*In February 2013, GlaxoSmithKline (GSK) announced a commitment to further clinical transparency through the public disclosure of GSK Clinical Study Reports (CSRs) on the GSK Clinical Study Register.*

*The following guiding principles have been applied to the disclosure:*

- *Information will be excluded in order to protect the privacy of patients and all named persons associated with the study*
- *Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the* ***GSK Clinical Study Register****.*
- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

As of September 27, 2023

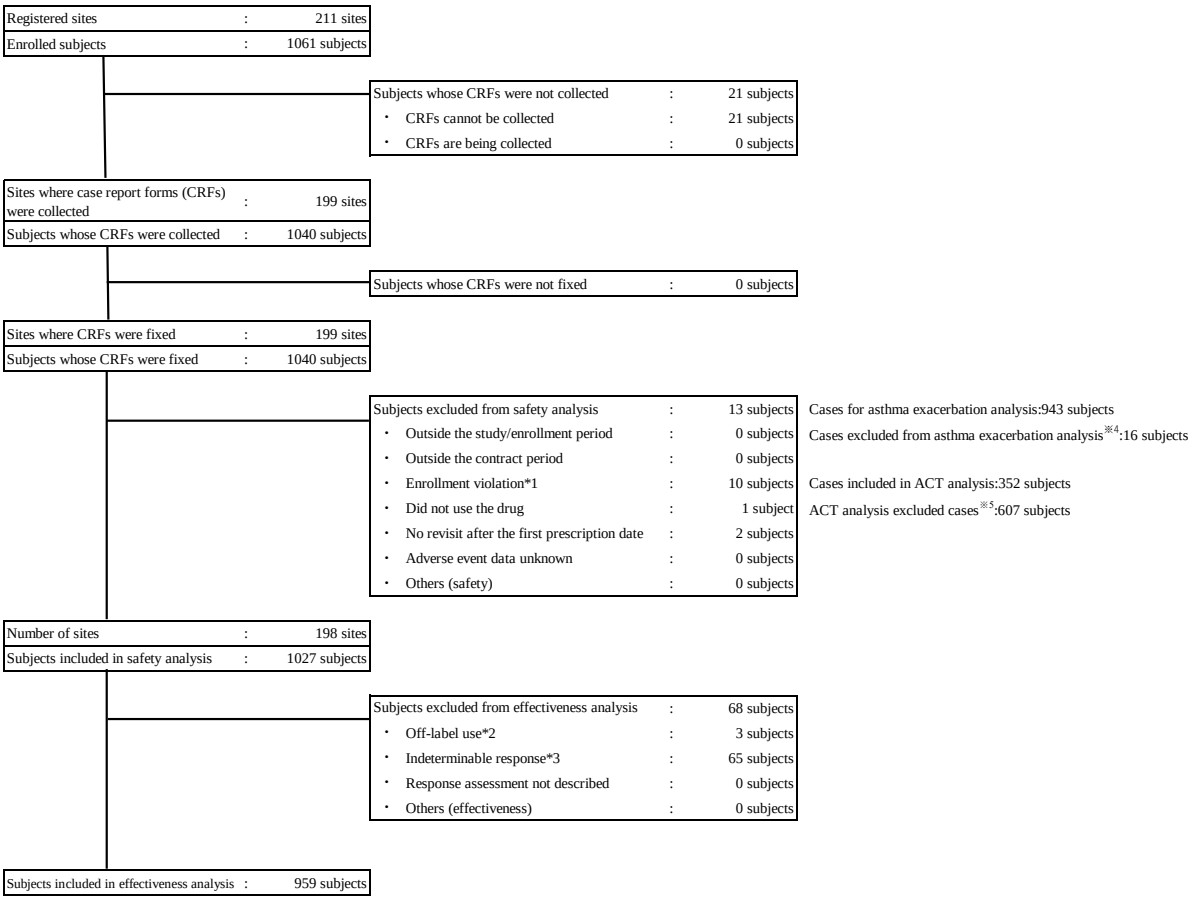



Figure 1 Subject disposition

*1: Subjects who were found to have been enrolled in violation of the enrollment deadline specified in the implementation guideline (within 14 days after the start of administration of this drug (the start date of administration is defined as Day 1)) after collection of the CRF. No adverse drug reactions were observed in these subjects.

*2: Bronchiectasis (1 subject), bronchiolitis (1 subject), and eosinophilic granulomatosis with polyangiitis (1 subject)

*3: Subjects considered indeterminable by the investigator for the following reasons: "indeterminable because the drug was administered only once," "the subject did not visit the hospital after only one administration," "because the drug was administered only once," "because the drug was discontinued since EGPA occurred after the first administration and steroid pulse therapy was administered," "unable to evaluate because of the comorbidity of bronchial asthma attack after the first administration," "because the drug was discontinued for adverse events after the first administration," "because the drug was administered only twice," "the subject did not visit the hospital for three months," "the subject stopped visiting the hospital after the third administration," "because the drug was discontinued for aggravation of EGPA," "because the drug was discontinued too early," "because the patient was transferred too early (personal reason)," "because Fasenra was recommended by the primary care physician, and the drug was discontinued," "the subject stopped visiting the hospital due to coronavirus pandemic," "the subject said he/she had an effect for a few days although the data did not show that," "dropout," "request to discontinue the treatment only once due to high medical expenses," "because the treatment was discontinued after the subject had temporal effects but lost the effect," "because the subject did not visit the hospital," "because the drug was discontinued due to the subject's intention," "due to the subject's request," "because Nucala was discontinued and Fasenra was used at the subject's request," "smoking," "because the subject was dead of disease during the clinical course," "economic reason," "inability to continue the treatment due to economic reason," "discontinuation due to economic reason," "administration only once due to economic reason," "discontinuation after the third administration due to economic reason," "it was found that eosinophilic sinusitis was not improved and the subject had been diagnosed as atopic dermatitis", "changed to Dupixent because eosinophilic sinusitis did not improve", "because the number of times of use was small", "because the duration of use was short", "because the drug was discontinued for less than 2 months", "Unevaluable due to interruption of treatment", "no visit to the primary physician", "the subject did not visit to the hospital. Unable to contact the subject," "insufficient treatment duration," "due to early transfer to another hospital," "due to early discontinuation," "no change despite after-hours visit due to exacerbation," "discontinued in a short period," "discontinued in a short period of time at the subject's request," "interrupted," "the visit was irregular and the drug was administered only twice, and therefore the condition was not markedly changed," "unevaluable due to transfer to another hospital," "no visit due to transfer to another hospital," "discontinued at 1 year after the start of administration," "the administration duration was short," "the administration duration was too short," "the details of the statement were unclear due to dementia," "discontinued at the subject's request due to exacerbation of comorbidity," "oral steroid was required even after administration of this drug," "the subject's complaint was unclear," "treatment was discontinued after one dose due to the drug price," "adverse events," "early discontinuation due to adverse events," "the drug was effective but the subject wished to discontinue on Februarv 12 due to malaise." and "no visits."

*4: Subjects included in effectiveness analysis for whom the number of asthma exacerbation before and after the start of administration of this drug was not described.

