0.00)	1(100.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	1(100.00)	1(1.28)
Neoplasms	0(0.00)	1(100.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.28)
Psychiatric disorders	0(0.00)	1(100.00)	1(1.28)
INSOMNIA	0(0.00)	1(100.00)	1(1.28)
Reproductive disorders, female	0(0.00)	1(100.00)	1(1.28)
VAGINITIS	0(0.00)	1(100.00)	1(1.28)
Respiratory system disorders	0(0.00)	1(100.00)	1(1.28)
THROAT PAIN	0(0.00)	1(100.00)	1(1.28)
Skin and appendages disorders	1(100.00)	0(0.00)	1(1.28)
DRUG ERUPTION	1(100.00)	0(0.00)	1(1.28)
Secondary terms - events	0(0.00)	2(100.00)	2(2.56)
ALCOHOL PROBLEM	0(0.00)	1(100.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.28)
Total	48(61.54)	30(38.46)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

B. Seriousness

Incidence of AEs based on the seriousness is presented in the table below (Table 157).

Table 157. AEs onset status based on the seriousness by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Serious n(%)	Non-serious n(%)	Total n(%)
Urinary system disorders	0(0.00)	24(100.00)	24(30.77)
URINARY RETENTION	0(0.00)	9(100.00)	9(11.54)
DYSURIA	0(0.00)	5(100.00)	5(6.41)
HAEMATURIA	0(0.00)	2(100.00)	2(2.56)
PYURIA	0(0.00)	2(100.00)	2(2.56)
URODYNIA	0(0.00)	2(100.00)	2(2.56)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	1(1.28)
URETHRAL PAIN	0(0.00)	1(100.00)	1(1.28)
URINARY FREQUENCY	0(0.00)	1(100.00)	1(1.28)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.28)
Gastro-intestinal system disorders	1(9.09)	10(90.91)	11(14.10)
NAUSEA	0(0.00)	3(100.00)	3(3.85)

	Serious n(%)	Non-serious n(%)	Total n(%)
ABDOMINAL DISCOMFORT	0(0.00)	1(100.00)	1(1.28)
ANAL PAIN	1(100.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.28)
CONSTIPATION	0(0.00)	1(100.00)	1(1.28)
DYSPEPSIA	0(0.00)	1(100.00)	1(1.28)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.28)
HEARTBURN	0(0.00)	1(100.00)	1(1.28)
MOUTH DRY	0(0.00)	1(100.00)	1(1.28)
Resistance mechanism disorders	2(20.00)	8(80.00)	10(12.82)
URINARY TRACT INFECTION	0(0.00)	7(100.00)	7(8.97)
CYSTITIS	1(50.00)	1(50.00)	2(2.56)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	0(0.00)	8(100.00)	8(10.26)
FEVER	0(0.00)	2(100.00)	2(2.56)
PELVIC PAIN	0(0.00)	2(100.00)	2(2.56)
PAIN GROIN	0(0.00)	1(100.00)	1(1.28)
PAIN IN LIMB	0(0.00)	1(100.00)	1(1.28)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.28)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	1(1.28)
Central & peripheral nervous system disorders	2(25.00)	6(75.00)	8(10.26)
DIZZINESS	0(0.00)	3(100.00)	3(3.85)
HEADACHE	0(0.00)	2(100.00)	2(2.56)
DEMENTIA	1(100.00)	0(0.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	1(100.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	2(40.00)	3(60.00)	5(6.41)
MYALGIA	0(0.00)	2(100.00)	2(2.56)
ARTHRALGIA	1(100.00)	0(0.00)	1(1.28)
ARTHRITIS	1(100.00)	0(0.00)	1(1.28)
BACK PAIN	0(0.00)	1(100.00)	1(1.28)
Metabolic and nutritional disorders	1(50.00)	1(50.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	1(100.00)	1(1.28)
HYPONATRAEMIA	1(100.00)	0(0.00)	1(1.28)
Reproductive disorders, male	0(0.00)	2(100.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	1(1.28)
TESTIS DISORDER	0(0.00)	1(100.00)	1(1.28)
Endocrine disorders	0(0.00)	1(100.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	1(100.00)	1(1.28)
Neoplasms	0(0.00)	1(100.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.28)
Psychiatric disorders	0(0.00)	1(100.00)	1(1.28)
INSOMNIA	0(0.00)	1(100.00)	1(1.28)
Reproductive disorders, female	0(0.00)	1(100.00)	1(1.28)
VAGINITIS	0(0.00)	1(100.00)	1(1.28)
Respiratory system disorders	0(0.00)	1(100.00)	1(1.28)
THROAT PAIN	0(0.00)	1(100.00)	1(1.28)
Skin and appendages disorders	0(0.00)	1(100.00)	1(1.28)
DRUG ERUPTION	0(0.00)	1(100.00)	1(1.28)
Secondary terms - events	1(50.00)	1(50.00)	2(2.56)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.28)

	Serious n(%)	Non-serious n(%)	Total n(%)
Total	9(11.54)	69(88.46)	78(100.00)

C. Severity of AEs

Incidence of AEs based on the severity is presented in the table below (Table 158).

Table 158. AEs onset status based on the severity by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)
Urinary system disorders	11(45.83)	13(54.17)	0(0.00)	24(30.77)
URINARY RETENTION	3(33.33)	6(66.67)	0(0.00)	9(11.54)
DYSURIA	1(20.00)	4(80.00)	0(0.00)	5(6.41)
HAEMATURIA	1(50.00)	1(50.00)	0(0.00)	2(2.56)
PYURIA	1(50.00)	1(50.00)	0(0.00)	2(2.56)
URODYNIA	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URETHRAL PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	0(0.00)	1(100.00)	0(0.00)	1(1.28)
URINARY HESITATION	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Gastro-intestinal system disorders	10(90.91)	1(9.09)	0(0.00)	11(14.10)
NAUSEA	2(66.67)	1(33.33)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANAL PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CONSTIPATION	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DYSPEPSIA	1(100.00)	0(0.00)	0(0.00)	1(1.28)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	1(1.28)
HEARTBURN	1(100.00)	0(0.00)	0(0.00)	1(1.28)
MOUTH DRY	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	6(60.00)	4(40.00)	0(0.00)	10(12.82)
URINARY TRACT INFECTION	6(85.71)	1(14.29)	0(0.00)	7(8.97)
CYSTITIS	0(0.00)	2(100.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	0(0.00)	1(100.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	7(87.50)	1(12.50)	0(0.00)	8(10.26)
FEVER	2(100.00)	0(0.00)	0(0.00)	2(2.56)
PELVIC PAIN	2(100.00)	0(0.00)	0(0.00)	2(2.56)
PAIN GROIN	1(100.00)	0(0.00)	0(0.00)	1(1.28)
PAIN IN LIMB	1(100.00)	0(0.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	1(1.28)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	5(62.50)	3(37.50)	0(0.00)	8(10.26)
DIZZINESS	2(66.67)	1(33.33)	0(0.00)	3(3.85)
HEADACHE	1(50.00)	1(50.00)	0(0.00)	2(2.56)
DEMENTIA	1(100.00)	0(0.00)	0(0.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	1(100.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	3(60.00)	2(40.00)	0(0.00)	5(6.41)

	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)
MYALGIA	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ARTHRALGIA	0(0.00)	1(100.00)	0(0.00)	1(1.28)
ARTHRITIS	0(0.00)	1(100.00)	0(0.00)	1(1.28)
BACK PAIN	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Metabolic and nutritional disorders	1(50.00)	1(50.00)	0(0.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	1(100.00)	0(0.00)	1(1.28)
HYPONATRAEMIA	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, male	1(50.00)	1(50.00)	0(0.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	1(100.00)	0(0.00)	1(1.28)
TESTIS DISORDER	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Endocrine disorders	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Neoplasms	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CERVICAL CARCINOMA	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Psychiatric disorders	0(0.00)	1(100.00)	0(0.00)	1(1.28)
INSOMNIA	0(0.00)	1(100.00)	0(0.00)	1(1.28)
Reproductive disorders, female	1(100.00)	0(0.00)	0(0.00)	1(1.28)
VAGINITIS	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Respiratory system disorders	0(0.00)	1(100.00)	0(0.00)	1(1.28)
THROAT PAIN	0(0.00)	1(100.00)	0(0.00)	1(1.28)
Skin and appendages disorders	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DRUG ERUPTION	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Secondary terms - events	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Total	50(64.10)	28(35.90)	0(0.00)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

D. Outcome of AEs

Incidence of AEs based on the outcome is presented in the table below (Table 159).

Table 159. Outcome of AEs by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
Urinary system disorders	9(37.50)	15(62.50)	0(0.00)	0(0.00)	24(30.77)
URINARY RETENTION	3(33.33)	6(66.67)	0(0.00)	0(0.00)	9(11.54)
DYSURIA	2(40.00)	3(60.00)	0(0.00)	0(0.00)	5(6.41)
HAEMATURIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PYURIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
URODYNIA	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URETHRAL PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Gastro-intestinal system disorders	2(18.18)	9(81.82)	0(0.00)	0(0.00)	11(14.10)
NAUSEA	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANAL PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
CONSTIPATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DYSPEPSIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
HEARTBURN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
MOUTH DRY	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	0(0.00)	9(90.00)	1(10.00)	0(0.00)	10(12.82)
URINARY TRACT INFECTION	0(0.00)	7(100.00)	0(0.00)	0(0.00)	7(8.97)
CYSTITIS	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	2(25.00)	6(75.00)	0(0.00)	0(0.00)	8(10.26)
FEVER	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
PELVIC PAIN	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PAIN GROIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
PAIN IN LIMB	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
WEAKNESS GENERALIZED	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	2(25.00)	6(75.00)	0(0.00)	0(0.00)	8(10.26)
DIZZINESS	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(3.85)
HEADACHE	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DEMENTIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	1(20.00)	4(80.00)	0(0.00)	0(0.00)	5(6.41)
MYALGIA	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ARTHRALGIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ARTHRITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
BACK PAIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Metabolic and nutritional disorders	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(2.56)
DIABETES MELLITUS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
HYPONATRAEMIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, male	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PERINEAL PAIN MALE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
TESTIS DISORDER	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Endocrine disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Neoplasms	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
CERVICAL CARCINOMA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Psychiatric disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
INSOMNIA	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, female	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
VAGINITIS	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Respiratory system disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
THROAT PAIN	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Skin and appendages disorders	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)

	Ongoing n(%)	Resolved without sequelae n(%)	Resolved with sequelae n(%)	Death n(%)	Total n(%)
DRUG ERUPTION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Secondary terms - events	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(2.56)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Total	21(26.92)	55(70.51)	2(2.56)	0(0.00)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

E. Relationship to the study drug

Incidence of AEs based on the relationship to the study drug is presented in the table below (Table 160).

Table 160. AEs onset status based on the relationship to the study drug by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Certain n(%)	Probable/Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/ Unclassified n(%)	Unassessible/Unclassifiable n(%)	Total n(%)
Urinary system disorders	7(29.17)	5(20.83)	6(25.00)	4(16.67)	2(8.33)	0(0.00)	24(30.77)
URINARY RETENTION	5(55.56)	2(22.22)	2(22.22)	0(0.00)	0(0.00)	0(0.00)	9(11.54)
DYSURIA	0(0.00)	1(20.00)	3(60.00)	0(0.00)	1(20.00)	0(0.00)	5(6.41)
HAEMATURIA	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PYURIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
URODYNIA	0(0.00)	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(2.56)
DIFFICULTY IN MICTURITION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
URETHRAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	1(9.09)	9(81.82)	1(9.09)	0(0.00)	11(14.10)
NAUSEA	0(0.00)	0(0.00)	1(33.33)	2(66.67)	0(0.00)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(1.28)
DYSPEPSIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
FAECAL INCONTINENCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
HEARTBURN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
MOUTH DRY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	0(0.00)	0(0.00)	3(30.00)	6(60.00)	0(0.00)	1(10.00)	10(12.82)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	1(14.29)	5(71.43)	0(0.00)	1(14.29)	7(8.97)
CYSTITIS	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	0(0.00)	0(0.00)	0(0.00)	8(100.00)	0(0.00)	0(0.00)	8(10.26)
FEVER	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)

	Certain	Probable/Likely	Possible	Unlikely	Conditional/ Unclassified	Unassessible/Unclassifiable	Total
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
PAIN GROIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
PAIN IN LIMB	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
WEAKNESS GENERALIZED	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	8(100.00)	0(0.00)	0(0.00)	8(10.26)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(3.85)
HEADACHE	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	0(0.00)	1(20.00)	1(20.00)	3(60.00)	0(0.00)	0(0.00)	5(6.41)
MYALGIA	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	0(0.00)	2(2.56)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, male	0(0.00)	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	1(1.28)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Psychiatric disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
INSOMNIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Respiratory system disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
THROAT PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Secondary terms - events	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Total	7(8.97)	6(7.69)	12(15.38)	48(61.54)	4(5.13)	1(1.28)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

F. Relationship to the study drug administration procedure

Incidence of AEs based on the relationship to the study drug administration procedure is presented by AE type in the table below (Table 161).

