



Product registry report – Erratum

Compound(s): Toujeo® / Insulin Glargine 300 U/mL

A 6-month, Multicenter, single-Arm, observational study with a 6-month extension evaluating patient-reported outcomes of insulin Glargine 300 U/mL (Gla-300) in basal/bolus-treated people with T2 diabetes on therapy in a rReal world setting (MAGE study)

Registry number: GLARGL07973

Registry name: MAGE

Registry initiation date [date first patient in (FPI)]: 02-Jun-2016

Registry completion date [last patient completed/last patient out (LPO)]: 28-Aug-2018

Registry design: 6-month, multicenter, prospective, single-arm observational Belgian study with Gla-300 with a 6-month extension.

Report date: 12-Feb-2019

Erratum date: 16-Jul-2019

This registry was performed in compliance with the guidelines for Good Epidemiology Practice. This report has been prepared based on the publication 'Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) – Guidelines for reporting observational studies – Ann Intern Med. 2007'.

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1 HYPOGLYCEMIC EVENTS

In the Clinical Study Report, the descriptive statistics of hypoglycemic events (HEs) and HEs per patient-year were overestimated by the fact that patients having reported no HEs were excluded from the analysis. This analysis had been performed on 49 patients only.

The analyses were therefore performed again in the whole ITT population of 87 patients minus 5 patients who had reported HEs only as adverse events in the AE section of the eCRF (Table 3). The 3 patients having reported HEs both on the appropriate page of the eCRF and as AEs were kept in the analysis. The total population for the new analysis was equal to 82. The whole study period of approximately one year was considered for all patients.

The results are summarized in Table 1 and Table 2.

A total of 1,509 HEs were reported in the 82 patients. This corresponds to a mean \pm SD of 18.4 ± 41.1 HEs per patient and to a mean \pm SD of 20.9 ± 41.0 HEs per patient-year.

A total of 1,244 HEs necessitated counter measures. This corresponds to a mean \pm SD of 15.2 ± 38.4 HEs with counter measures per patient and to a mean \pm SD of 17.4 ± 38.8 HEs with counter measures per patient-year.

A total of 1,346 HEs were symptomatic. This corresponds to a mean \pm SD of 16.4 ± 39.7 symptomatic HEs per patient and to a mean \pm SD of 18.7 ± 39.7 symptomatic HEs per patient-year.

A total of 140 HEs were nocturnal. This corresponds to a mean \pm SD of 1.8 ± 3.8 nocturnal HEs per patient and to a mean \pm SD of 2.3 ± 5.2 nocturnal HEs per patient-year.

A total of 1,497 HEs were confirmed by glucose concentrations below or equal to 70 mg/dL. This corresponds to a mean \pm SD of 18.5 ± 41.2 confirmed HEs per patient and to a mean \pm SD of 21.0 ± 41.1 HEs confirmed by glucose concentrations below or equal to 70 mg/dL per patient-year.

A total of 493 HEs were confirmed by glucose concentrations below 54 mg/dL. This corresponds to a mean \pm SD of 6.1 ± 17.7 confirmed HEs per patient and to a mean \pm SD of 6.6 ± 17.5 confirmed (glucose concentrations below 54 mg/dL) HEs per patient-year.

A total of 16 HEs were severe and only 3 of them required assistance. This corresponds to a mean \pm SD of 0.20 ± 0.85 severe HE per patient and to a mean \pm SD of 0.18 ± 0.75 severe HEs per patient-year.

Table 1 Hypoglycemic events (descriptive statistics) (ITT cohort – 5 patients)

	N		Mean	Median	SD	Min	Max	Sum
	Valid	Missing						
Total number of HEs	82	0	18.4024	2.0000	41.09335	0	245	1509
Number of HEs with counter measures	82	0	15.1707	1.0000	38.35307	0	245	1244
Number of symptomatic HEs	82	0	16.4146	1.0000	39.68361	0	245	1346
Number of nocturnal HEs	78	4	1.7949	.0000	3.82187	0	21	140
Number of HEs confirmed <=70 mg/dL	81	1	18.4815	2.0000	41.20289	0	244	1497
Number of HEs confirmed <54 mg/dL	81	1	6.0864	.0000	17.69477	0	108	493
Number of severe HEs	82	0	.1951	.0000	.85258	0	6	16

Table 2 Hypoglycemic events per patient-year (descriptive statistics) (ITT cohort – 5 patients)