*5: Subjects included in effectiveness analysis for whom the ACT score before and after the start of administration of this drug was not measured.

As of September 27, 2023

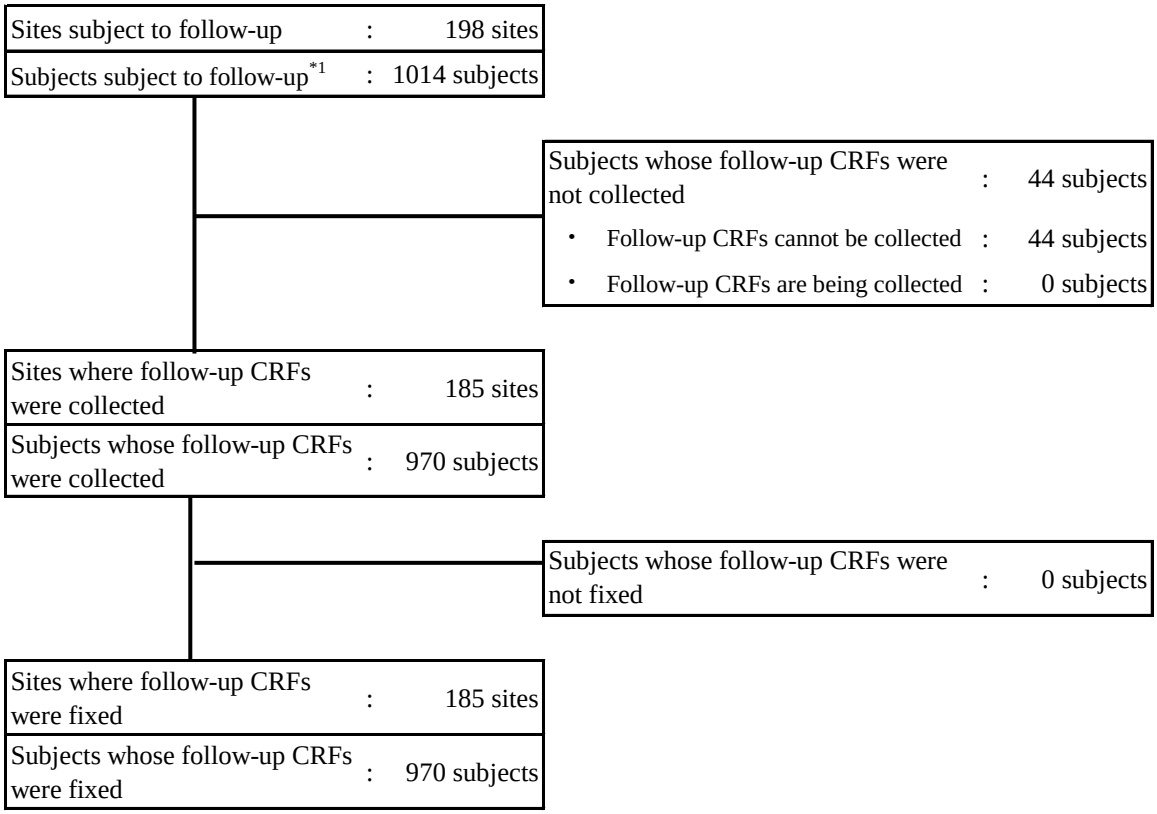



Figure 2 Subject disposition (follow-up)

*1: Among the subjects included in the safety analysis, those who completed the observation period and those who discontinued/completed the administration of this drug (excluding fatal cases) were followed up.

Table 1 Subject characteristics

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Subject characteristics | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| Total | | 1027 | 100.0 | 959 | 100.0 |
| Gender | Male | 386 | 37.6 | 355 | 37.0 |
| | Female | 641 | 62.4 | 604 | 63.0 |
| Pregnancy status "Female only" | No | 623 | 97.2 | 589 | 97.5 |
| | PPD | | | | |
| Age 1 [years] | <15 | 11 | 1.1 | 11 | 1.1 |
| Mean ± SD: 62.7±16.1/62.6±16.1 | 15≤ to <65 | 461 | 44.9 | 431 | 44.9 |
| Minimum: 12/12 | 65≤ to <75 | 280 | 27.3 | 257 | 26.8 |
| Median: 66.0/66.0 | 75≤ | 275 | 26.8 | 260 | 27.1 |
| Maximum: 93/93 | | | | | |
| Age 2 [years] | <65 | 472 | 46.0 | 442 | 46.1 |
| | 65≤ | 555 | 54.0 | 517 | 53.9 |
| Age 3 [years] | <12 | 0 | 0.0 | 0 | 0.0 |
| | 12≤ to <18 | 14 | 1.4 | 14 | 1.5 |
| | 18≤ | 1013 | 98.6 | 945 | 98.5 |
| Hospitalization status | Inpatient | 59 | 5.7 | 50 | 5.2 |
| | Outpatient | 968 | 94.3 | 909 | 94.8 |
| Reason for use of this drug | Bronchial asthma | 1024 | 99.7 | 959 | 100.0 |
| | Other | 3 | 0.3 | 0 | 0.0 |
| Breakdown of other reasons for use of this drug (name of disease)(multiple reasons) | Bronchiectasis | 1 | 0.1 | 0 | 0.0 |
| | Bronchiolitis | 1 | 0.1 | 0 | 0.0 |
| | Eosinophilic granulomatosis with polyangiitis | 1 | 0.1 | 0 | 0.0 |
| Comorbidity | No | 290 | 28.2 | 280 | 29.2 |
| | Yes | 737 | 71.8 | 679 | 70.8 |
| Comorbidity (renal impairment) | No | 1002 | 97.6 | 938 | 97.8 |
| | Yes | 25 | 2.4 | 21 | 2.2 |
| Comorbidity (hepatic impairment) | No | 997 | 97.1 | 931 | 97.1 |
| | Yes | 30 | 2.9 | 28 | 2.9 |
| Comorbidities (allergies) | No | 625 | 60.9 | 592 | 61.7 |
| | Yes | 402 | 39.1 | 367 | 38.3 |
| Comorbidities (other conditions) | No | 411 | 40.0 | 392 | 40.9 |
| | Yes | 616 | 60.0 | 567 | 59.1 |
| Smoking history | Never-smoker | 702 | 68.4 | 668 | 69.7 |
| | Ex-smoker | 289 | 28.1 | 260 | 27.1 |
| | Current-smoker | 36 | 3.5 | 31 | 3.2 |
| Primary disease (disease duration [years]) | ≤2 | 33 | 3.2 | 29 | 3.0 |
| | 2< to ≤5 | 68 | 6.6 | 60 | 6.3 |
| | 5< to ≤10 | 143 | 13.9 | 137 | 14.3 |
| | 10< | 638 | 62.1 | 589 | 61.4 |
| | Unknown | 145 | 14.1 | 144 | 15.0 |
| Primary disease (severity before administration) | Mild intermittent | 0 | 0.0 | 0 | 0.0 |
| | Mild persistent | 2 | 0.2 | 2 | 0.2 |
| | Moderate persistent | 30 | 2.9 | 29 | 3.0 |
| | Severe persistent | 688 | 67.0 | 642 | 66.9 |
| | Most severe persistent | 307 | 29.9 | 286 | 29.8 |
| Primary disease (disease type) | Atopic | 532 | 51.8 | 485 | 50.6 |
| | Non-atopic | 382 | 37.2 | 364 | 38.0 |
| | Unknown | 113 | 11.0 | 110 | 11.5 |
| Blood eosinophil count (9 to 52 weeks before start of administration of this drug)[/μL] | <150 | 110 | 10.7 | 97 | 10.1 |
| Mean ± SD: 701.0±935.1/708.1±938.0 | 150≤ to <300 | 95 | 9.3 | 93 | 9.7 |
| Minimum: 0/0 | 300≤ to <500 | 143 | 13.9 | 134 | 14.0 |
| Median: 460.0/466.0 | 500≤ | 308 | 30.0 | 290 | 30.2 |
| Maximum: 9999/9999 | Unknown | 371 | 36.1 | 345 | 36.0 |
| Blood eosinophil count (baseline)[/μL] | <150 | 163 | 15.9 | 150 | 15.6 |
| Mean ± SD: 641.5±822.9/634.7±813.8 | 150≤ to <300 | 110 | 10.7 | 103 | 10.7 |
| Minimum: 0/0 | 300≤ to <500 | 196 | 19.1 | 182 | 19.0 |
| Median: 418.0/409.0 | 500≤ | 350 | 34.1 | 325 | 33.9 |
| Maximum: 7500/7500 | Unknown | 208 | 20.3 | 199 | 20.8 |
| History of omalizumab use | No | 871 | 84.8 | 813 | 84.8 |
| | Yes | 156 | 15.2 | 146 | 15.2 |
| Prior medications for bronchial asthma | No | 7 | 0.7 | 7 | 0.7 |
| | Yes | 1020 | 99.3 | 952 | 99.3 |
| Concomitant medications | No | 75 | 7.3 | 69 | 7.2 |
| | Yes | 952 | 92.7 | 890 | 92.8 |
| Concomitant therapies for bronchial asthma (other than drug therapy) | No | 1013 | 98.6 | 946 | 98.6 |
| | Yes | 14 | 1.4 | 13 | 1.4 |