Table 161. AEs onset status based on the relationship to the study drug administration procedure by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Certain	Probable/Likely	Possible	Unlikely	Conditional/Unclassified	Unassessible/Unclassifiable	Total
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Urinary system disorders	1(4.17)	5(20.83)	4(16.67)	11(45.83)	1(4.17)	2(8.33)	24(30.77)
URINARY RETENTION	0(0.00)	2(22.22)	0(0.00)	7(77.78)	0(0.00)	0(0.00)	9(11.54)
DYSURIA	0(0.00)	1(20.00)	3(60.00)	0(0.00)	0(0.00)	1(20.00)	5(6.41)
HAEMATURIA	0(0.00)	1(50.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PYURIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
URODYNIA	0(0.00)	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	2(2.56)
DIFFICULTY IN MICTURITION	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
URETHRAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
URINARY HESITATION	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Gastro-intestinal system disorders	0(0.00)	0(0.00)	0(0.00)	11(100.00)	0(0.00)	0(0.00)	11(14.10)
NAUSEA	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DYSPEPSIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
FAECAL INCONTINENCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
HEARTBURN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
MOUTH DRY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	0(0.00)	0(0.00)	3(30.00)	6(60.00)	0(0.00)	1(10.00)	10(12.82)
URINARY TRACT INFECTION	0(0.00)	0(0.00)	1(14.29)	5(71.43)	0(0.00)	1(14.29)	7(8.97)
CYSTITIS	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	0(0.00)	0(0.00)	1(12.50)	7(87.50)	0(0.00)	0(0.00)	8(10.26)
FEVER	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
PAIN GROIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
PAIN IN LIMB	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
WEAKNESS GENERALIZED	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	0(0.00)	0(0.00)	0(0.00)	8(100.00)	0(0.00)	0(0.00)	8(10.26)
DIZZINESS	0(0.00)	0(0.00)	0(0.00)	3(100.00)	0(0.00)	0(0.00)	3(3.85)
HEADACHE	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
GAIT DISTURBANCE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	0(0.00)	0(0.00)	0(0.00)	5(100.00)	0(0.00)	0(0.00)	5(6.41)
MYALGIA	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)

	Certain n(%)	Probable/Likely n(%)	Possible n(%)	Unlikely n(%)	Conditional/Unclassified n(%)	Unassessible/Unclassifiable n(%)	Total n(%)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, male	0(0.00)	0(0.00)	1(50.00)	1(50.00)	0(0.00)	0(0.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Psychiatric disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
INSOMNIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Respiratory system disorders	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
THROAT PAIN	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Secondary terms - events	0(0.00)	0(0.00)	0(0.00)	2(100.00)	0(0.00)	0(0.00)	2(2.56)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	0(0.00)	0(0.00)	1(1.28)
Total	1(1.28)	5(6.41)	10(12.82)	58(74.36)	1(1.28)	3(3.85)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

G. Change in the study drug administration after AE

Incidence of AEs based on the change in the study drug administration after AE is presented by AE type in the table below (Table 162).

Table 162. AEs onset status based on the actions taken to the study drug by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	None n(%)	Regimen changed n(%)	Discontinued n(%)	Not applicable n(%)	Total n(%)
Urinary system disorders	12(50.00)	0(0.00)	0(0.00)	12(50.00)	24(30.77)
URINARY RETENTION	5(55.56)	0(0.00)	0(0.00)	4(44.44)	9(11.54)
DYSURIA	3(60.00)	0(0.00)	0(0.00)	2(40.00)	5(6.41)
HAEMATURIA	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
PYURIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(2.56)
URODYNIA	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(2.56)
DIFFICULTY IN MICTURITION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
URETHRAL PAIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
URINARY HESITATION	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Gastro-intestinal system disorders	9(81.82)	0(0.00)	0(0.00)	2(18.18)	11(14.10)
NAUSEA	3(100.00)	0(0.00)	0(0.00)	0(0.00)	3(3.85)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)

	None n(%)	Regimen changed n(%)	Discontinued n(%)	Not applicable n(%)	Total n(%)
ANAL PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
ANUS DISCOMFORT	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
CONSTIPATION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
DYSPEPSIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
FAECAL INCONTINENCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
HEARTBURN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
MOUTH DRY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Resistance mechanism disorders	3(30.00)	0(0.00)	0(0.00)	7(70.00)	10(12.82)
URINARY TRACT INFECTION	2(28.57)	0(0.00)	0(0.00)	5(71.43)	7(8.97)
CYSTITIS	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
PYELONEPHRITIS	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	4(50.00)	0(0.00)	0(0.00)	4(50.00)	8(10.26)
FEVER	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
PELVIC PAIN	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
PAIN GROIN	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
PAIN IN LIMB	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	6(75.00)	0(0.00)	0(0.00)	2(25.00)	8(10.26)
DIZZINESS	3(100.00)	0(0.00)	0(0.00)	0(0.00)	3(3.85)
HEADACHE	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(2.56)
DEMENTIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
GAIT DISTURBANCE	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Musculo-skeletal system disorders	2(40.00)	0(0.00)	0(0.00)	3(60.00)	5(6.41)
MYALGIA	2(100.00)	0(0.00)	0(0.00)	0(0.00)	2(2.56)
ARTHRALGIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
ARTHRITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
BACK PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Metabolic and nutritional disorders	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
DIABETES MELLITUS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
HYPONATRAEMIA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Reproductive disorders, male	0(0.00)	0(0.00)	0(0.00)	2(100.00)	2(2.56)
PERINEAL PAIN MALE	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
TESTIS DISORDER	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Endocrine disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Neoplasms	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Psychiatric disorders	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
INSOMNIA	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Reproductive disorders, female	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
VAGINITIS	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Respiratory system disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
THROAT PAIN	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Skin and appendages disorders	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
DRUG ERUPTION	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
Secondary terms - events	1(50.00)	0(0.00)	0(0.00)	1(50.00)	2(2.56)
ALCOHOL PROBLEM	0(0.00)	0(0.00)	0(0.00)	1(100.00)	1(1.28)
CLOSED HEAD INJURY	1(100.00)	0(0.00)	0(0.00)	0(0.00)	1(1.28)
Total	38(48.72)	0(0.00)	0(0.00)	40(51.28)	78(100.00)

	None n(%)	Regimen changed n(%)	Discontinued n(%)	Not applicable n(%)	Total n(%)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

H. AE treatment

Incidence of AEs based on the use of AE treatment is presented by AE type in the table below (Table 163).

Table 163. AEs onset status based on the use of AE treatment by AE type (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Yes n(%)	No n(%)	Total n(%)
Urinary system disorders	15(62.50)	9(37.50)	24(30.77)
URINARY RETENTION	5(55.56)	4(44.44)	9(11.54)
DYSURIA	4(80.00)	1(20.00)	5(6.41)
HAEMATURIA	1(50.00)	1(50.00)	2(2.56)
PYURIA	2(100.00)	0(0.00)	2(2.56)
URODYNIA	1(50.00)	1(50.00)	2(2.56)
DIFFICULTY IN MICTURITION	0(0.00)	1(100.00)	1(1.28)
URETHRAL PAIN	1(100.00)	0(0.00)	1(1.28)
URINARY FREQUENCY	1(100.00)	0(0.00)	1(1.28)
URINARY HESITATION	0(0.00)	1(100.00)	1(1.28)
Gastro-intestinal system disorders	5(45.45)	6(54.55)	11(14.10)
NAUSEA	2(66.67)	1(33.33)	3(3.85)
ABDOMINAL DISCOMFORT	1(100.00)	0(0.00)	1(1.28)
ANAL PAIN	1(100.00)	0(0.00)	1(1.28)
ANUS DISCOMFORT	0(0.00)	1(100.00)	1(1.28)
CONSTIPATION	1(100.00)	0(0.00)	1(1.28)
DYSPEPSIA	0(0.00)	1(100.00)	1(1.28)
FAECAL INCONTINENCE	0(0.00)	1(100.00)	1(1.28)
HEARTBURN	0(0.00)	1(100.00)	1(1.28)
MOUTH DRY	0(0.00)	1(100.00)	1(1.28)
Resistance mechanism disorders	9(90.00)	1(10.00)	10(12.82)
URINARY TRACT INFECTION	6(85.71)	1(14.29)	7(8.97)
CYSTITIS	2(100.00)	0(0.00)	2(2.56)
PYELONEPHRITIS	1(100.00)	0(0.00)	1(1.28)
Body as a whole - general disorders	2(25.00)	6(75.00)	8(10.26)
FEVER	0(0.00)	2(100.00)	2(2.56)
PELVIC PAIN	0(0.00)	2(100.00)	2(2.56)
PAIN GROIN	0(0.00)	1(100.00)	1(1.28)
PAIN IN LIMB	1(100.00)	0(0.00)	1(1.28)
UROGENITAL PROLAPSE	0(0.00)	1(100.00)	1(1.28)
WEAKNESS GENERALIZED	1(100.00)	0(0.00)	1(1.28)
Central & peripheral nervous system disorders	5(62.50)	3(37.50)	8(10.26)
DIZZINESS	1(33.33)	2(66.67)	3(3.85)
HEADACHE	1(50.00)	1(50.00)	2(2.56)
DEMENTIA	1(100.00)	0(0.00)	1(1.28)

	Yes n(%)	No n(%)	Total n(%)
GAIT DISTURBANCE	1(100.00)	0(0.00)	1(1.28)
NORMAL PRESSURE HYDROCEPHALUS	1(100.00)	0(0.00)	1(1.28)
Musculo-skeletal system disorders	3(60.00)	2(40.00)	5(6.41)
MYALGIA	0(0.00)	2(100.00)	2(2.56)
ARTHRALGIA	1(100.00)	0(0.00)	1(1.28)
ARTHRITIS	1(100.00)	0(0.00)	1(1.28)
BACK PAIN	1(100.00)	0(0.00)	1(1.28)
Metabolic and nutritional disorders	2(100.00)	0(0.00)	2(2.56)
DIABETES MELLITUS	1(100.00)	0(0.00)	1(1.28)
HYPONATRAEMIA	1(100.00)	0(0.00)	1(1.28)
Reproductive disorders, male	2(100.00)	0(0.00)	2(2.56)
PERINEAL PAIN MALE	1(100.00)	0(0.00)	1(1.28)
TESTIS DISORDER	1(100.00)	0(0.00)	1(1.28)
Endocrine disorders	1(100.00)	0(0.00)	1(1.28)
ADRENAL CORTICAL INSUFFICIENCY	1(100.00)	0(0.00)	1(1.28)
Neoplasms	0(0.00)	1(100.00)	1(1.28)
CERVICAL CARCINOMA	0(0.00)	1(100.00)	1(1.28)
Psychiatric disorders	1(100.00)	0(0.00)	1(1.28)
INSOMNIA	1(100.00)	0(0.00)	1(1.28)
Reproductive disorders, female	1(100.00)	0(0.00)	1(1.28)
VAGINITIS	1(100.00)	0(0.00)	1(1.28)
Respiratory system disorders	1(100.00)	0(0.00)	1(1.28)
THROAT PAIN	1(100.00)	0(0.00)	1(1.28)
Skin and appendages disorders	1(100.00)	0(0.00)	1(1.28)
DRUG ERUPTION	1(100.00)	0(0.00)	1(1.28)
Secondary terms - events	1(50.00)	1(50.00)	2(2.56)
ALCOHOL PROBLEM	1(100.00)	0(0.00)	1(1.28)
CLOSED HEAD INJURY	0(0.00)	1(100.00)	1(1.28)
Total	49(62.82)	29(37.18)	78(100.00)

The denominator is number of total AE counts
Dictionary: WHO-ART 092

3.1.6 Adverse events by factors

The 78 AEs reported in the safety population were analyzed by factor.

A. Background factors

When analyzing AE incidence by age group, it was 10.49% (17/162 subjects, 22 events) in '< 50 years', 8.68% (19/219 subjects, 29 events) in '≥ 70 years', 7.69% (12/156 subjects, 13 events) in '≥ 60 years to < 70 years', and 7.38% (11/149 subjects, 14 events) in '≥ 50 years to < 60 years'. Difference in AE incidences among the groups was not statistically significant (p=0.7566) (Table 164).

When analyzing AE incidence by sex, it was 8.47% (20/236 subjects, 25 events) in 'Male' and 8.67% (39/450 subjects, 53 events) in 'Female', and difference in AE incidences between the groups was not statistically significant (p=0.9321) (Table 164).