	N		Mean	Median	SD	Min	Max
	Valid	Missing					
Total number of HEs per patient-year	82	0	20.8970	2.5810	40.97655	.00	243.83
Number of HEs with counter measure per patient-year	82	0	17.4402	1.9692	38.79763	.00	243.83
Number of symptomatic HEs per patient-year	82	0	18.7178	1.9692	39.69367	.00	243.83
Number of nocturnal HEs per patient year	78	4	2.3435	.0000	5.21023	.00	31.92
Number of HEs confirmed <=70 mg/dL per patient-year	81	1	20.9686	2.0069	41.09896	.00	242.84
Number of HEs confirmed <54 mg/dL per patient-year	81	1	6.5546	.0000	17.50893	.00	107.49
Number of severe HEs per patient-year	82	0	.1765	.0000	.74693	.00	5.07

Table 3 Identification of 8 patients for whom hypoglycemia events had been reported as AEs and/or also on the appropriate HE form of the eCRF (ITT cohort)

Number	Patient number	Hypoglycemia reported as AE	Hypoglycemic events reported in the appropriate form of the eCRF	Number of hypoglycemic events reported in the appropriate form of the eCRF
1	056-004-005	Yes	Yes	18
2	056-004-009	Yes	No	0
3	056-004-010	Yes	No	0
4	056-004-011	Yes	No	0
5	056-004-015	Yes	Yes	5
6	056-008-004	Yes	No	0
7	056-009-012	Yes	No	0
8	056-010-007	Yes	Yes	17

2 ADVERSE EVENTS

A total of 150 AEs were reported in 55 patients (63.2%) of the ITT cohort during the whole study of approximately one year. They are listed in Table 4. The most frequent AEs, at the exclusion of HEs already reported before, are diarrhea (4.6%), bronchitis (4.6%) and myalgia (3.2%).

In Table 4, the line in yellow indicates that 9 hypoglycemic events have been reported by 8 patients (9.2% of the ITT population). This has to be considered cautiously since we know that at least 54 patients (49 + 5 patients; 62.0% of the ITT population) have reported at least one HE in the appropriate form of the eCRF or in the Adverse Event section of the eCRF. In fact as described previously in Table 3, 5 patients have reported an undetermined number of HEs using a single verbatim in the AE section of the eCRF and 3 have reported HEs both in the appropriate section of the eCRF and in the adverse event section of the eCRF.

Table 4 Adverse events classified according to System Organ Class (SOC) and Preferred Term (PT) (MedDRA Version 21.0; ITT cohort)

SOC	PT	Number of events	% of events	Number of patients	% of patients
Blood and lymphatic system disorders	Anaemia	1	0.7	1	1.1
	Microcytic anaemia	1	0.7	1	1.1
Cardiac disorders	Arteriosclerosis coronary artery	1	0.7	1	1.1
	Cardiac failure	3	2.0	2	2.3
	Ventricular tachycardia	1	0.7	1	1.1
Ear and labyrinth disorders	Cerumen impaction	1	0.7	1	1.1
	Vertigo	2	1.3	1	1.1
Endocrine disorders	Hypothyroidism	1	0.7	1	1.1
	Silent thyroiditis	1	0.7	1	1.1
Eye disorders	Cataract	2	1.3	1	1.1
	Diabetic retinopathy	1	0.7	1	1.1
Gastrointestinal disorders	Abdominal distension	1	0.7	1	1.1
	Colitis	1	0.7	1	1.1
	Constipation	2	1.3	2	2.3
	Dental discomfort	1	0.7	1	1.1
	Diarrhoea	4	2.7	4	4.6
	Gastritis	1	0.7	1	1.1
	Gastroesophageal reflux disease	1	0.7	1	1.1
	Nausea	1	0.7	1	1.1
	Oesophagitis	1	0.7	1	1.1
	Pancreatic steatosis	1	0.7	1	1.1
	Umbilical hernia	1	0.7	1	1.1
	Vomiting	2	1.3	2	2.3