The "mean ± SD," "minimum," "median," and "maximum" for each subject factor are presented in the order of "safety analysis set" / "effectiveness analysis set."

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| Comorbidities: Other conditions | Hypertension | 204 | 19.9 | 189 | 19.7 |
| | Gastroesophageal reflux disease | 102 | 9.9 | 92 | 9.6 |
| | Osteoporosis | 87 | 8.5 | 81 | 8.4 |
| | Diabetes mellitus | 86 | 8.4 | 79 | 8.2 |
| | Insomnia | 86 | 8.4 | 75 | 7.8 |
| | Chronic obstructive pulmonary disease | 73 | 7.1 | 67 | 7.0 |
| | Dyslipidaemia | 72 | 7.0 | 67 | 7.0 |
| | Chronic sinusitis | 56 | 5.5 | 54 | 5.6 |
| | Constipation | 48 | 4.7 | 43 | 4.5 |
| | Hyperuricaemia | 43 | 4.2 | 40 | 4.2 |
| | Hyperlipidaemia | 40 | 3.9 | 39 | 4.1 |
| | Chronic gastritis | 39 | 3.8 | 36 | 3.8 |
| | Eosinophilic otitis media | 36 | 3.5 | 35 | 3.6 |
| | Sinusitis | 30 | 2.9 | 28 | 2.9 |
| | Bronchitis chronic | 28 | 2.7 | 26 | 2.7 |
| | Atrial fibrillation | 22 | 2.1 | 17 | 1.8 |
| | Gastric ulcer | 22 | 2.1 | 15 | 1.6 |
| | Hypercholesterolaemia | 22 | 2.1 | 22 | 2.3 |
| | Benign prostatic hyperplasia | 21 | 2.0 | 19 | 2.0 |
| | Eosinophilic granulomatosis with polyangiitis | 21 | 2.0 | 19 | 2.0 |
| | Angina pectoris | 17 | 1.7 | 15 | 1.6 |
| | Cardiac failure | 17 | 1.7 | 11 | 1.1 |
| | Back pain | 16 | 1.6 | 15 | 1.6 |
| | Depression | 16 | 1.6 | 14 | 1.5 |
| | Sleep apnoea syndrome | 16 | 1.6 | 14 | 1.5 |
| | Type 2 diabetes mellitus | 16 | 1.6 | 14 | 1.5 |
| | Cardiac failure chronic | 15 | 1.5 | 15 | 1.6 |
| | Bronchitis | 14 | 1.4 | 13 | 1.4 |
| | Rheumatoid arthritis | 14 | 1.4 | 13 | 1.4 |
| | Eosinophilic pneumonia | 12 | 1.2 | 11 | 1.1 |
| | Anxiety disorder | 12 | 1.2 | 12 | 1.3 |
| | Hypertonic bladder | 11 | 1.1 | 8 | 0.8 |
| | Upper respiratory tract inflammation | 11 | 1.1 | 10 | 1.0 |
| | Emphysema | 10 | 1.0 | 9 | 0.9 |
| | Arrhythmia | 9 | 0.9 | 8 | 0.8 |
| | Cerebral infarction | 9 | 0.9 | 8 | 0.8 |
| | Gastritis | 9 | 0.9 | 8 | 0.8 |
| | Breast cancer | 8 | 0.8 | 8 | 0.8 |
| | Hypothyroidism | 8 | 0.8 | 6 | 0.6 |
| | Neuropathy peripheral | 8 | 0.8 | 7 | 0.7 |
| | Otitis media | 8 | 0.8 | 6 | 0.6 |
| | Pharyngitis | 8 | 0.8 | 8 | 0.8 |
| | Adrenal insufficiency | 7 | 0.7 | 7 | 0.7 |
| | Bronchiectasis | 7 | 0.7 | 6 | 0.6 |
| | Cataract | 7 | 0.7 | 6 | 0.6 |
| | Dementia | 7 | 0.7 | 6 | 0.6 |
| | Dizziness | 7 | 0.7 | 4 | 0.4 |
| | Eosinophilia | 7 | 0.7 | 7 | 0.7 |
| | Gout | 7 | 0.7 | 5 | 0.5 |
| | Lumbar spinal stenosis | 7 | 0.7 | 6 | 0.6 |
| | Pneumonia | 7 | 0.7 | 7 | 0.7 |
| | Eosinophilic pneumonia chronic | 7 | 0.7 | 7 | 0.7 |
| | Spinal stenosis | 7 | 0.7 | 5 | 0.5 |
| | Colon cancer | 6 | 0.6 | 5 | 0.5 |
| | Iron deficiency anaemia | 6 | 0.6 | 6 | 0.6 |
| | Osteoarthritis | 6 | 0.6 | 6 | 0.6 |
| | Pruritus | 6 | 0.6 | 6 | 0.6 |
| | Lipid metabolism disorder | 6 | 0.6 | 5 | 0.5 |
| | Diffuse panbronchiolitis | 6 | 0.6 | 6 | 0.6 |