When analyzing AE incidence by treatment setting, it was 7.93% (26/328 subjects, 34 events) in 'Outpatient' and 9.22% (33/358 subjects, 44 events) in 'Inpatient', and difference in AE incidences between the groups was not statistically significant (p=0.5469) (Table 164).

When analyzing AE incidence by diagnosed indications, it was 11.80% (19/161 subjects, 27 events) in subjects with NDO and 7.62% (40/525 subjects, 51 events) in subjects with OAB, and difference in AE incidences between the groups was not statistically significant (p=0.0978) (Table 164).

When analyzing AE incidence by underlying neurologic conditions in subjects diagnosed with NDO in the safety population (multiple counting allowed), it was 20.00% (1/5 subjects, 1 event) in 'Multiple Sclerosis' and 11.54% (18/156 subjects, 26 events) in 'Spinal Cord Injury' (Table 164).

When analyzing AE incidence by symptoms in subjects diagnosed with OAB in the safety population (multiple counting allowed), it was 9.31% (35/376 subjects, 46 events) in 'Urge urinary incontinence', 8.62% (30/348 subjects, 38 events) in 'Urgency', 7.27% (28/385 subjects, 36 events) in 'Frequency', and 7.07% (7/99 subjects, 8 events) in 'Other' (Table 164).

Among female subjects, there was no pregnant subject (Table 164).

Table 164. AEs onset status by background factor (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Age	< 50years	17(10.49)	(5.77, 15.21)	22	162(23.62)	0.7566 Chi-square test
	≥ 50years to < 60years	11(7.38)	(3.18, 11.58)	14	149(21.72)	
	≥ 60years to < 70years	12(7.69)	(3.51, 11.87)	13	156(22.74)	
	≥ 70years	19(8.68)	(4.95, 12.40)	29	219(31.92)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Sex	Male	20(8.47)	(4.92, 12.03)	25	236(34.40)	0.9321 Chi-square test
	Female	39(8.67)	(6.07, 11.27)	53	450(65.60)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Treatment Setting	Outpatient	26(7.93)	(5.00, 10.85)	34	328(47.81)	0.5469 Chi-square test
	Inpatient	33(9.22)	(6.22, 12.21)	44	358(52.19)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Currently pregnant * for female	Yes	0(0.00)	(0.00, 0.00)	0	0(0.00)	NA
	No	39(8.67)	(6.07, 11.27)	53	450(100.00)	
	Total	39(8.67)	(6.07, 11.27)	53	450(100.00)	
Diagnosis	NDO	19(11.80)	(6.82, 16.78)	27	161(23.47)	0.0978 Chi-square test
	OAB	40(7.62)	(5.35, 9.89)	51	525(76.53)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Underlying neurologic condition§ * for patients with NDO Overlapped¶	Multiple Sclerosis	1(20.00)	(0.00, 55.06)	1	5(3.11)	NA
	Spinal Cord Injury	18(11.54)	(6.52, 16.55)	26	156(96.89)	
	Other	0(0.00)	(0.00, 0.00)	0	1(0.62)	

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
	Total	19(11.80)	(6.82, 16.78)	27	161(100.00)	
Symptoms	Urge urinary incontinence	35(9.31)	(6.37, 12.25)	46	376(71.62)	NA
* for patients with OAB Overlapped¶	Urgency	30(8.62)	(5.67, 11.57)	38	348(66.29)	
	Frequency	28(7.27)	(4.68, 9.87)	36	385(73.33)	
	Other	7(7.07)	(2.02, 12.12)	8	99(18.86)	
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%
‡ 95% Confidence Interval for adverse event Incidence rate
95% Confidence Interval was calculated using the normal approximation method.
* The p-value is about that relation between Category and Incidence rate of AEs.
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).

B. Past treatment history

When analyzing AE incidence by previous anticholinergic therapy, it was 8.74% (59/675 subjects, 78 events) in subjects who had received anticholinergic therapy, and no AE was reported in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.6118) (Table 165).

When analyzing AE incidence by use of other OAB drugs after anticholinergic therapy in subjects diagnosed with OAB, it was 8.84% (26/294 subjects, 32 events) in subjects who had used other OAB drugs and 6.06% (14/231 subjects, 19 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.2328) (Table 165).

When analyzing AE incidence by previous use of sacral neuromodulation therapy, it was 20.00% (2/10 subjects, 2 events) in subjects who had received sacral neuromodulation therapy and 8.43% (57/676 subjects, 76 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.2097) (Table 165).

When analyzing AE incidence by past treatment history with the study drug or other botulinum toxin, it was 12.50% (4/32 subjects, 4 events) in subjects who had used the study drug or other botolinum toxin and 8.41% (55/654 subjects, 74 events) in subjects who had not. Difference in AE incidences between the groups was not statistically significant (p=0.3453) (Table 165).

Table 165. AEs onset status by past treatment history (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Previous Anticholinergic Therapy	Yes	59(8.74)	(6.61, 10.87)	78	675(98.40)	0.6118
	No	0(0.00)	(0.00, 0.00)	0	11(1.60)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Another OAB drug also used after anticholinergic therapy	Yes	26(8.84)	(5.60, 12.09)	32	294(56.00)	0.2328
* for patients with OAB	No	14(6.06)	(2.98, 9.14)	19	231(44.00)	Chi-square test
	Total	40(7.62)	(5.35, 9.89)	51	525(100.00)	
Previous Use of Sacral Neuromodulation Therapy	Yes	2(20.00)	(0.00, 44.79)	2	10(1.46)	0.2097
	No	57(8.43)	(6.34, 10.53)	76	676(98.54)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	4(12.50)	(1.04, 23.96)	4	32(4.66)	0.3453
	None	55(8.41)	(6.28, 10.54)	74	654(95.34)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

C. Medical history

When analyzing AE incidence by medical history including surgeries and complications of underlying diseases, it was 9.70% (55/567 subjects, 74 events) in subjects with medical history and 3.48% (4/115 subjects, 4 events) in subjects without medical history. The difference in AE incidences between the groups was statistically significant (p=0.0305) (Table 166).

When analyzing AE incidence by the type of medical history (multiple counting allowed), it was 36.36% (4/11 subjects, 7 events) in 'Diseases of the ear and mastoid process', followed by 'Injury, poisoning and certain other consequences of external causes' in 19.57% (9/46 subjects, 12 events) and ‘Symptoms, signs and abnormal clinical and laboratory findings, NEC' in 16.67% (11/66 subjects, 15 events) (Table 166).

When analyzing AE incidence by allergy history, it was 13.89% (5/36 subjects, 7 events) in subjects with allergy history and 8.31% (54/650 subjects, 71 events) in subject without allergy history. Difference in AE incidences between the groups was not statistically significant (p=0.2249) (Table 166).

When analyzing AE incidence by the type of allergy history, it was 22.22% (4/18 subjects, 6 events) in 'Factors influencing health status and contact with health services', followed by 'Injury, poisoning and certain other consequences of external causes' in 5.56% (1/18 subjects, 1 event) (Table 166).

Table 166. AEs onset status by medical history (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Medical History, Including Surgeries and Complications of Underlying Diseases	Yes	55(9.70)	(7.26, 12.14)	74	567(83.14)	0.0305
	None	4(3.48)	(0.13, 6.83)	4	115(16.86)	Chi-square test
	Total	59(8.65)	(6.54, 10.76)	78	682(100.00)	
	Details for Medical History by dictionary (Overlapped¶)					
	Diseases of the circulatory system	22(7.61)	(4.55, 10.67)	29	289(50.97)	
	Factors influencing health status and contact with health services	24(10.04)	(6.23, 13.85)	32	239(42.15)	
	Endocrine, nutritional and metabolic diseases	15(7.69)	(3.95, 11.43)	25	195(34.39)	
	Diseases of the genitourinary system	17(11.72)	(6.49, 16.96)	22	145(25.57)	
	Diseases of the digestive system	15(10.64)	(5.55, 15.73)	20	141(24.87)	
	Diseases of the musculoskeletal system and connective tissue	20(14.71)	(8.75, 20.66)	25	136(23.99)	
	Neoplasms	5(5.00)	(0.73, 9.27)	7	100(17.64)	
	Mental and behavioural disorders	12(12.12)	(5.69, 18.55)	16	99(17.46)	
	Diseases of the nervous system	12(13.19)	(6.23, 20.14)	21	91(16.05)	
	Diseases of the respiratory system	5(9.09)	(1.49, 16.69)	8	55(9.70)	
	Diseases of the eye and adnexa	6(14.29)	(3.70, 24.87)	9	42(7.41)	
	Injury, poisoning and certain other consequences of external causes	9(19.57)	(8.10, 31.03)	12	46(8.11)	
	Certain infectious and parasitic diseases	4(10.81)	(0.81, 20.82)	5	37(6.53)	
	Diseases of the skin and subcutaneous tissue	4(13.33)	(1.17, 25.50)	5	30(5.29)	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1(7.14)	(0.00, 20.63)	1	14(2.47)	
	Diseases of the ear and mastoid process	4(36.36)	(7.94, 64.79)	7	11(1.94)	
	Congenital malformations, deformations and chromosomal abnormalities	0(0.00)	(0.00, 0.00)	0	5(0.88)	
	Pregnancy, childbirth and the puerperium	0(0.00)	(0.00, 0.00)	0	1(0.18)	
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	11(16.67)	(7.68, 25.66)	15	66(11.64)	
History of Allergies	Yes	5(13.89)	(2.59, 25.19)	7	36(5.25)	0.2249
	None	54(8.31)	(6.19, 10.43)	71	650(94.75)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
	Details for History of Allergies by dictionary					
	Factors influencing health status and contact with health services	4(22.22)	(3.02, 41.43)	6	18(50.00)	
	Injury, poisoning and certain other consequences of external causes	1(5.56)	(0.00, 16.14)	1	18(50.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

Dictionary: KCD 7 and ICD 10

Unknown: 4 (Medical History, Including Surgeries and Complications of Underlying Diseases)

D. Concomitant medications

When analyzing AE incidence by use of concomitant medications, it was 9.09% (59/649 subjects, 78 events) in subjects with concomitant medications, and no AE was reported in subjects without concomitant medications. Difference in AE incidences between the groups was not statistically significant (p=0.0646) (Table 167).

When analyzing AE incidence by concomitant medications (multiple counting allowed), it was 51.61% (16/31 subjects, 22 events) in 'Anti-infectives (systemic)', followed by 'Dermatologicals' in 36.36% (4/11 subjects, 5 event) and 'Eye' in 25.00% (3/12 subjects, 5 events) (Table 167).