SOC	PT	Number of events	% of events	Number of patients	% of patients	
General disorders and administration site conditions	Chest pain	3	2.0	2	2.3	
	Decreased activity	1	0.7	1	1.1	
	Oedema peripheral	1	0.7	1	1.1	
	Pain	1	0.7	1	1.1	
	Pyrexia	1	0.7	1	1.1	
	Sudden death	1	0.7	1	1.1	
Hepatobiliary disorders	Hepatic steatosis	2	1.3	2	2.3	
Infections and infestations	Bronchitis	4	2.7	4	4.6	
	Candida infection	1	0.7	1	1.1	
	Cellulitis	2	1.3	1	1.1	
	Conjunctivitis	1	0.7	1	1.1	
	Cystitis	2	1.3	2	2.3	
	Diverticulitis	1	0.7	1	1.1	
	Ear infection	1	0.7	1	1.1	
	Erysipelas	1	0.7	1	1.1	
	Escherichia urinary tract infection	1	0.7	1	1.1	
	Fungal infection	1	0.7	1	1.1	
	Gastroenteritis	1	0.7	1	1.1	
	Groin infection	1	0.7	1	1.1	
	Influenza	1	0.7	1	1.1	
	Nasopharyngitis	2	1.3	2	2.3	
	Otitis externa	1	0.7	1	1.1	
	Postoperative wound infection	1	0.7	1	1.1	
	Urinary tract infection	1	0.7	1	1.1	
	Urinary tract infection bacterial	1	0.7	1	1.1	
	Injury, poisoning and procedural complications	Chest injury	1	0.7	1	1.1
		Eye injury	1	0.7	1	1.1
Fall		1	0.7	1	1.1	
Fibula fracture		1	0.7	1	1.1	
Joint injury		1	0.7	1	1.1	
Limb injury		3	2.0	2	2.3	
Post-traumatic neck syndrome		1	0.7	1	1.1	
Upper limb fracture		1	0.7	1	1.1	
Wound complication		1	0.7	1	1.1	
Investigations	Blood pressure increased	1	0.7	1	1.1	
	Glomerular filtration rate abnormal	1	0.7	1	1.1	
	Serum ferritin decreased	1	0.7	1	1.1	
Metabolism and nutrition disorders	Dyslipidaemia	1	0.7	1	1.1	
	Gout	3	2.0	3	3.4	
	Haemochromatosis	1	0.7	1	1.1	

SOC	PT	Number of events	% of events	Number of patients	% of patients
	Hypercholesterolaemia	1	0.7	1	1.1
	Hypoglycaemia	9	6.0	8	9.2
	Hypomagnesaemia	1	0.7	1	1.1
	Vitamin B complex deficiency	1	0.7	1	1.1
	Vitamin B12 deficiency	2	1.3	2	2.3
	Vitamin D deficiency	1	0.7	1	1.1
Musculoskeletal and connective tissue disorders	Arthralgia	1	0.7	1	1.1
	Back pain	2	1.3	2	2.3
	Bursitis	2	1.3	2	2.3
	Dupuytren's contracture	1	0.7	1	1.1
	Haemarthrosis	1	0.7	1	1.1
	Myalgia	3	2.0	3	3.4
	Neck pain	2	1.3	2	2.3
	Osteoarthritis	2	1.3	2	2.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Adenocarcinoma of colon	1	0.7	1	1.1
	Urinary bladder adenoma	1	0.7	1	1.1
Nervous system disorders	Carpal tunnel syndrome	1	0.7	1	1.1
	Headache	2	1.3	2	2.3
	Radial nerve palsy	1	0.7	1	1.1
	Restless legs syndrome	1	0.7	1	1.1
	Tremor	1	0.7	1	1.1
Psychiatric disorders	Depression	1	0.7	1	1.1
	Insomnia	2	1.3	2	2.3
	Sleep disorder	1	0.7	1	1.1
	Stress	1	0.7	1	1.1
Renal and urinary disorders	Acute kidney injury	1	0.7	1	1.1
	Chronic kidney disease	2	1.3	2	2.3
	Renal failure	1	0.7	1	1.1
Reproductive system and breast disorders	Erectile dysfunction	1	0.7	1	1.1
Respiratory, thoracic and mediastinal disorders	Dyspnoea	3	2.0	2	2.3
	Dyspnoea exertional	1	0.7	1	1.1
	Oropharyngeal pain	1	0.7	1	1.1
	Respiratory failure	1	0.7	1	1.1
	Upper respiratory tract inflammation	1	0.7	1	1.1
Skin and subcutaneous tissue disorders	Blister	1	0.7	1	1.1
	Lipodystrophy acquired	1	0.7	1	1.1
	Skin ulcer	1	0.7	1	1.1
Surgical and medical procedures	Coronary arterial stent insertion	1	0.7	1	1.1
Vascular disorders	Hypotension	1	0.7	1	1.1
	Intermittent claudication	2	1.3	2	2.3

SOC	PT	Number of events	% of events	Number of patients	% of patients
	Peripheral arterial occlusive disease	<i>1</i>	<i>0.7</i>	<i>1</i>	<i>1.1</i>
	Peripheral ischaemia	<i>1</i>	<i>0.7</i>	<i>1</i>	<i>1.1</i>
	Phlebitis	<i>1</i>	<i>0.7</i>	<i>1</i>	<i>1.1</i>
	Poor peripheral circulation	<i>1</i>	<i>0.7</i>	<i>1</i>	<i>1.1</i>
	Total	<i>150</i>	<i>100.0</i>	<i>55</i>	<i>63.2</i>