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| | Steroid diabetes | 6 | 0.6 | 6 | 0.6 |
| | Chronic respiratory failure | 5 | 0.5 | 5 | 0.5 |
| | Dementia Alzheimer's type | 5 | 0.5 | 5 | 0.5 |
| | Enterocolitis | 5 | 0.5 | 4 | 0.4 |
| | Epilepsy | 5 | 0.5 | 5 | 0.5 |
| | Gastroenteritis | 5 | 0.5 | 5 | 0.5 |
| | Glaucoma | 5 | 0.5 | 3 | 0.3 |
| | Headache | 5 | 0.5 | 5 | 0.5 |
| | Hypokalaemia | 5 | 0.5 | 5 | 0.5 |
| | Pollakiuria | 5 | 0.5 | 5 | 0.5 |
| | Anaemia | 4 | 0.4 | 4 | 0.4 |
| | Bronchopulmonary aspergillosis | 4 | 0.4 | 3 | 0.3 |
| | Diarrhea | 4 | 0.4 | 4 | 0.4 |
| | Dry eye | 4 | 0.4 | 3 | 0.3 |
| | Eczema | 4 | 0.4 | 2 | 0.2 |
| | Interstitial lung disease | 4 | 0.4 | 4 | 0.4 |
| | Myocardial infarction | 4 | 0.4 | 4 | 0.4 |
| | Neuralgia | 4 | 0.4 | 4 | 0.4 |
| | Pain | 4 | 0.4 | 4 | 0.4 |
| | Panic disorder | 4 | 0.4 | 3 | 0.3 |
| | Spinal compression fracture | 4 | 0.4 | 4 | 0.4 |
| | Deep vein thrombosis | 4 | 0.4 | 4 | 0.4 |
| | Asteatosis | 4 | 0.4 | 4 | 0.4 |
| | Lung neoplasm malignant | 4 | 0.4 | 4 | 0.4 |
| | Prostate cancer | 4 | 0.4 | 3 | 0.3 |
| | Cardiac failure congestive | 3 | 0.3 | 3 | 0.3 |
| | Cerebrovascular disorder | 3 | 0.3 | 3 | 0.3 |
| | Dermatitis | 3 | 0.3 | 3 | 0.3 |
| | Eczema asteatotic | 3 | 0.3 | 3 | 0.3 |
| | Irritable bowel syndrome | 3 | 0.3 | 3 | 0.3 |
| | Lower respiratory tract infection | 3 | 0.3 | 3 | 0.3 |
| | Migraine | 3 | 0.3 | 1 | 0.1 |
| | Nasopharyngitis | 3 | 0.3 | 2 | 0.2 |
| | Oral candidiasis | 3 | 0.3 | 3 | 0.3 |
| | Otitis media chronic | 3 | 0.3 | 2 | 0.2 |
| | Pancreatitis chronic | 3 | 0.3 | 3 | 0.3 |
| | Prinzmetal angina | 3 | 0.3 | 2 | 0.2 |
| | Pulmonary tuberculosis | 3 | 0.3 | 3 | 0.3 |
| | Schizophrenia | 3 | 0.3 | 3 | 0.3 |
| | Spinal osteoarthritis | 3 | 0.3 | 3 | 0.3 |
| | Tendon rupture | 3 | 0.3 | 0 | 0.0 |
| | Tracheitis | 3 | 0.3 | 3 | 0.3 |
| | Uterine leiomyoma | 3 | 0.3 | 3 | 0.3 |
| | Viral infection | 3 | 0.3 | 3 | 0.3 |
| | Tachyarrhythmia | 3 | 0.3 | 3 | 0.3 |
| | Large intestine polyp | 3 | 0.3 | 2 | 0.2 |
| | Spondylitis | 3 | 0.3 | 3 | 0.3 |
| | Respiratory tract infection | 3 | 0.3 | 3 | 0.3 |
| | Abdominal distension | 2 | 0.2 | 2 | 0.2 |
| | Aortic valve disease mixed | 2 | 0.2 | 2 | 0.2 |
| | Arthralgia | 2 | 0.2 | 2 | 0.2 |
| | Bipolar I disorder | 2 | 0.2 | 2 | 0.2 |
| | Blood insulin abnormal | 2 | 0.2 | 2 | 0.2 |
| | Cholecystectomy | 2 | 0.2 | 2 | 0.2 |
| | Cholelithiasis | 2 | 0.2 | 2 | 0.2 |
| | Cough | 2 | 0.2 | 2 | 0.2 |
| | Dissociative disorder | 2 | 0.2 | 2 | 0.2 |
| | Duodenal ulcer | 2 | 0.2 | 2 | 0.2 |
| | Dyspepsia | 2 | 0.2 | 2 | 0.2 |
| | Essential hypertension | 2 | 0.2 | 2 | 0.2 |