Table 167. AEs onset status by concomitant medications (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Yes	59(9.08)	(6.87, 11.29)	78	650(94.48)	0.0646 Fisher's Exact test
No	0(0.00)	(0.00, 0.00)	0	38(5.52)	
Total	59(8.58)	(6.48, 10.67)	78	688(100.00)	
Details for Concomitant Medication by dictionary (Overlapped¶)					
Anaesthetics- Local & General	51(8.85)	(6.53, 11.17)	68	576(88.75)	
Anaesthetics - Local & General	51(8.85)	(6.53, 11.17)	68	576(88.75)	
Central Nervous System	46(10.13)	(7.36, 12.91)	63	454(69.95)	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	25(12.20)	(7.72, 16.67)	38	205(31.59)	
Analgesics (Non-Opioid) & Antipyretics	22(12.43)	(7.57, 17.29)	33	177(27.27)	
Analgesics (Opioid)	11(9.48)	(4.15, 14.81)	16	116(17.87)	
Hypnotics & Sedatives	6(7.23)	(1.66, 12.80)	8	83(12.79)	
Antidepressants	14(17.50)	(9.17, 25.83)	22	80(12.33)	
Drugs For Neuropathic Pain	4(6.35)	(0.33, 12.37)	4	63(9.71)	
Anxiolytics	7(12.96)	(4.00, 21.92)	14	54(8.32)	
Anticonvulsants	6(12.24)	(3.07, 21.42)	7	49(7.55)	
Nootropics & Neurotonics	2(6.06)	(0.00, 14.20)	4	33(5.08)	
Neurodegenerative Disease Drugs	2(9.09)	(0.00, 21.10)	3	22(3.39)	
Antiparkinsonian Drugs	0(0.00)	(0.00, 0.00)	0	19(2.93)	
Antipsychotics	2(14.29)	(0.00, 32.62)	3	14(2.16)	
Antivertigo Drugs	1(20.00)	(0.00, 55.06)	3	5(0.77)	
Antimigraine Preparations	0(0.00)	(0.00, 0.00)	0	2(0.31)	
Other CNS Drugs & Agents for ADHD	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Gastrointestinal & Hepatobiliary System	44(11.52)	(8.32, 14.72)	60	382(58.86)	
Antacids, Antireflux Agents & Antiulcerants	28(11.34)	(7.38, 15.29)	35	247(38.06)	
GIT Regulators, Antiflatulents & Anti-inflammatories	16(12.12)	(6.55, 17.69)	26	132(20.34)	
Digestives	7(7.87)	(2.27, 13.46)	10	89(13.71)	
Laxatives, Purgatives	15(18.52)	(10.06, 26.98)	23	81(12.48)	
Antiemetics	6(17.65)	(4.83, 30.46)	6	34(5.24)	
Antispasmodics	3(11.54)	(0.00, 23.82)	6	26(4.01)	
Antidiarrheals	0(0.00)	(0.00, 0.00)	0	12(1.85)	
Cholagogues, Cholelitholytics & Hepatic	3(33.33)	(2.53, 64.13)	4	9(1.39)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Protectors					
Other Gastrointestinal Agents	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	4(0.62)	
Cardiovascular & Hematopoietic System	26(10.08)	(6.40, 13.75)	33	258(39.75)	
Dyslipidaemic Agents	8(8.79)	(2.97, 14.61)	11	91(14.02)	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	8(8.99)	(3.05, 14.93)	13	89(13.71)	
Calcium Antagonists	5(7.35)	(1.15, 13.56)	7	68(10.48)	
Angiotensin II Antagonists	3(5.45)	(0.00, 11.46)	4	55(8.47)	
Other Antihypertensives	2(5.00)	(0.00, 11.75)	2	40(6.16)	
Haemostatics	2(5.26)	(0.00, 12.36)	2	38(5.86)	
Beta-Blockers	4(11.11)	(0.84, 21.38)	5	36(5.55)	
Peripheral Vasodilators & Cerebral Activators	2(8.70)	(0.00, 20.21)	3	23(3.54)	
Diuretics	1(6.67)	(0.00, 19.29)	2	15(2.31)	
Anti-Anginal Drugs	1(6.25)	(0.00, 18.11)	1	16(2.47)	
Other Cardiovascular Drugs	3(23.08)	(0.17, 45.98)	4	13(2.00)	
Vasoconstrictors	3(30.00)	(1.60, 58.40)	4	10(1.54)	
Cardiac Drugs	1(16.67)	(0.00, 46.49)	2	6(0.92)	
Phlebitis & Varicose Preparations	3(75.00)	(32.56, 100.00)	3	4(0.62)	
Antidiuretics	1(33.33)	(0.00, 86.68)	1	3(0.46)	
Haematopoietic Agents	0(0.00)	(0.00, 0.00)	0	2(0.31)	
ACE Inhibitors/Direct Renin Inhibitors	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	7(1.08)	
Musculo-Skeletal System	12(10.91)	(5.08, 16.74)	14	110(16.95)	
Muscle Relaxants	7(9.86)	(2.92, 16.79)	9	71(10.94)	
Neuromuscular Disorder Drugs	6(16.22)	(4.34, 28.09)	6	37(5.70)	
Other Drugs Acting on the Musculo-Skeletal System	2(11.11)	(0.00, 25.63)	2	18(2.77)	
Anti-Inflammatory Enzymes	0(0.00)	(0.00, 0.00)	0	13(2.00)	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	0(0.00)	(0.00, 0.00)	0	5(0.77)	
Hyperuricemia & Gout Preparations	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Endocrine & Metabolic System	7(6.48)	(1.84, 11.12)	12	108(16.64)	
Antidiabetic Agents	6(8.11)	(1.89, 14.33)	11	74(11.40)	
Other Agents Affecting Metabolism	0(0.00)	(0.00, 0.00)	0	21(3.24)	
Thyroid Hormones	0(0.00)	(0.00, 0.00)	0	13(2.00)	
Agents Affecting Bone Metabolism	0(0.00)	(0.00, 0.00)	0	10(1.54)	
Insulin Preparations	1(20.00)	(0.00, 55.06)	1	5(0.77)	
Antithyroid Agents	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Intravenous & Other Sterile Solutions	11(12.50)	(5.59, 19.41)	17	88(13.56)	
Intravenous & other sterile solutions	11(12.50)	(5.59, 19.41)	17	88(13.56)	
Genito-Urinary System	10(12.20)	(5.11, 19.28)	15	82(12.63)	
Drugs for Bladder & Prostate Disorders	10(12.66)	(5.33, 19.99)	15	79(12.17)	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	2(33.33)	(0.00, 71.05)	2	6(0.92)	
Other Drugs Acting on the Genito-Urinary System	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Respiratory System	6(10.53)	(2.56, 18.49)	9	57(8.78)	
Antiasthmatic & COPD Preparations	5(13.51)	(2.50, 24.53)	6	37(5.70)	
Cough & Cold Preparations	4(12.50)	(1.04, 23.96)	4	32(4.93)	
Nasal Decongestant & Other Nasal Preparations	1(20.00)	(0.00, 55.06)	3	5(0.77)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Oncology	9(16.98)	(6.87, 27.09)	12	53(8.17)	
Supportive Care Therapy	9(19.15)	(7.90, 30.40)	12	47(7.24)	
Hormonal Chemotherapy	0(0.00)	(0.00, 0.00)	0	4(0.62)	
Cytotoxic Chemotherapy	0(0.00)	(0.00, 0.00)	0	2(0.31)	
Vitamins & Minerals	7(14.58)	(4.60, 24.57)	9	48(7.40)	
Calcium / with Vitamins	4(15.38)	(1.52, 29.25)	5	26(4.01)	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	1(9.09)	(0.00, 26.08)	2	11(1.69)	
Vitamin B-complex / with C	1(11.11)	(0.00, 31.64)	1	9(1.39)	
Vitamins &/or Minerals	2(25.00)	(0.00, 55.01)	3	8(1.23)	
Vitamin C	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Vitamins & Minerals (Geriatric)	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Vitamins A, D & E	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Miscellaneous	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Anti-infectives (systemic)	16(51.61)	(34.02, 69.21)	22	31(4.78)	
Cephalosporins	12(92.31)	(77.82, 100.00)	17	13(2.00)	
Quinolones	7(77.78)	(50.62, 100.00)	9	9(1.39)	
Antivirals	0(0.00)	(0.00, 0.00)	0	6(0.92)	
Antifungals	1(20.00)	(0.00, 55.06)	1	5(0.77)	
Antiamoebics	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Macrolides	1(50.00)	(0.00, 100.00)	1	2(0.31)	
Aminoglycosides	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Anti-TB Agents	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Antibacterial Combinations	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Other Antibiotics	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Tetracyclines	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Allergy & Immune System	3(11.11)	(0.00, 22.97)	3	27(4.16)	
Antihistamines & Antiallergics	3(13.64)	(0.00, 27.98)	3	22(3.39)	
Immunosuppressants	0(0.00)	(0.00, 0.00)	0	4(0.62)	
Vaccines, Antisera & Immunologicals	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	4(19.05)	(2.25, 35.84)	7	21(3.24)	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	4(19.05)	(2.25, 35.84)	7	21(3.24)	
Hormones	4(21.05)	(2.72, 39.38)	6	19(2.93)	
Corticosteroid Hormones	3(21.43)	(0.00, 42.92)	5	14(2.16)	
Oestrogens & Progesterones & Related Synthetic Drugs	1(33.33)	(0.00, 86.68)	1	3(0.46)	
Other Drugs Affecting Hormonal Regulation	0(0.00)	(0.00, 0.00)	0	2(0.31)	
Trophic Hormones & Related Synthetic Drugs	1(100.00)	(100.00, 100.00)	3	1(0.15)	
Nutrition	2(10.53)	(0.00, 24.33)	6	19(2.93)	
Parenteral Nutritional Products	2(15.38)	(0.00, 35.00)	6	13(2.00)	
Electrolytes	1(12.50)	(0.00, 35.42)	1	8(1.23)	
Appetite Enhancers	0(0.00)	(0.00, 0.00)	0	3(0.46)	
Enteral / Nutritional Products	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Supplements & Adjuvant Therapy	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Eye	3(25.00)	(0.50, 49.50)	5	12(1.85)	
Ophthalmic Lubricants	1(20.00)	(0.00, 55.06)	1	5(0.77)	
Eye Anti-infectives & Antiseptics	1(33.33)	(0.00, 86.68)	2	3(0.46)	
Eye Corticosteroids	0(0.00)	(0.00, 0.00)	0	2(0.31)	
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	0(0.00)	(0.00, 0.00)	0	2(0.31)	

	Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Other Eye Preparations	1(50.00)	(0.00, 100.00)	2	2(0.31)	
Antiglaucoma Preparations	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Mydriatic Drugs	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Dermatologicals	4(36.36)	(7.94, 64.79)	5	11(1.69)	
Topical Corticosteroids	1(20.00)	(0.00, 55.06)	1	5(0.77)	
Other Dermatologicals	0(0.00)	(0.00, 0.00)	0	2(0.31)	
Topical Antibiotics	1(50.00)	(0.00, 100.00)	2	2(0.31)	
Topical Antifungals & Antiparasites	1(50.00)	(0.00, 100.00)	1	2(0.31)	
Emollients & Skin Protectives	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Psoriasis, Seborrhea & Ichthyosis Preparations	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Skin Antiseptics & Disinfectants	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Topical Anti-infectives with Corticosteroids	1(100.00)	(100.00, 100.00)	1	1(0.15)	
Ear & Mouth / Throat	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Mouth / Throat Preparations	0(0.00)	(0.00, 0.00)	0	1(0.15)	
Miscellaneous	1(12.50)	(0.00, 35.42)	2	8(1.23)	
Miscellaneous	1(12.50)	(0.00, 35.42)	2	8(1.23)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

¶ The same subject may appear in different categories.

Dictionary: KIMS

E. Special population

When classifying and analyzing AE incidence in elderly group who was '65 or/and over', it was 9.03% (27/299 subjects, 38 events) in subjects of '65 or/and over' and 8.27% (32/387 subjects, 40 events) in subjects of 'below 65 years'. Difference in AE incidences between the groups was not statistically significant (p=0.7243) (Table 168).

When analyzing AE incidence by renal impairment, no AE was reported in subjects with renal impairment, and it was 8.70% (59/678 subjects, 78 events) in subject without renal impairment. Difference in AE incidences between the groups was not statistically significant (p=1.0000) (Table 168).

When analyzing AE incidence by hepatic impairment, it was 10.00% (1/10 subjects, 1 event) in subjects with hepatic impairment and 8.58% (58/676 subjects, 77 events) in subject without hepatic impairment. Difference in AE incidences between the groups was not statistically significant (p=0.5957) (Table 168).

Details of AE in subject with hepatic impairment are presented in the table below (Table 169).

Table 168. AEs onset status in special population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Elderly	below 65 years	32(8.27)	(5.52, 11.01)	40	387(56.41)	0.7243
	65 or/and over	27(9.03)	(5.78, 12.28)	38	299(43.59)	Chi-square test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Renal impairment	Yes	0(0.00)	(0.00, 0.00)	0	8(1.17)	1.0000
	No	59(8.70)	(6.58, 10.82)	78	678(98.83)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Hepatic impairment	Yes	1(10.00)	(0.00, 28.59)	1	10(1.46)	0.5957
	No	58(8.58)	(6.47, 10.69)	77	676(98.54)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

Table 169. AEs onset status in the subjects with hepatic impairment (Neurogenic Detrusor Overactivity and Overactive Bladder)

caseno	Liver	SOC	PT	Onset Date	Stop Date	Severity	Change in BOTOX treatment after AE	Current Status	Causal Relationship	BOTOX Injection procedure	Treatment received	Expected
[redacted]	r/o toxic liver injury;r/o non-alcoholic steatohepatitis	Neoplasms	CERVICAL CARCINOMA	2015-10-20		Mild	Not applicable	Ongoing	Unlikely	Unlikely	No	Unexpected AE

F. Information of the study drug administration

All subjects diagnosed with NDO in the safety population received total 200 U in 30 sites, while all subjects diagnosed with OAB in the safety population received total 100 U in 20 sites. Thus, the AE incidence was the same as that in each indication-specific safety population. Difference in AE incidences between the groups was not statistically significant (p=0.0978) (Table 170).

When analyzing AE incidence by use of anesthesia at the study drug administration, 'Local' was used in 9.43% (41/435 subjects, 56 events), 'None' in 8.43% (7/83 subjects, 8 events), and 'General' in 6.55% (11/168 subjects, 14 events), and difference in AE incidences among the groups was not statistically significant (p=0.5273)(Table 170).

When analyzing AE incidence by use of prophylactic antibiotics before, during, and after the study drug administration, it was 9.35% (59/631 subjects, 78 events) in subjects with antibiotics, and no AE was reported in subjects without antibiotics. The difference in AE incidences between the groups was statistically significant (p=0.0102) (Table 170).