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| | Gangrene | 2 | 0.2 | 0 | 0.0 |
| | Gastroenteritis eosinophilic | 2 | 0.2 | 2 | 0.2 |
| | Graves' disease | 2 | 0.2 | 2 | 0.2 |
| | Herpes zoster | 2 | 0.2 | 2 | 0.2 |
| | Hyperkalaemia | 2 | 0.2 | 2 | 0.2 |
| | Hypoaesthesia | 2 | 0.2 | 2 | 0.2 |
| | Inguinal hernia | 2 | 0.2 | 2 | 0.2 |
| | Intracranial aneurysm | 2 | 0.2 | 2 | 0.2 |
| | Meniere's disease | 2 | 0.2 | 2 | 0.2 |
| | Mitral valve incompetence | 2 | 0.2 | 2 | 0.2 |
| | Muscle spasms | 2 | 0.2 | 2 | 0.2 |
| | Myocardial ischaemia | 2 | 0.2 | 1 | 0.1 |
| | Oedema peripheral | 2 | 0.2 | 1 | 0.1 |
| | Polymyalgia rheumatica | 2 | 0.2 | 2 | 0.2 |
| | Sarcoidosis | 2 | 0.2 | 2 | 0.2 |
| | Sciatica | 2 | 0.2 | 2 | 0.2 |
| | Systemic lupus erythematosus | 2 | 0.2 | 1 | 0.1 |
| | Vitamin B1 deficiency | 2 | 0.2 | 2 | 0.2 |
| | Vomiting | 2 | 0.2 | 2 | 0.2 |
| | Autoimmune thyroiditis | 2 | 0.2 | 2 | 0.2 |
| | Intervertebral disc protrusion | 2 | 0.2 | 2 | 0.2 |
| | Dilated cardiomyopathy | 2 | 0.2 | 2 | 0.2 |
| | Chronic inflammatory demyelinating polyradiculoneuropathy | 2 | 0.2 | 2 | 0.2 |
| | Tinea infection | 2 | 0.2 | 2 | 0.2 |
| | Sudden hearing loss | 2 | 0.2 | 2 | 0.2 |
| | Atypical mycobacterial infection | 2 | 0.2 | 2 | 0.2 |
| | Pneumocystis jirovecii pneumonia | 2 | 0.2 | 2 | 0.2 |
| | Ureterolithiasis | 2 | 0.2 | 2 | 0.2 |
| | Mixed anxiety and depressive disorder | 2 | 0.2 | 2 | 0.2 |
| | Immune thrombocytopenia | 2 | 0.2 | 2 | 0.2 |
| | Pancreatic cystadenoma | 2 | 0.2 | 2 | 0.2 |
| | Abdominal pain | 1 | 0.1 | 1 | 0.1 |
| | Acne | 1 | 0.1 | 1 | 0.1 |
| | Acute myocardial infarction | 1 | 0.1 | 1 | 0.1 |
| | Adenoma benign | 1 | 0.1 | 1 | 0.1 |
| | Angle closure glaucoma | 1 | 0.1 | 0 | 0.0 |
| | Aortic aneurysm | 1 | 0.1 | 0 | 0.0 |
| | Aortic dissection | 1 | 0.1 | 1 | 0.1 |
| | Aortic stenosis | 1 | 0.1 | 1 | 0.1 |
| | Aortic valve incompetence | 1 | 0.1 | 1 | 0.1 |
| | Aortic valve replacement | 1 | 0.1 | 1 | 0.1 |
| | Appendicitis | 1 | 0.1 | 1 | 0.1 |
| | Asbestosis | 1 | 0.1 | 1 | 0.1 |
| | Asthenia | 1 | 0.1 | 1 | 0.1 |
| | Atelectasis | 1 | 0.1 | 1 | 0.1 |
| | Atrioventricular block complete | 1 | 0.1 | 1 | 0.1 |
| | Autonomic nervous system imbalance | 1 | 0.1 | 1 | 0.1 |
| | Behaviour disorder | 1 | 0.1 | 1 | 0.1 |
| | Behcet's syndrome | 1 | 0.1 | 1 | 0.1 |
| | Blood immunoglobulin G increased | 1 | 0.1 | 1 | 0.1 |
| | Body tinea | 1 | 0.1 | 1 | 0.1 |
| | Bronchiolitis | 1 | 0.1 | 1 | 0.1 |
| | Bronchogram abnormal | 1 | 0.1 | 1 | 0.1 |
| | Bursitis | 1 | 0.1 | 1 | 0.1 |
| | Calculus urinary | 1 | 0.1 | 0 | 0.0 |
| | Cardiac hypertrophy | 1 | 0.1 | 1 | 0.1 |
| | Carotid artery stenosis | 1 | 0.1 | 1 | 0.1 |
| | Carotid artery thrombosis | 1 | 0.1 | 0 | 0.0 |
| | Cerebellar haemorrhage | 1 | 0.1 | 1 | 0.1 |
| | Cerebellar infarction | 1 | 0.1 | 1 | 0.1 |

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| | Cervical spinal stenosis | 1 | 0.1 | 1 | 0.1 |
| | Cholecystitis | 1 | 0.1 | 1 | 0.1 |
| | Cholesteatoma | 1 | 0.1 | 1 | 0.1 |
| | Chronic myeloid leukaemia | 1 | 0.1 | 1 | 0.1 |
| | Compression fracture | 1 | 0.1 | 1 | 0.1 |
| | Conversion disorder | 1 | 0.1 | 1 | 0.1 |
| | Coronary artery disease | 1 | 0.1 | 1 | 0.1 |
| | Cystitis | 1 | 0.1 | 1 | 0.1 |
| | Deafness | 1 | 0.1 | 1 | 0.1 |
| | Dermal cyst | 1 | 0.1 | 1 | 0.1 |
| | Dermatophytosis of nail | 1 | 0.1 | 1 | 0.1 |
| | Diabetic neuropathy | 1 | 0.1 | 1 | 0.1 |
| | Diabetic retinopathy | 1 | 0.1 | 1 | 0.1 |
| | Diplopia | 1 | 0.1 | 1 | 0.1 |
| | Diverticulitis | 1 | 0.1 | 1 | 0.1 |
| | Diverticulum intestinal haemorrhagic | 1 | 0.1 | 0 | 0.0 |
| | Dysphagia | 1 | 0.1 | 1 | 0.1 |
| | Dysuria | 1 | 0.1 | 1 | 0.1 |
| | Eosinophilic myocarditis | 1 | 0.1 | 1 | 0.1 |
| | Fat tissue increased | 1 | 0.1 | 1 | 0.1 |
| | Femoral neck fracture | 1 | 0.1 | 1 | 0.1 |
| | Femur fracture | 1 | 0.1 | 1 | 0.1 |
| | Fungal infection | 1 | 0.1 | 1 | 0.1 |
| | Gastric cancer | 1 | 0.1 | 1 | 0.1 |
| | Glucose tolerance impaired | 1 | 0.1 | 0 | 0.0 |
| | Goitre | 1 | 0.1 | 1 | 0.1 |
| | Haematuria | 1 | 0.1 | 0 | 0.0 |
| | Hemiparesis | 1 | 0.1 | 1 | 0.1 |
| | Hiatus hernia | 1 | 0.1 | 1 | 0.1 |
| | Hyperparathyroidism | 1 | 0.1 | 0 | 0.0 |
| | Hypertrophic cardiomyopathy | 1 | 0.1 | 1 | 0.1 |
| | Hypocalcaemia | 1 | 0.1 | 1 | 0.1 |
| | Hyponatraemia | 1 | 0.1 | 1 | 0.1 |
| | Hypopituitarism | 1 | 0.1 | 1 | 0.1 |
| | Hypovitaminosis | 1 | 0.1 | 1 | 0.1 |
| | Infection susceptibility increased | 1 | 0.1 | 1 | 0.1 |
| | Influenza | 1 | 0.1 | 1 | 0.1 |
| | Joint dislocation | 1 | 0.1 | 1 | 0.1 |
| | Lacrimation increased | 1 | 0.1 | 1 | 0.1 |
| | Large intestine perforation | 1 | 0.1 | 1 | 0.1 |
| | Lipids abnormal | 1 | 0.1 | 0 | 0.0 |
| | Lung adenocarcinoma | 1 | 0.1 | 1 | 0.1 |
| | Mania | 1 | 0.1 | 1 | 0.1 |
| | Metastases to liver | 1 | 0.1 | 1 | 0.1 |
| | Mitral valve replacement | 1 | 0.1 | 1 | 0.1 |
| | Muscle hypertrophy | 1 | 0.1 | 1 | 0.1 |
| | Myasthenia gravis | 1 | 0.1 | 0 | 0.0 |
| | Nail disorder | 1 | 0.1 | 1 | 0.1 |
| | Nasal polyps | 1 | 0.1 | 1 | 0.1 |
| | Nausea | 1 | 0.1 | 1 | 0.1 |
| | Nephrectomy | 1 | 0.1 | 1 | 0.1 |
| | Neurogenic bladder | 1 | 0.1 | 1 | 0.1 |
| | Oedema | 1 | 0.1 | 1 | 0.1 |
| | Oesophageal candidiasis | 1 | 0.1 | 1 | 0.1 |
| | Oesophagitis | 1 | 0.1 | 1 | 0.1 |
| | Open angle glaucoma | 1 | 0.1 | 1 | 0.1 |
| | Orthostatic hypotension | 1 | 0.1 | 1 | 0.1 |
| | Osteogenesis imperfecta | 1 | 0.1 | 1 | 0.1 |
| | Osteonecrosis | 1 | 0.1 | 1 | 0.1 |
| | Pain in extremity | 1 | 0.1 | 1 | 0.1 |

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| | Palmoplantar keratoderma | 1 | 0.1 | 1 | 0.1 |
| | Pancreatic cyst | 1 | 0.1 | 1 | 0.1 |
| | Patent ductus arteriosus | 1 | 0.1 | 1 | 0.1 |
| | Peptic ulcer | 1 | 0.1 | 1 | 0.1 |
| | Periarthritis | 1 | 0.1 | 1 | 0.1 |
| | Periodontitis | 1 | 0.1 | 1 | 0.1 |
| | Pleurisy | 1 | 0.1 | 1 | 0.1 |
| | Pneumonia aspiration | 1 | 0.1 | 1 | 0.1 |
| | Post herpetic neuralgia | 1 | 0.1 | 1 | 0.1 |
| | Primary hyperaldosteronism | 1 | 0.1 | 1 | 0.1 |
| | Prurigo | 1 | 0.1 | 1 | 0.1 |
| | Pulmonary embolism | 1 | 0.1 | 0 | 0.0 |
| | Punctate keratitis | 1 | 0.1 | 1 | 0.1 |
| | Pyelonephritis acute | 1 | 0.1 | 1 | 0.1 |
| | Rash | 1 | 0.1 | 1 | 0.1 |
| | Renal cancer | 1 | 0.1 | 1 | 0.1 |
| | Right ventricular failure | 1 | 0.1 | 0 | 0.0 |
| | Scleroderma | 1 | 0.1 | 1 | 0.1 |
| | Scoliosis | 1 | 0.1 | 1 | 0.1 |
| | Secondary adrenocortical insufficiency | 1 | 0.1 | 1 | 0.1 |
| | Senile pruritus | 1 | 0.1 | 1 | 0.1 |
| | Sinus congestion | 1 | 0.1 | 1 | 0.1 |
| | Skin infection | 1 | 0.1 | 1 | 0.1 |
| | Skin papilloma | 1 | 0.1 | 1 | 0.1 |
| | Squamous cell carcinoma of lung | 1 | 0.1 | 1 | 0.1 |
| | Still's disease | 1 | 0.1 | 1 | 0.1 |
| | Stomatitis | 1 | 0.1 | 1 | 0.1 |
| | Subarachnoid haemorrhage | 1 | 0.1 | 1 | 0.1 |
| | Supraventricular extrasystoles | 1 | 0.1 | 1 | 0.1 |
| | Supraventricular tachycardia | 1 | 0.1 | 1 | 0.1 |
| | Tachycardia | 1 | 0.1 | 1 | 0.1 |
| | Thromboangiitis obliterans | 1 | 0.1 | 1 | 0.1 |
| | Thrombophlebitis | 1 | 0.1 | 1 | 0.1 |
| | Thrombosis | 1 | 0.1 | 1 | 0.1 |
| | Thyroid neoplasm | 1 | 0.1 | 1 | 0.1 |
| | Tooth abscess | 1 | 0.1 | 1 | 0.1 |
| | Tuberculosis | 1 | 0.1 | 1 | 0.1 |
| | Turner's syndrome | 1 | 0.1 | 1 | 0.1 |
| | Upper respiratory tract infection | 1 | 0.1 | 1 | 0.1 |
| | Uterine cancer | 1 | 0.1 | 1 | 0.1 |
| | Uterine polyp | 1 | 0.1 | 1 | 0.1 |
| | Varicose vein | 1 | 0.1 | 1 | 0.1 |
| | Venous thrombosis | 1 | 0.1 | 1 | 0.1 |
| | Vitamin C deficiency | 1 | 0.1 | 0 | 0.0 |
| | Fibromyalgia | 1 | 0.1 | 1 | 0.1 |
| | Hypereosinophilic syndrome | 1 | 0.1 | 1 | 0.1 |
| | Hypoacusis | 1 | 0.1 | 1 | 0.1 |
| | Sinobronchitis | 1 | 0.1 | 1 | 0.1 |
| | Gallbladder polyp | 1 | 0.1 | 1 | 0.1 |
| | Intercostal neuralgia | 1 | 0.1 | 1 | 0.1 |
| | Castleman's disease | 1 | 0.1 | 1 | 0.1 |
| | Oropharyngeal candidiasis | 1 | 0.1 | 1 | 0.1 |
| | Sinusitis aspergillus | 1 | 0.1 | 1 | 0.1 |
| | Lacunar infarction | 1 | 0.1 | 1 | 0.1 |
| | Facet joint syndrome | 1 | 0.1 | 1 | 0.1 |
| | Adenomyosis | 1 | 0.1 | 1 | 0.1 |
| | Pulmonary mass | 1 | 0.1 | 1 | 0.1 |
| | Cognitive disorder | 1 | 0.1 | 1 | 0.1 |
| | Mycobacterium avium complex infection | 1 | 0.1 | 1 | 0.1 |
| | Carnitine deficiency | 1 | 0.1 | 1 | 0.1 |