Table 170. AEs onset status based on the information of study drug administration (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Number of Injection Sites	20	40(7.62)	(5.35, 9.89)	51	525(76.53)	0.0978
	30	19(11.80)	(6.82, 16.78)	27	161(23.47)	Chi-square test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Total Units Injected	100	40(7.62)	(5.35, 9.89)	51	525(76.53)	0.0978
	200	19(11.80)	(6.82, 16.78)	27	161(23.47)	Chi-square test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Anesthesia	None	7(8.43)	(2.46, 14.41)	8	83(12.10)	0.5273
	Local	41(9.43)	(6.68, 12.17)	56	435(63.41)	Chi-square test
	General	11(6.55)	(2.81, 10.29)	14	168(24.49)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Prophylactic Antibiotic Use	Yes	59(9.35)	(7.08, 11.62)	78	631(91.98)	0.0102
	No	0(0.00)	(0.00, 0.00)	0	55(8.02)	Fisher's Exact test
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%

‡ 95% Confidence Interval for adverse event Incidence rate

95% Confidence Interval was calculated using the normal approximation method.

* The p-value is about that relation between Category and Incidence rate of AEs.

G. Clean intermittent catheterization

When analyzing AE incidence by use of clean intermittent catheterization before the study drug administration, it was 9.20% (23/250 subjects, 32 events) in subjects with clean intermittent catheterization and 8.26% (36/436 subjects, 46 events) in subjects without clean intermittent catheterization, and difference in AE incidences between the groups was not statistically significant (p=0.6716) (Table 171).

When analyzing AE incidence by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, it was 16.07% (18/112 subjects, 22 events) in subjects with urinary catheterization and 5.56% (18/324 subjects, 24 events) in subjects without urinary catheterization, and difference in AE incidences between the groups was statistically significant (p=0.0005). Among the subjects with urinary catheterization, AE incidence was 44.44% (8/18 subjects, 9 events) in subjects who initiated catheterization due to urinary retention and 11.58% (11/95 subjects, 14 events) in subjects who initiated catheterization due to other reason (Table 171).

Table 171. AEs onset status by clean intermittent catheterization (Neurogenic Detrusor Overactivity and Overactive Bladder)

		Incidence rate† n(%)	95% CI‡ (Lower, Upper)	No. of AE n	Total n(%)	p-value*
Routine Urinary Catheterization(before BOTOX)	Yes	23(9.20)	(5.62, 12.78)	32	250(36.44)	0.6716 Chi-square test
	No	36(8.26)	(5.67, 10.84)	46	436(63.56)	
	Total	59(8.60)	(6.50, 10.70)	78	686(100.00)	
Initiation of CIC after BOTOX injection§	Yes	18(16.07)	(9.27, 22.87)	22	112(25.69)	0.0005** Chi-square test
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	8(44.44)	(21.4, 967.40)	9	18(4.13)	
	initiated CIC due to "Other Reason"	11(11.58)	(5.14, 18.01)	14	95(21.79)	
	No	18(5.56)	(3.06, 8.05)	24	324(74.31)	
	Total	36(8.26)	(5.67, 10.84)	46	436(100.00)	

† The percentage of 'Incidence rate of AE' = (No. subjects of AE in each category/No. subjects in each category)*100%
‡ 95% Confidence Interval for adverse event incidence rate
95% Confidence Interval was calculated using the normal approximation method.
* The p-value is about that relation between Category and incidence rate of AEs
**The p-value is about that relation between Yes/No and incidence rate of AEs
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

H. Factors that may affect safety

Regarding the safety in this PMS, incidence of AEs was investigated by age, sex, treatment setting, pregnancy status, underlying neurological conditions (NDO), symptoms (OAB), past treatment history, medical history, concomitant medications, information of study drug administration, and clean intermittent catheterization as well as in special population such as the elderly and subjects with renal or hepatic impairment.

The analysis results showed statistically significant difference in AE incidence by 3 factors: presence of medical history including surgeries and complications of underlying diseases (p=0.0305), use of prophylactic antibiotics before, during, and after the study drug administration (p=0.0102), and use of urinary catheterization after the study drug administration in subjects who had not used use of urinary catheterization before the study drug administration (p=0.0005).

When analyzing AE incidence by medical history including surgeries and complications of underlying diseases, it was 9.70% (55/567 subjects, 74 events) in subjects with the history and

3.48% (4/115 subjects, 4 events) in subjects without medical history. The difference in AE incidences between the groups was statistically significant (p=0.0305). These results are not surprising as generally, patients with other medical histories or comorbidities may have more reports of AEs as they are a "sicker" population than those without medical histories. It seemed that the above reason may have affected the results, but it was considered difficult to determine clinical significance solely with the data.

When analyzing AE incidence by use of of prophylactic antibiotics before, during, and after the study drug administration, it was 9.35% (59/631 subjects, 78 events) in subjects with antibiotics, and no AE was reported in subjects without antibiotics (0/55 subjects, 0 events). The difference in AE incidence between the groups was statistically significant (p=0.0102). Since so few patients did not use antibiotics, it is difficult to draw any conclusions or determine clinical significance from this analysis.

When analyzing AE incidence by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, it was 16.07% (18/112 subjects, 22 events) in subjects using urinary catheterization and 5.56% (18/324 subjects, 24 events) in subjects without urinary catheterization, and difference in AE incidences between the groups was statistically significant (p=0.0005). It should be noted that subjects who initiate catheterization are at increased risk to develop a urinary tract infection. However, as the analysis did not specify the type of AEs experienced in the group of patients who initiated catheterization after BOTOX treatment, it is difficult to draw any conclusions or determine clinical significance from this analysis.

3.1.7 Other AEs

No distant spread of toxin was identified.

3.2 Effectiveness data (Neurogenic Detrusor Overactivity and Overactive Bladder)

3.2.1 Effectiveness evaluation

Effectiveness evaluation was conducted by the subject using incontinence questionnaire (ICIQ-SF) before the study drug administration and 1 ~ 4 month(s) after the study drug administration. Evaluation should be carried out based on the change in total score before and after the study drug administration. A decrease in score represents an improvement.

When comparing and analyzing changes in the ICIQ score in 612 subjects of the effectiveness population, the mean score decreased by 6.19±6.24 from 12.67±6.30 before the study drug administration to 6.48±6.20 after the study drug administration. The mean change in ICIQ from baseline was statistically significant (p<0.0001) (Table 172).

Table 172. ICIQ Score Variation (Neurogenic Detrusor Overactivity and Overactive Bladder)

	n	mean± std	median	min~ max

	n	mean± std	median	min~ max
before BOTOX injection	612	12.67± 6.30	15.00	0.00~ 21.00
after BOTOX injection	612	6.48± 6.20	6.00	0.00~ 21.00
after BOTOX injection - before BOTOX injection	612	-6.19± 6.24	-6.00	-21.00~ 13.00
p-value(paired t-test)		<0.0001		

When analyzing changes in ICIQ scores in the effectiveness population by range, it was '< 5' in 51.14% (313/612 subjects), '≥ -5 to < 0' in 23.53% (144/612 subjects), '≥ 0 to < 5' in 23.37% (143/612 subjects), and '≥ 5' in 1.96% (12/612 subjects) (Table 173).

Table 173. Change in ICIQ Score by range (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total n(%)
< -5	313(51.14)
≥ -5 to < 0	144(23.53)
≥ 0 to < 5	143(23.37)
≥ 5	12(1.96)
Total	612(100.00)

The denominator is number of total subjects.

The mean time to ICIQ assessment completion from baseline was 60.87±109.80 days (Table 174).

Table 174. Time to ICIQ assessment completion (Neurogenic Detrusor Overactivity and Overactive Bladder)

	Total (N=612)
n	612
mean±std (days)	60.87± 109.80
median	44.00
min ~ max	17.00~ 2,184.00

Duration between baseline and follow-up ICIQ completion = Date of after BOTOX treatment - Date of before BOTOX treatment + 1

When investigating the degree of urine leaks before/after the study drug administration by multiple counting, 'Never-urine does not leak' accounted for 14.33% (87/607 subjects) before the study drug administration, but it accounted for 46.70% (283/606 subjects) after the administration (Table 175).

'Leaks before you can get to the toilet' accounted for 45.14% (274/607 subjects) before the study drug administration, but it accounted for 23.27% (141/606 subjects) after the administration (Table 175).

'Leaks when you cough or sneeze' accounted for 25.54% (155/607 subjects) before the study drug administration, but it accounted for 14.36% (87/606 subjects) after the administration (Table 175). Note that 'Leaks when you cough or sneeze' is a symptom of stress incontinence, which is not indicated for BOTOX.

'Leaks when you are asleep' accounted for 19.93% (121/607 subjects) before the study drug administration, but it accounted for 10.40% (63/606 subjects) after the study drug administration (Table 175).

'Leaks when are physically active/exercising' accounted for 19.60% (119/607 subjects) before the study drug administration, but it accounted for 9.90% (60/606 subjects) after the study drug administration (Table 175). Note that 'Leaks when are physically active/exercising' is a symptom of stress incontinence, which is not indicated for BOTOX.

'Leaks when you have finished urinating and are dressed' accounted for 13.18% (80/607 subjects) before the study drug administration, but it accounted for 7.59% (46/606 subjects) after the study drug administration (Table 175).

'Leaks for no obvious reason' accounted for 42.67% (259/607 subjects) before the study drug administration, but it accounted for 18.32% (111/606 subjects) after the study drug administration (Table 175).

'Leaks all the time' accounted for 14.66% (89/607 subjects) before the study drug administration , but it accounted for 4.95% (30/606 subjects) after the study drug administration (Table 175).

Table 175. Degree of urine leaks before/after the study drug administration (Neurogenic Detrusor Overactivity and Overactive Bladder)

Overlapped¶	Before BOTOX n(%)	After BOTOX n(%)
Never-urine does not leak	87(14.33)	283(46.70)
Leaks before you can get to the toilet	274(45.14)	141(23.27)
Leaks when you cough or sneeze	155(25.54)	87(14.36)
Leaks when you are asleep	121(19.93)	63(10.40)
Leaks when are physically active/exercising	119(19.60)	60(9.90)
Leaks when you have finished urinating and are dressed	80(13.18)	46(7.59)
Leaks for no obvious reason	259(42.67)	111(18.32)
Leaks all the time	89(14.66)	30(4.95)
Total	607(100.00)	606(100.00)

The denominator is number of total subjects.
¶ The same subject may appear in different categories.
Missing: 5 (Before BOTOX), 6 (After BOTOX)

3.2.2 Effectiveness evaluation by factor

A. Background factors

When analyzing ICIQ score change before/after the study drug administration by age, the mean decrease of 6.36±5.82 was found in subjects '< 50 years', and it was statistically significant

(p<0.0001). The mean decrease of 6.47±6.33 was found in '≥ 50 years to < 60 years', which was statistically significant (p<0.0001). The mean decrease of 5.20±6.17 was found in '≥ 60 years to < 70 years', which was statistically significant (p<0.0001). The mean decrease of 6.52±6.46 was found in '≥ 70 years', which was statistically significant (p<0.0001). Difference in ICIQ score change among the groups was not statistically significant (p=0.2330) (Table 176).

When analyzing ICIQ score change before/after the study drug administration by sex, the mean decrease of 5.56±5.41 was found in 'Male' subjects, and it was statistically significant (p<0.0001). The mean decrease of 6.51±6.60 was found in 'Female' subjects, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.0587) (Table 176).

When analyzing ICIQ score change before/after the study drug administration by treatment setting, the mean decrease of 6.59±5.89 was found in 'Outpatient' subjects, and it was statistically significant (p<0.0001). The mean decrease of 5.88±6.48 was found in 'Inpatient', which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1602) (Table 176).

When analyzing ICIQ score change before/after the study drug administration by indication which subjects were diagnosed with, the mean decrease of 6.84±5.53 was found in subjects diagnosed with NDO, which was statistically significant (p<0.0001). The mean decrease of 6.00±6.41 was found in OAB, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1394) (Table 176).

When analyzing ICIQ score change before/after the study drug administration by underlying neurologic conditions (multiple counting allowed) in subjects diagnosed with NDO, subjects with 'Urge urinary incontinence' showed the mean decrease of 7.80±6.26, which was statistically significant (p=0.0495). The mean decrease of 6.80±5.53 was found in 'Spinal Cord Injury' subjects, which was statistically significant (p<0.0001). Decrease of 10.00 was found in 'Other' (Table 176).

When analyzing ICIQ score change before/after the study drug administration by symptoms (multiple counting allowed) in subjects diagnosed with OAB, subjects with 'Urge urinary incontinence' showed the mean decrease of 7.02±6.48, which was statistically significant (p<0.0001). The mean decrease of 5.77±6.34 was found in 'Urgency', which was statistically significant (p<0.0001). The mean decrease of 5.71±6.18 was found in 'Frequency', which was statistically significant (p<0.0001). The mean decrease of 4.66±5.61 was found in 'Other', which was statistically significant (p<0.0001) (Table 176).

Among female subjects, there was no pregnant subject (Table 176).

Table 176. Effectiveness evaluation by background factor (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Age	< 50 years	139	-6.36± 5.82	-6.00	-21.00~ 5.00	<0.0001	0.2330
	≥ 50 years to < 60 years	132	-6.47± 6.33	-6.50	-21.00~ 9.00	<0.0001	
	≥ 60 years to < 70 years	133	-5.20± 6.17	-4.00	-20.00~ 10.00	<0.0001	
	≥ 70 years	208	-6.52± 6.46	-6.00	-21.00~ 13.00	<0.0001	
Sex	Male	208	-5.56± 5.41	-6.00	-21.00~ 9.00	<0.0001	0.0587

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
	Female	404	-6.51± 6.60	-6.00	-21.00~ 13.00	<0.0001	
Treatment Setting	Outpatient	266	-6.59± 5.89	-7.00	-21.00~ 9.00	<0.0001	0.1602
	Inpatient	346	-5.88± 6.48	-5.00	-21.00~ 13.00	<0.0001	
Currently pregnant	Yes	0					NA
* for female	No	404	-6.51± 6.60	-6.00	-21.00~ 13.00	<0.0001	
Diagnosis	NDO	134	-6.84± 5.53	-7.00	-21.00~ 10.00	<0.0001	0.1394
	OAB	478	-6.00± 6.41	-5.00	-21.00~ 13.00	<0.0001	
Underlying neurologic condition§	Multiple Sclerosis	5	-7.80± 6.26	-6.00	-16.00~ 0.00	0.0495	NA
* for patients with NDO	Spinal Cord Injury	129	-6.80± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Overlapped¶	Other	1	-10.00	-10.00	-10.00~ -10.00		
Symptoms	Urge urinary incontinence	351	-7.02± 6.48	-6.00	-21.00~ 13.00	<0.0001	NA
* for patients with OAB	Urgency	320	-5.77± 6.34	-5.00	-21.00~ 13.00	<0.0001	
Overlapped¶	Frequency	348	-5.71± 6.18	-4.00	-21.00~ 13.00	<0.0001	
	Other	86	-4.66± 5.61	-3.00	-18.00~ 7.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.
§ subject had 2 underlying neurologic conditions (Spinal Cord Injury and Other (Stroke)).

B. Past treatment history

When analyzing ICIQ score change before/after the study drug administration by previous anticholinergic therapy, subjects who had received anticholinergic therapy showed the mean decrease of 6.20±6.23, which was statistically significant (p<0.0001). Subjects without previous anticholinergic therapy showed the mean decrease of 5.20±7.07, which was statistically significant (p=0.0450). Difference in ICIQ score change between the groups was not statistically significant (p=0.6145) (Table 177).

When analyzing ICIQ score change before/after the study drug administration by past use of other OAB drugs after anticholinergic therapy in subjects diagnosed with OAB in the safety population, subjects who had used OAB drug showed the mean decrease of 5.61±6.17, which was statistically significant (p=0.0001). Subjects without experience of other treatments showed the mean decrease of 6.47±6.67, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1441) (Table 177).

When analyzing ICIQ score change before/after the study drug administration by previous use of sacral neuromodulation therapy, the mean decrease of 7.00±7.00 was found in subjects who had received sacral neuromodulation therapy, which was statistically significant (p=0.0171). Subjects without previous sacral neuromodulation therapy showed the mean decrease of 6.17±6.23, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.6936) (Table 177).

When analyzing ICIQ score change before/after the study drug administration by past treatment history with the study drug for other indication or other botulinum toxin, the mean decrease of 4.43±5.63 were found in subjects who had used the study drug or other botolimum toxin, which was statistically significant (p=0.0002). Subjects who had not been previously treated with BOTOX or other botulinum toxin showed the mean decrease of 6.28±6.26, which was

statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.1145) (Table 177).

Table 177. Effectiveness evaluation by past treatment history (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Previous Anticholinergic Therapy	Yes	602	-6.20± 6.23	-6.00	-21.00~ 13.00	<0.0001	0.6145
	No	10	-5.20± 7.07	-1.50	-16.00~ 3.00	0.0450	
Another OAB drug also used after anticholinergic therapy * for patients with OAB	Yes	259	-5.61± 6.17	-4.00	-21.00~ 9.00	<0.0001	0.1441
	No	219	-6.47± 6.67	-6.00	-21.00~ 13.00	<0.0001	
Previous Use of Sacral Neuromodulation Therapy	Yes	9	-7.00± 7.00	-10.00	-18.00~ 0.00	0.0171	0.6936
	No	603	-6.17± 6.23	-6.00	-21.00~ 13.00	<0.0001	
Previous BOTOX or Other Botulinum Toxin Treatment	Yes	30	-4.43± 5.63	-2.00	-21.00~ 2.00	0.0002	0.1145
	None	582	-6.28± 6.26	-6.00	-21.00~ 13.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

C. Medical history

When analyzing ICIQ score change before/after the study drug administration by medical history including surgeries and complications of underlying diseases, the mean decrease of 6.15±6.38 was found in subjects with medical history, which was statistically significant (p<0.0001). Subjects without medical history showed the mean decrease of 6.15±5.31, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.9983) (Table 178).

ICIQ score change before/after the study drug administration by medical history type (multiple counting allowed) are presented in the table below (Table 178).

When analyzing ICIQ score change before/after the study drug administration by allergy history, the mean decrease of 5.09±6.69 was found in subjects with allergy history, which was statistically significant (p=0.0001). Subjects without allergy history showed the mean decrease of 6.25±6.21, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.2911) (Table 178).

ICIQ score change before/after the study drug administration by allergens (multiple counting allowed) are presented in the table below (Table 178).

Table 178. Effectiveness evaluation by medical history (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Medical History, Including Surgeries and	Yes	518	-6.15± 6.38	-6.00	-21.00~ 13.00	<0.0001	0.9983
	None	91	-6.15± 5.31	-6.00	-21.00~ 2.00	<0.0001	

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Complications of Underlying Diseases							
	Details for Medical History by dictionary (Overlapped¶)						
	Diseases of the circulatory system	272	-6.25± 6.17	-6.00	-21.00~ 10.00	<0.0001	
	Factors influencing health status and contact with health services	225	-6.23± 6.68	-5.00	-21.00~ 10.00	<0.0001	
	Endocrine, nutritional and metabolic diseases	183	-6.27± 6.18	-6.00	-21.00~ 10.00	<0.0001	
	Diseases of the genitourinary system	130	-4.99± 5.94	-3.00	-21.00~ 9.00	<0.0001	
	Diseases of the digestive system	130	-5.88± 6.82	-4.50	-21.00~ 13.00	<0.0001	
	Diseases of the musculoskeletal system and connective tissue	131	-5.85± 6.53	-5.00	-21.00~ 10.00	<0.0001	
	Neoplasms	98	-5.80± 6.88	-5.00	-21.00~ 13.00	<0.0001	
	Mental and behavioural disorders	95	-5.93± 6.62	-6.00	-21.00~ 13.00	<0.0001	
	Diseases of the nervous system	87	-6.22± 6.95	-4.00	-21.00~ 13.00	<0.0001	
	Diseases of the respiratory system	52	-5.69± 6.55	-3.00	-21.00~ 5.00	<0.0001	
	Diseases of the eye and adnexa	42	-4.83± 6.60	-4.00	-18.00~ 10.00	<0.0001	
	Injury, poisoning and certain other consequences of external causes	41	-5.78± 6.22	-5.00	-19.00~ 3.00	<0.0001	
	Certain infectious and parasitic diseases	35	-6.09± 6.23	-5.00	-21.00~ 1.00	<0.0001	
	Diseases of the skin and subcutaneous tissue	27	-6.52± 7.02	-3.00	-19.00~ 1.00	<0.0001	
	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	14	-5.43± 4.65	-6.00	-14.00~ 1.00	0.0008	
	Diseases of the ear and mastoid process	11	-5.82± 5.88	-3.00	-15.00~ 1.00	0.0083	
	Congenital malformations, deformations and chromosomal abnormalities	5	-6.80± 4.32	-7.00	-12.00~ -2.00	0.0245	
	Pregnancy, childbirth and the puerperium	1	-18.00	-18.00	-18.00~ -18.00		
	Symptoms, signs and abnormal clinical and laboratory findings, NEC	65	-5.54± 6.13	-4.00	-19.00~ 5.00	<0.0001	
History of Allergies	Yes	34	-5.09± 6.69	-4.50	-20.00~ 7.00	<0.0001	0.2911
	None	578	-6.25± 6.21	-6.00	-21.00~ 13.00	<0.0001	
	Details for History of Allergies by dictionary						
	Factors influencing health status and contact with health services	17	-5.41± 6.04	-5.00	-20.00~ 1.00	0.0020	
	Injury, poisoning and certain other consequences of external causes	17	-4.76± 7.46	-4.00	-17.00~ 7.00	0.0181	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.
Dictionary: KCD 7 and ICD 10
Unknown: 3 (Medical History, Including Surgeries and Complications of Underlying Diseases)

D. Concomitant medications

When analyzing ICIQ score change before/after the study drug administration by use of concomitant medications, the mean decrease 6.27±6.23 was found in subjects with concomitant medications, which was statistically significant (p<0.0001). Subjects without concomitant medications showed the mean decrease of 4.59±6.19, which was statistically significant (p=0.0004). Difference in ICIQ score change between the groups was not statistically

significant (p=0.1570) (Table 179).

ICIQ score change before/after the study drug administration by concomitant medication type (multiple counting allowed) are presented in the table below (Table 179).

Table 179. Effectiveness evaluation by concomitant medications (Neurogenic Detrusor Overactivity and Overactive Bladder)

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Yes	583	-6.27± 6.23	-6.00	-21.00~ 13.00	<0.0001	0.1570
No	29	-4.59± 6.19	-5.00	-18.00~ 9.00	0.0004	
Details for Concomitant Medication by dictionary (Overlapped¶)						
Anaesthetics- Local & General	522	-6.32± 6.21	-6.00	-21.00~ 13.00	<0.0001	
Anaesthetics - Local & General	522	-6.32± 6.21	-6.00	-21.00~ 13.00	<0.0001	
Central Nervous System	396	-6.51± 6.30	-6.00	-21.00~ 13.00	<0.0001	
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	165	-7.13± 6.27	-8.00	-21.00~ 7.00	<0.0001	
Analgesics (Non-Opioid) & Antipyretics	156	-6.88± 6.43	-7.00	-21.00~ 7.00	<0.0001	
Analgesics (Opioid)	115	-6.07± 6.38	-5.00	-21.00~ 7.00	<0.0001	
Hypnotics & Sedatives	81	-4.30± 6.48	-2.00	-21.00~ 13.00	<0.0001	
Antidepressants	72	-6.96± 6.48	-8.00	-21.00~ 13.00	<0.0001	
Drugs For Neuropathic Pain	48	-7.27± 4.78	-7.50	-21.00~ 1.00	<0.0001	
Anxiolytics	46	-6.89± 6.18	-8.00	-18.00~ 13.00	<0.0001	
Anticonvulsants	44	-7.82± 7.37	-7.00	-21.00~ 13.00	<0.0001	
Nootropics & Neurotonics	33	-6.12± 5.70	-7.00	-18.00~ 5.00	<0.0001	
Neurodegenerative Disease Drugs	22	-5.55± 6.91	-3.00	-21.00~ 3.00	0.0011	
Antiparkinsonian Drugs	19	-7.79± 7.78	-6.00	-21.00~ 3.00	0.0004	
Antipsychotics	14	-7.86± 7.62	-7.50	-18.00~ 2.00	0.0020	
Antivertigo Drugs	4	-3.00± 6.00	0.00	-12.00~ 0.00	0.3910	
Antimigraine Preparations	2	-8.00± 2.83	-8.00	-10.00~ -6.00	0.1560	
Other CNS Drugs & Agents for ADHD	1	-18.00	-18.00	-18.00~ -18.00		
Gastrointestinal & Hepatobiliary System	329	-6.57± 6.31	-7.00	-21.00~ 13.00	<0.0001	
Antacids, Antireflux Agents & Antiulcerants	212	-6.48± 6.41	-7.00	-21.00~ 13.00	<0.0001	
GIT Regulators, Antiflatulents & Anti-inflammatories	111	-5.79± 5.83	-7.00	-21.00~ 13.00	<0.0001	
Digestives	70	-7.40± 6.92	-6.50	-21.00~ 5.00	<0.0001	
Laxatives, Purgatives	70	-7.60± 6.37	-7.00	-21.00~ 2.00	<0.0001	
Antiemetics	32	-7.16± 6.85	-5.50	-21.00~ 2.00	<0.0001	
Antispasmodics	22	-4.50± 6.38	-1.00	-17.00~ 7.00	0.0034	
Antidiarrheals	12	-7.50± 7.37	-6.50	-20.00~ 0.00	0.0047	
Cholagogues, Cholelitholytics & Hepatic Protectors	9	-7.56± 7.91	-5.00	-21.00~ 2.00	0.0209	
Other Gastrointestinal Agents	1	-18.00	-18.00	-18.00~ -18.00		
Miscellaneous	4	-9.25± 6.80	-10.50	-16.00~ 0.00	0.0725	
Cardiovascular & Hematopoietic System	244	-6.34± 6.17	-6.00	-21.00~ 10.00	<0.0001	
Dyslipidaemic Agents	88	-6.70± 6.07	-7.00	-21.00~ 7.00	<0.0001	
Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)	89	-6.85± 6.33	-6.00	-21.00~ 10.00	<0.0001	
Calcium Antagonists	67	-5.27± 5.78	-4.00	-19.00~ 10.00	<0.0001	
Angiotensin II Antagonists	52	-6.42± 6.00	-7.00	-21.00~ 10.00	<0.0001	
Other Antihypertensives	38	-6.21± 4.77	-5.50	-17.00~ 1.00	<0.0001	
Haemostatics	34	-4.12± 4.91	-2.50	-13.00~ 7.00	<0.0001	
Beta-Blockers	33	-5.36± 6.07	-5.00	-21.00~ 3.00	<0.0001	

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Peripheral Vasodilators & Cerebral Activators	23	-8.30± 6.65	-7.00	-19.00~ 1.00	<0.0001	
Diuretics	14	-5.79± 6.17	-3.50	-19.00~ 0.00	0.0038	
Anti-Anginal Drugs	15	-6.07± 5.19	-6.00	-16.00~ 0.00	0.0005	
Other Cardiovascular Drugs	13	-9.69± 6.14	-9.00	-21.00~ -1.00	0.0001	
Vasoconstrictors	8	-5.00± 6.76	-3.50	-18.00~ 2.00	0.0748	
Cardiac Drugs	6	-3.67± 6.35	-1.50	-16.00~ 1.00	0.2161	
Phlebitis & Varicose Preparations	4	-8.00± 10.42	-7.50	-20.00~ 3.00	0.2224	
Antidiuretics	3	-2.33± 4.04	0.00	-7.00~ 0.00	0.4226	
Haematopoietic Agents	2	-0.50± 0.71	-0.50	-1.00~ 0.00	0.5000	
ACE Inhibitors/Direct Renin Inhibitors	1	-18.00	-18.00	-18.00~ -18.00		
Miscellaneous	7	-7.86± 7.56	-11.00	-17.00~ 0.00	0.0333	
Musculo-Skeletal System	97	-7.43± 6.51	-7.00	-21.00~ 10.00	<0.0001	
Muscle Relaxants	60	-6.58± 5.70	-6.00	-21.00~ 7.00	<0.0001	
Neuromuscular Disorder Drugs	35	-8.63± 6.58	-9.00	-21.00~ 0.00	<0.0001	
Other Drugs Acting on the Musculo-Skeletal System	17	-6.53± 8.19	-5.00	-21.00~ 7.00	0.0046	
Anti-Inflammatory Enzymes	12	-9.75± 7.07	-9.00	-21.00~ 0.00	0.0006	
Disease-Modifying Anti-Rheumatic Drugs (DMARDs)	5	-1.40± 7.70	-3.00	-11.00~ 10.00	0.7052	
Hyperuricemia & Gout Preparations	1	-14.00	-14.00	-14.00~ -14.00		
Endocrine & Metabolic System	102	-5.76± 6.22	-5.00	-21.00~ 10.00	<0.0001	
Antidiabetic Agents	73	-6.47± 6.01	-6.00	-21.00~ 10.00	<0.0001	
Other Agents Affecting Metabolism	17	-2.76± 5.09	0.00	-11.00~ 7.00	0.0398	
Thyroid Hormones	12	-8.08± 8.05	-10.00	-19.00~ 7.00	0.0052	
Agents Affecting Bone Metabolism	10	-5.10± 6.30	-4.50	-17.00~ 3.00	0.0306	
Insulin Preparations	5	-7.20± 7.16	-6.00	-18.00~ 0.00	0.0876	
Antithyroid Agents	1	-2.00	-2.00	-2.00~ -2.00		
Miscellaneous	1	0.00	0.00	0.00~ 0.00		
Intravenous & Other Sterile Solutions	86	-6.70± 6.36	-7.00	-21.00~ 5.00	<0.0001	
Intravenous & other sterile solutions	86	-6.70± 6.36	-7.00	-21.00~ 5.00	<0.0001	
Genito-Urinary System	67	-6.21± 6.13	-5.00	-21.00~ 9.00	<0.0001	
Drugs for Bladder & Prostate Disorders	64	-6.45± 6.16	-6.00	-21.00~ 9.00	<0.0001	
Drugs for Erectile Dysfunction and Ejaculatory Disorders	6	-3.17± 8.57	-1.50	-16.00~ 9.00	0.4067	
Other Drugs Acting on the Genito-Urinary System	1	-11.00	-11.00	-11.00~ -11.00		
Respiratory System	54	-6.28± 7.71	-4.50	-21.00~ 7.00	<0.0001	
Antiasthmatic & COPD Preparations	36	-6.08± 7.95	-4.00	-21.00~ 7.00	<0.0001	
Cough & Cold Preparations	30	-7.87± 7.44	-6.50	-21.00~ 7.00	<0.0001	
Nasal Decongestant & Other Nasal Preparations	3	-4.33± 12.06	-3.00	-17.00~ 7.00	0.5971	
Oncology	52	-6.56± 5.07	-7.00	-18.00~ 2.00	<0.0001	
Supportive Care Therapy	46	-6.54± 5.27	-7.00	-18.00~ 2.00	<0.0001	
Hormonal Chemotherapy	4	-6.50± 2.89	-6.50	-10.00~ -3.00	0.0204	
Cytotoxic Chemotherapy	2	-7.00± 5.66	-7.00	-11.00~ -3.00	0.3305	
Vitamins & Minerals	47	-7.21± 5.81	-7.00	-21.00~ 3.00	<0.0001	
Calcium / with Vitamins	26	-6.54± 5.46	-5.50	-18.00~ 3.00	<0.0001	
Vitamins & Minerals (Pre & Post Natal) / Antianemics	10	-5.40± 4.14	-4.50	-11.00~ 0.00	0.0026	
Vitamin B-complex / with C	9	-6.78± 5.91	-9.00	-16.00~ 3.00	0.0088	
Vitamins &/or Minerals	8	-8.50± 6.14	-8.00	-21.00~ 0.00	0.0058	
Vitamin C	1	-2.00	-2.00	-2.00~ -2.00		
Vitamins & Minerals (Geriatric)	1	-21.00	-21.00	-21.00~ -21.00		
Vitamins A, D & E	1	-12.00	-12.00	-12.00~ -12.00		
Miscellaneous	1	-14.00	-14.00	-14.00~ -14.00		
Anti-infectives (systemic)	27	-6.15± 6.74	-3.00	-21.00~ 2.00	<0.0001	
Cephalosporins	12	-5.17± 7.15	-2.50	-21.00~ 2.00	0.0293	

	n	mean± std	median	min~ max	p-value (a)	p-value (b)
Quinolones	8	-6.25± 6.11	-6.00	-16.00~ 2.00	0.0232	
Antivirals	5	-6.40± 6.69	-3.00	-17.00~ -1.00	0.0993	
Antifungals	4	-3.75± 5.56	-1.50	-12.00~ 0.00	0.2702	
Macrolides	1	-12.00	-12.00	-12.00~ -12.00		
Anti-TB Agents	1	-16.00	-16.00	-16.00~ -16.00		
Antibacterial Combinations	1	-2.00	-2.00	-2.00~ -2.00		
Tetracyclines	1	0.00	0.00	0.00~ 0.00		
Allergy & Immune System	26	-7.46± 5.81	-7.50	-19.00~ 0.00	<0.0001	
Antihistamines & Antiallergics	21	-6.71± 5.62	-4.00	-19.00~ 0.00	<0.0001	
Immunosuppressants	4	-11.00± 6.98	-12.50	-17.00~ -2.00	0.0511	
Vaccines, Antisera & Immunologicals	1	-9.00	-9.00	-9.00~ -9.00		
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	21	-6.14± 6.44	-4.00	-21.00~ 1.00	0.0003	
Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	21	-6.14± 6.44	-4.00	-21.00~ 1.00	0.0003	
Hormones	18	-7.44± 6.51	-9.00	-19.00~ 2.00	0.0001	
Corticosteroid Hormones	13	-7.85± 6.72	-9.00	-19.00~ 0.00	0.0012	
Oestrogens & Progesterones & Related Synthetic Drugs	3	-7.67± 6.11	-9.00	-13.00~ -1.00	0.1618	
Other Drugs Affecting Hormonal Regulation	2	-4.50± 9.19	-4.50	-11.00~ 2.00	0.6145	
Trophic Hormones & Related Synthetic Drugs	1	-12.00	-12.00	-12.00~ -12.00		
Nutrition	19	-9.42± 7.78	-10.00	-21.00~ 7.00	<0.0001	
Parenteral Nutritional Products	13	-11.62± 6.59	-11.00	-21.00~ 0.00	<0.0001	
Electrolytes	8	-8.75± 7.91	-10.00	-18.00~ 7.00	0.0166	
Appetite Enhancers	3	-7.33± 12.10	-3.00	-21.00~ 2.00	0.4039	
Enteral / Nutritional Products	1	-7.00	-7.00	-7.00~ -7.00		
Supplements & Adjuvant Therapy	1	-17.00	-17.00	-17.00~ -17.00		
Eye	12	-7.00± 5.98	-7.50	-18.00~ 1.00	0.0019	
Ophthalmic Lubricants	5	-4.60± 3.21	-5.00	-8.00~ 0.00	0.0327	
Eye Anti-infectives & Antiseptics	3	-7.67± 7.51	-8.00	-15.00~ 0.00	0.2189	
Eye Corticosteroids	2	-13.00± 7.07	-13.00	-18.00~ -8.00	0.2338	
Ophthalmic Decongestants, Anesthetics, Anti-inflammatories	2	-9.00± 12.73	-9.00	-18.00~ 0.00	0.5000	
Other Eye Preparations	2	-4.50± 7.78	-4.50	-10.00~ 1.00	0.5635	
Antiglaucoma Preparations	1	-11.00	-11.00	-11.00~ -11.00		
Mydriatic Drugs	1	-8.00	-8.00	-8.00~ -8.00		
Dermatologicals	11	-6.36± 5.33	-5.00	-16.00~ 2.00	0.0027	
Topical Corticosteroids	5	-6.60± 5.59	-5.00	-16.00~ -2.00	0.0577	
Other Dermatologicals	2	-6.50± 2.12	-6.50	-8.00~ -5.00	0.1444	
Topical Antibiotics	2	-0.50± 3.54	-0.50	-3.00~ 2.00	0.8743	
Topical Antifungals & Antiparasites	2	-5.00± 4.24	-5.00	-8.00~ -2.00	0.3440	
Emollients & Skin Protectives	1	-2.00	-2.00	-2.00~ -2.00		
Psoriasis, Seborrhea & Ichthyosis Preparations	1	-2.00	-2.00	-2.00~ -2.00		
Skin Antiseptics & Disinfectants	1	-11.00	-11.00	-11.00~ -11.00		
Topical Anti-infectives with Corticosteroids	1	-13.00	-13.00	-13.00~ -13.00		
Ear & Mouth / Throat	1	-8.00	-8.00	-8.00~ -8.00		
Mouth / Throat Preparations	1	-8.00	-8.00	-8.00~ -8.00		
Miscellaneous	8	-1.25± 4.98	-0.50	-8.00~ 7.00	0.5006	
Miscellaneous	8	-1.25± 4.98	-0.50	-8.00~ 7.00	0.5006	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
¶ The same subject may appear in different categories.

	n	mean± std	median	min~ max	p-value (a)	p-value (b)

Dictionary: KIMS

E. Special population

When analyzing ICIQ score change before/after the study drug administration in elderly and non-elderly groups, the mean decrease of 6.13±6.42 was found in the group of '65 or/and over', which was statistically significant (p<0.0001). The mean decrease of 6.23±6.09 was found in 'below 65 years', which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.8355) (Table 180).

When analyzing ICIQ score change before/after the study drug administration by presence of renal impairment, the mean decrease of 2.14±5.93 was found in subjects with renal impairment which was not statistically significant (p=0.3758), and the mean decrease of 6.23±6.23 was found in subjects without renal impairment which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.0845) (Table 180).

When analyzing ICIQ score change before/after the study drug administration by hepatic impairment, the mean decrease of 3.88±5.89 was found in subjects with hepatic impairment, which was not statistically significant (p=0.1051). Subjects without hepatic impairment showed the mean decrease of 6.22±6.24, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.2917) (Table 180).

Table 180. Effectiveness evaluation in special population (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Elderly	below 65 years	333	-6.23± 6.09	-6.00	-21.00~ 10.00	<0.0001	0.8355
	65 or/and over	279	-6.13± 6.42	-6.00	-21.00~ 13.00	<0.0001	
Renal impairment	Yes	7	-2.14± 5.93	-1.00	-14.00~ 4.00	0.3758	0.0845
	No	605	-6.23± 6.23	-6.00	-21.00~ 13.00	<0.0001	
Hepatic impairment	Yes	8	-3.88± 5.89	-1.50	-16.00~ 1.00	0.1051	0.2917
	No	604	-6.22± 6.24	-6.00	-21.00~ 13.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

F. Information of the study drug administration

All subjects diagnosed with NDO in the effectiveness population received total 200 U in 30 sites, while all subjects diagnosed with OAB in the effectiveness population received total 100 U in 20 sites. Thus, the ICIQ score change before/after the study drug administration was the same as that in each indication-specific population (Table 181).

When analyzing ICIQ score change before/after the study drug administration by use of

anesthesia at the study drug administration, the mean decrease of 5.32±6.31 was found in 'None' anesthesia group, which was statistically significant (p<0.0001). The mean decrease of 6.30±6.03 was found in 'Local' anesthesia group, which was statistically significant (p=0.0001). The mean decrease of 6.25±6.74 was found in 'General' anesthesia group, which was statistically significant (p=0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.5045) (Table 181).

When analyzing the ICIQ score change by use of prophylactic antibiotics before, during, and after the study drug administration, the mean decrease of 6.26±6.21 was found in subjects with antibiotics, which was statistically significant (p<0.0001). Subjects without antibiotics showed the mean decrease of 5.47±6.55, which was statistically significant (p=0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.3742) (Table 181).

Table 181. Effectiveness evaluation by the information of study drug administration (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Number of Injection Sites	20	478	-6.00± 6.41	-5.00	-21.00~ 13.00	<0.0001	0.1394
	30	134	-6.84± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Total Units Injected	100	478	-6.00± 6.41	-5.00	-21.00~ 13.00	<0.0001	0.1394
	200	134	-6.84± 5.53	-7.00	-21.00~ 10.00	<0.0001	
Anesthesia	None	63	-5.32± 6.31	-5.00	-18.00~ 9.00	<0.0001	0.5045
	Local	399	-6.30± 6.03	-6.00	-21.00~ 13.00	<0.0001	
	General	150	-6.25± 6.74	-4.00	-21.00~ 7.00	<0.0001	
Prophylactic Antibiotic Use	Yes	557	-6.26± 6.21	-6.00	-21.00~ 13.00	<0.0001	0.3742
	No	55	-5.47± 6.55	-4.00	-21.00~ 8.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA

G. Clean intermittent catheterization

When analyzing ICIQ score change before/after the study drug administration by use of clean intermittent catheterization before the study drug administration, the mean decrease of 6.13±5.88 was found in subjects with clean intermittent catheterization, which was statistically significant (p<0.0001). Subjects without clean intermittent catheterization showed the mean decrease of 6.22±6.43, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.8628) (Table 182).

When analyzing ICIQ score change before/after the study drug administration by use of urinary catheterization after the study drug administration among subjects who did not use urinary catheterization before the study drug administration, the mean decrease of 6.20±6.44 was found in subjects with urinary catheterization, which was statistically significant (p<0.0001). Subjects without urinary catheterization showed the mean decrease of 6.23±6.44, which was statistically significant (p<0.0001). Difference in ICIQ score change between the groups was not statistically significant (p=0.9742). Among the subjects with urinary catheterization, the mean decrease of 9.18±6.34 was found in subjects who initiated catheterization due to urinary retention (p<0.0001) and the mean decrease of 5.62±6.31 was found in subjects who initiated

catheterization due to other reason (p<0.0001) (Table 182).

Table 182. Effectiveness evaluation by use of clean intermittent catheterization (Neurogenic Detrusor Overactivity and Overactive Bladder)

		n	mean± std	median	min~ max	p-value (a)	p-value (b)
Routine Urinary Catheterization(before BOTOX)	Yes	219	-6.13±5.88	-6.00	-21.00~ 10.00	<0.0001	0.8628
	No	393	-6.22±6.43	-5.00	-21.00~ 13.00	<0.0001	
Initiation of CIC after BOTOX injection§	Yes	109	-6.20±6.44	-5.00	-20.00~ 13.00	<0.0001	0.9742**
§ In subjects not performing CIC before BOTOX	initiated CIC due to "Urinary Retention"	17	-9.18±6.34	-10.00	-18.00~ 0.00	<0.0001	
	initiated CIC due to "Other Reason"	93	-5.62±6.31	-4.00	-20.00~ 13.00	<0.0001	
	No	284	-6.23±6.44	-5.50	-21.00~ 9.00	<0.0001	

The p-value(a) is about that the ICIQ Score change by the subject characteristics.
The p-value(b) is about that relation between Category and the amount of ICIQ Score Change.
(a): Paired t-test
(b): T-test or ANOVA
**The p-value is about that relation between Yes/No and the amount of ICIQ Score Change
Subject of [redacted] initiated CIC after BOTOX injection 2 times due to "Other Reason(insertion immediately after surgery)" and "Urinary Retention".

H. Factors that may affect effectiveness

For the effectiveness evaluation in this PMS, evaluation was conducted by age, sex, treatment setting, pregnancy status, underlying neurological conditions (NDO), symptoms (OAB), past treatment history, medical history, concomitant medications, and the information of study drug administration as well as in special subjects such as the elderly and subject with renal or hepatic impairment. In the evaluation results, there was no factor that significantly affected the effectiveness.

Ⅳ. Discussion on Results and Further Measures (Neurogenic Detrusor Overactivity and Overactive Bladder)

4. Discussion on Results and Further Measures (Neurogenic Detrusor Overactivity and Overactive Bladder)

During this re-examination period, CRFs were collected from a total of 739 subjects. Among the subjects whose CRFs were retrieved, a total of 686 subjects were included in the safety evaluation except 35 subjects who didn't receive Botox for this sutdy due to consent withdrawal or other reasons, 2 subjects of follow-up failure, 6 subjects who were prescribedBOTOX for a neurologic condition other than SCI or MS (ie, indications not included in the local Prescibed Information), and 10 subjects who violate the dosage (ie, subject received an unapproved dosage). Among these safety population, 612 subjects were included in the effectiveness evaluation, except 74 subjects whose record ICIQ Scores at baseline or follow-up on the CRF are not completed.

During the PMS period, 78 AEs occurred in 59 out of 686 subjects in the safety population, which indicated that incidence of AEs was 8.60%. Examining the AEs by PT, 'URINARY RETENTION' accounted for 1.31% (9/686 subjects), 'URINARY TRACT INFECTION' for 1.02% (7/686 subjects) and 'DYSURIA' for 0.73% (5/686 subjects). Among them, 30 events occurred in 26 subjects (3.79%) were ADRs which cannot rule out the relationship to the study drug. Examining the ADRs by PT, 'URINARY RETENTION' accounted for 1.31% (9/686 subjects), 'DYSURIA' for 0.73% (5/686 subjects) and 'URINARY TRACT INFECTION' and 'MYALGIA' for 0.29% (2/686 subjects) each.

During the PMS period, 30 unexpected AEs were reported from 30 subjects (4.36%) in the safety population. Examining the unexpected AEs by PT, 'PELVIC PAIN' and 'HEADACHE' accounted for 0.29% (2/686 subjects) each and others accounted for 0.15% (1/686 subjects) each. Among them, 3 events occurred in 3 subjects (0.44%) were unexpected ADRs which cannot rule out the relationship to the study drug: 'URINARY HESITATION', 'PERINEAL PAIN MALE' and 'TESTIS DISORDER' accounted for 0.15% (1/686 subjects) each. But the causal relationship between 'URINARY HESITATION', 'PERINEAL PAIN MALE', and 'TESTIS DISORDER', and the study drug could not be established based on the study data.

During the PMS period, 9 SAEs were reported from 8 subjects (1.17%) in the safety population. Examining the SAEs by PT, 'PYELONEPHRITIS', 'ANAL PAIN', 'CYSTITIS', 'DEMENTIA', 'NORMAL PRESSURE HYDROCEPHALUS', 'ARTHRALGIA', 'ARTHRITIS', 'HYPONATRAEMIA', and 'ALCOHOL PROBLEM' occurred in 0.15% (1/686 subjects) each. Among them, 1 event of 'PYELONEPHRITIS' occurred in 1 subject (0.15%) was an SADR which cannot rule out the relationship to the study drug.

When classifying and evaluating the expectedness of AEs, 'Expected AE' accounted for 61.54% (48/78 events) and 'Unexpected AE' accounted for 38.46% (30/78 events).

When classifying and evaluating the seriousness of AEs into two of 'Serious' and 'Non-serious', 'Serious' accounted for 11.54% (9/78 events) and 'Non-serious' accounted for 88.46% (69/78 events).

When classifying and evaluating the severity of AEs, 'Mild' occurred in 64.10% (50/78 events) and 'Moderate' in 35.90% (28/78 events).

When classifying and evaluating the outcome of AEs, 'Resolved without sequelae' was reported in 70.51% (55/78 events), 'Ongoing' in 26.92% (21/78 events), and 'Resolved with sequelae' in 2.56% (2/78 events). No fatal outcome has been reported.

When classifying and evaluating the causal relationship of AEs to the study drug, 'Unlikely' was reported in 61.54% (48/78 events), 'Possible' was reported in 15.38% (12/78 events), and 'Certain' was reported in 8.97% (7/78 events).

When classifying and evaluating the causal relationship of AEs to the study drug administration procedure, 'Unlikely' was reported in 74.36% (58/78 events), 'Possible' was reported in 12.82% (10/78 events), and 'Probable/Likely' was reported in 6.41% (5/78 events).

Effectiveness evaluation in subjects with NDO and OAB was conducted using ICIQ before and after the study drug administration. The mean decrease of 6.19±6.24 was found from baseline, and it was statistically significant ($p<0.0001$).

In conclusion, the PMS study results showed no specific trend comparing to previously reported AE incidence and no specific matter that may affect the safety and effectiveness. Therefore, we will continuously monitor the use of BOTOX through routine pharmacovigilence activities.

D. Results Other than PMS

1. Results other than PMS

In addition to the events in PMS results, the following shows the AEs spontaneously reported in Korea during this PMS period (spontaneous reports, clinical studies, literature reports, etc.). Details of the AEs are listed in Annex 4 and 5 of this re-examination report. The names of AEs are coded using WHO-ART 092 convention. All AEs excluding 'not related' to the study drug were categorized into ADRs that cannot rule out the relationship to the study drug.

1.1 Serious AEs/ADRs (Other than PMS)

During this PMS period, 1 SAE was collected in Korea other than PMS: 'URINARY RETENTION' which was an SADR that cannot rule out the relationship to the study drug (Table 183).

Table 183. Onset status of SAEs and SADRs (Other then PMS)

	SAE	SADR
	No. of AE	No. of AE
URINARY RETENTION	1	1
Total	1	1

Dictionary: WHO-ART 092

1.2 Unexpected AEs/ADRs (Other than PMS)

During this PMS period, 1 unexpected AE was collected in Korea other than PMS: 'PARALYSIS PERIPHERAL' which was not an unexpected ADR that cannot rule out the relationship to the study drug (Table 184).

Table 184. Onset status of unexpected AEs and unexpected ADRs (Other than PMS)

	Unexpected AE	Unexpected ADR
	No. of AE	No. of AE
PARALYSIS PERIPHERAL	1	0
Total	1	0

Dictionary: WHO-ART 092

1.3 AEs and ADRs (Other than PMS)

During this PMS period, 3 AEs were collected in Korea other than PMS: 'DYSURIA', 'PARALYSIS PERIPHERAL', and 'URINARY RETENTION'. Among them, 'DYSURIA' and 'URINARY RETENTION' were ADRs that cannot rule out the relationship to the study drug (Table 185).

Table 185. Onset status of AEs and ADRs (Other than PMS)

	AE	ADR
	No. of AE	No. of AE
DYSURIA	1	1
PARALYSIS PERIPHERAL	1	0
URINARY RETENTION	1	1
Total	3	2

Dictionary: WHO-ART 092