Table 2 Subject characteristics (other comorbidities)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | Subjects included in effectiveness analysis | |
|---|---|---|---|---|---|
| | | Number of subjects studied | Composition ratio (%) | Number of subjects studied | Composition ratio (%) |
| | Sputum retention | 1 | 0.1 | 1 | 0.1 |
| | Monoclonal gammopathy | 1 | 0.1 | 1 | 0.1 |
| | Embolism | 1 | 0.1 | 1 | 0.1 |
| | Pseudomonas infection | 1 | 0.1 | 1 | 0.1 |
| | Salivary gland neoplasm | 1 | 0.1 | 1 | 0.1 |
| | Lip and/or oral cavity cancer | 1 | 0.1 | 1 | 0.1 |
| | Ovarian neoplasm | 1 | 0.1 | 1 | 0.1 |
| | Parkinson's disease | 1 | 0.1 | 1 | 0.1 |
| | Vitamin B complex deficiency | 1 | 0.1 | 1 | 0.1 |
| | Diverticular perforation | 1 | 0.1 | 1 | 0.1 |
| | Psychotic disorder | 1 | 0.1 | 1 | 0.1 |
| | Pigmentation disorder | 1 | 0.1 | 1 | 0.1 |
| | Seronegative arthritis | 1 | 0.1 | 1 | 0.1 |
| | Heparin-induced thrombocytopenia | 1 | 0.1 | 1 | 0.1 |
| | Peripheral arterial occlusive disease | 1 | 0.1 | 1 | 0.1 |
| | Arterial occlusive disease | 1 | 0.1 | 1 | 0.1 |
| | Hyperamylasaemia | 1 | 0.1 | 1 | 0.1 |
| | Gitelman's syndrome | 1 | 0.1 | 1 | 0.1 |
| | Spondylolisthesis | 1 | 0.1 | 1 | 0.1 |
| | Autism spectrum disorder | 1 | 0.1 | 1 | 0.1 |
| | Asthmatic crisis | 1 | 0.1 | 1 | 0.1 |
| | Nutritional condition abnormal | 1 | 0.1 | 0 | 0.0 |
| | Stress cardiomyopathy | 1 | 0.1 | 1 | 0.1 |
| | Carotid arteriosclerosis | 1 | 0.1 | 1 | 0.1 |
| | Type 1 diabetes mellitus | 1 | 0.1 | 1 | 0.1 |
| | Lupus enteritis | 1 | 0.1 | 0 | 0.0 |
| | Vascular graft | 1 | 0.1 | 1 | 0.1 |
| | Intellectual disability | 1 | 0.1 | 1 | 0.1 |
| | Oropharyngeal pain | 1 | 0.1 | 1 | 0.1 |
| | Lung cyst | 1 | 0.1 | 0 | 0.0 |
| | Upper-airway cough syndrome | 1 | 0.1 | 0 | 0.0 |
| | Functional gastrointestinal disorder | 1 | 0.1 | 1 | 0.1 |
| | Granulomatosis with polyangiitis | 1 | 0.1 | 1 | 0.1 |
| | Rheumatic disorder | 1 | 0.1 | 1 | 0.1 |
| | Candida infection | 1 | 0.1 | 0 | 0.0 |
| | Aspergillus infection | 1 | 0.1 | 1 | 0.1 |
| | Myeloproliferative neoplasm | 1 | 0.1 | 1 | 0.1 |
| | Somatic symptom disorder | 1 | 0.1 | 1 | 0.1 |
| | Colorectal adenoma | 1 | 0.1 | 1 | 0.1 |

Table 3 Subject characteristics (prior medications)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Daily dose for 4 weeks prior to the start of administration of this drug* | | | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | | Mean ± SD | Minimum | Median | Maximum | | | | | | | | |
| Prior medications | Inhaled corticosteroid alone | | | | | 126 | 12.3 | 4 | 3.2 | 118 | 12.3 | 101 | 85.6 |
| | Flutide | | | | | 14 | 1.4 | 0 | 0.0 | 13 | 1.4 | 11 | 84.6 |
| | Qvar | | | | | 22 | 2.1 | 0 | 0.0 | 22 | 2.3 | 21 | 95.5 |
| | Alvesco | | | | | 53 | 5.2 | 3 | 5.7 | 50 | 5.2 | 40 | 80.0 |
| | Pulmicort | | | | | 24 | 2.3 | 1 | 4.2 | 22 | 2.3 | 18 | 81.8 |
| | Asmanex | | | | | 11 | 1.1 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Other | | | | | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Amuity | | | | | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Aldecin | | | | | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Unknown | | | | | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Inhaled corticosteroid/long-acting β2-agonist combination | | | | | 922 | 89.8 | 40 | 4.3 | 861 | 89.8 | 781 | 90.7 |
| | Relvar | | | | | 334 | 32.5 | 15 | 4.5 | 315 | 32.8 | 294 | 93.3 |
| | Adoair | | | | | 135 | 13.1 | 1 | 0.7 | 131 | 13.7 | 117 | 89.3 |
| | Symbicort | | | | | 253 | 24.6 | 13 | 5.1 | 232 | 24.2 | 206 | 88.8 |
| | Flutiform | | | | | 207 | 20.2 | 11 | 5.3 | 190 | 19.8 | 171 | 90.0 |
| | Other | | | | | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Trelegy | | | | | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | BudeForu | | | | | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Oral corticosteroids | | | - | | 353 | 34.4 | 22 | 6.2 | 327 | 34.1 | 291 | 89.0 |
| | Prednisolone/predonine | 11.031±9.505 | 1.00 | 8.000 | 75.00 | 310 | 30.2 | 21 | 6.8 | 287 | 29.9 | 254 | 88.5 |
| | Cortril | 3.861±3.307 | 2.00 | 2.500 | 12.50 | 10 | 1.0 | 0 | 0.0 | 9 | 0.9 | 9 | 100.0 |
| | Medrol | 9.219±7.348 | 1.25 | 7.500 | 20.00 | 9 | 0.9 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Ledercort | 3.750±1.768 | 2.50 | 3.750 | 5.00 | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Orgadrone/decadron | 8.667±7.764 | 1.67 | 5.000 | 20.00 | 5 | 0.5 | 1 | 20.0 | 5 | 0.5 | 4 | 80.0 |
| | Rinderon | 9.298±7.784 | 0.87 | 6.667 | 26.67 | 14 | 1.4 | 0 | 0.0 | 12 | 1.3 | 11 | 91.7 |
| | Other | | | - | | 8 | 0.8 | 0 | 0.0 | 8 | 0.8 | 8 | 100.0 |
| | Celestamine | | | - | | 8 | 0.8 | 0 | 0.0 | 8 | 0.8 | 8 | 100.0 |
| | Unknown | | | - | | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Long-acting β2 agonist alone | | | | | 82 | 8.0 | 3 | 3.7 | 74 | 7.7 | 62 | 83.8 |
| | Leukotriene receptor antagonists | | | | | 685 | 66.7 | 29 | 4.2 | 644 | 67.2 | 579 | 89.9 |
| | Theophylline sustained-release preparation | | | | | 375 | 36.5 | 14 | 3.7 | 351 | 36.6 | 311 | 88.6 |
| | Long-acting anticholinergics | | | | | 484 | 47.1 | 18 | 3.7 | 457 | 47.7 | 404 | 88.4 |
| | Anti-IgE antibody | | | | | 74 | 7.2 | 3 | 4.1 | 69 | 7.2 | 59 | 85.5 |
| | Antiallergic agents other than leukotriene receptor antagonists | | | | | 255 | 24.8 | 17 | 6.7 | 236 | 24.6 | 198 | 83.9 |
| | Unknown | | | | | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |

*Calculated by prednisolone dose

Table 4 Usage ratio of oral corticosteroids for bronchial asthma

As of September 27, 2023

Subjects included in safety analysis

| Item/Category | | 4 weeks prior to the start of administration of this drug (1027 subjects) | | | | After the start of administration of this drug (1027 subjects) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Not used | | Used | | Not used | | Used | |
| | | Number of subjects | Percentage (%) | Number of subjects | Percentage (%) | Number of subjects | Percentage (%) | Number of subjects | Percentage (%) |
| Oral corticosteroids | | 674 | 65.6 | 353 | 34.4 | 803 | 78.2 | 224 | 21.8 |
| | Prednisolone/predonine | 717 | 69.8 | 310 | 30.2 | 832 | 81.0 | 195 | 19.0 |
| | Cortril | 1017 | 99.0 | 10 | 1.0 | 1016 | 98.9 | 11 | 1.1 |
| | Medrol | 1018 | 99.1 | 9 | 0.9 | 1019 | 99.2 | 8 | 0.8 |
| | Ledercort | 1025 | 99.8 | 2 | 0.2 | 1025 | 99.8 | 2 | 0.2 |
| | Orgadrone/decadron | 1022 | 99.5 | 5 | 0.5 | 1025 | 99.8 | 2 | 0.2 |
| | Rinderon | 1013 | 98.6 | 14 | 1.4 | 1019 | 99.2 | 8 | 0.8 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| Concomitant medications | Montelukast sodium | 499 | 48.6 | 16 | 3.2 | 471 | 49.1 | 429 | 91.1 |
| | Tiotropium bromide hydrate | 337 | 32.8 | 11 | 3.3 | 320 | 33.4 | 289 | 90.3 |
| | Vilanterol trifenatate/fluticasone furoate | 280 | 27.3 | 11 | 3.9 | 267 | 27.8 | 251 | 94.0 |
| | Theophylline | 256 | 24.9 | 7 | 2.7 | 241 | 25.1 | 211 | 87.6 |
| | Prednisolone | 251 | 24.4 | 13 | 5.2 | 230 | 24.0 | 193 | 83.9 |
| | Budesonide/formoterol fumarate hydrate | 178 | 17.3 | 8 | 4.5 | 163 | 17.0 | 147 | 90.2 |
| | Fluticasone propionate/formoterol fumarate hydrate | 173 | 16.8 | 9 | 5.2 | 157 | 16.4 | 143 | 91.1 |
| | L-carbocisteine | 158 | 15.4 | 10 | 6.3 | 147 | 15.3 | 132 | 89.8 |
| | Salmeterol xinafoate/fluticasone propionate | 103 | 10.0 | 0 | 0.0 | 100 | 10.4 | 94 | 94.0 |
| | Ambroxol hydrochloride | 100 | 9.7 | 4 | 4.0 | 94 | 9.8 | 81 | 86.2 |
| | Procaterol hydrochloride hydrate | 76 | 7.4 | 4 | 5.3 | 69 | 7.2 | 56 | 81.2 |
| | Clarithromycin | 74 | 7.2 | 4 | 5.4 | 70 | 7.3 | 63 | 90.0 |
| | Pranlukast hydrate | 61 | 5.9 | 3 | 4.9 | 57 | 5.9 | 50 | 87.7 |
| | Amlodipine besilate | 60 | 5.8 | 0 | 0.0 | 56 | 5.8 | 51 | 91.1 |
| | Epinastine hydrochloride | 60 | 5.8 | 1 | 1.7 | 57 | 5.9 | 52 | 91.2 |
| | Esomeprazole magnesium hydrate | 57 | 5.6 | 4 | 7.0 | 52 | 5.4 | 44 | 84.6 |
| | Levocetirizine hydrochloride | 57 | 5.6 | 5 | 8.8 | 51 | 5.3 | 41 | 80.4 |
| | Methylprednisolone sodium succinate | 56 | 5.5 | 3 | 5.4 | 50 | 5.2 | 34 | 68.0 |
| | Salbutamol sulfate | 51 | 5.0 | 2 | 3.9 | 48 | 5.0 | 39 | 81.3 |
| | Lansoprazole | 44 | 4.3 | 3 | 6.8 | 40 | 4.2 | 33 | 82.5 |
| | Fluticasone furoate | 40 | 3.9 | 4 | 10.0 | 35 | 3.6 | 32 | 91.4 |
| | Famotidine | 40 | 3.9 | 1 | 2.5 | 37 | 3.9 | 35 | 94.6 |
| | Fexofenadine hydrochloride | 38 | 3.7 | 2 | 5.3 | 35 | 3.6 | 31 | 88.6 |
| | Sodium rabeprazole | 37 | 3.6 | 2 | 5.4 | 33 | 3.4 | 31 | 93.9 |
| | Suplatast tosilate | 34 | 3.3 | 2 | 5.9 | 31 | 3.2 | 26 | 83.9 |
| | Sulfamethoxazole-trimethoprim | 33 | 3.2 | 2 | 6.1 | 29 | 3.0 | 24 | 82.8 |
| | Alendronate sodium hydrate | 32 | 3.1 | 3 | 9.4 | 28 | 2.9 | 24 | 85.7 |
| | Rosuvastatin calcium | 30 | 2.9 | 0 | 0.0 | 30 | 3.1 | 28 | 93.3 |
| | Tulobuterol | 29 | 2.8 | 1 | 3.4 | 27 | 2.8 | 24 | 88.9 |
| | Betamethasone sodium phosphate | 29 | 2.8 | 1 | 3.4 | 26 | 2.7 | 17 | 65.4 |
| | Alfacalcidol | 28 | 2.7 | 0 | 0.0 | 23 | 2.4 | 21 | 91.3 |
| | Ciclesonide | 27 | 2.6 | 1 | 3.7 | 26 | 2.7 | 25 | 96.2 |
| | Magnesium oxide | 27 | 2.6 | 3 | 11.1 | 23 | 2.4 | 18 | 78.3 |
| | Hydrocortisone | 27 | 2.6 | 2 | 7.4 | 25 | 2.6 | 24 | 96.0 |
| | Rebamipide | 26 | 2.5 | 0 | 0.0 | 20 | 2.1 | 15 | 75.0 |
| | Mometasone furoate hydrate | 25 | 2.4 | 2 | 8.0 | 25 | 2.6 | 18 | 72.0 |
| | Atorvastatin calcium hydrate | 25 | 2.4 | 0 | 0.0 | 24 | 2.5 | 24 | 100.0 |
| | Olopatadine hydrochloride | 25 | 2.4 | 0 | 0.0 | 22 | 2.3 | 19 | 86.4 |
| | Febuxostat | 21 | 2.0 | 1 | 4.8 | 20 | 2.1 | 19 | 95.0 |
| | Zolpidem tartrate | 20 | 1.9 | 0 | 0.0 | 20 | 2.1 | 15 | 75.0 |
| | Budesonide | 19 | 1.9 | 1 | 5.3 | 18 | 1.9 | 14 | 77.8 |
| | Bilastine | 19 | 1.9 | 1 | 5.3 | 18 | 1.9 | 18 | 100.0 |
| | Acetaminophen | 18 | 1.8 | 1 | 5.6 | 17 | 1.8 | 14 | 82.4 |
| | Vonoprazan fumarate | 18 | 1.8 | 1 | 5.6 | 13 | 1.4 | 11 | 84.6 |
| | Sitagliptin phosphate hydrate | 18 | 1.8 | 0 | 0.0 | 17 | 1.8 | 16 | 94.1 |
| | Brotizolam | 17 | 1.7 | 2 | 11.8 | 14 | 1.5 | 12 | 85.7 |
| | Telmisartan | 17 | 1.7 | 0 | 0.0 | 16 | 1.7 | 12 | 75.0 |
| | Olmesartan medoxomil | 17 | 1.7 | 0 | 0.0 | 16 | 1.7 | 16 | 100.0 |
| | Nifedipine | 17 | 1.7 | 1 | 5.9 | 17 | 1.8 | 15 | 88.2 |
| | Dextromethorphan hydrobromide hydrate | 17 | 1.7 | 1 | 5.9 | 16 | 1.7 | 15 | 93.8 |
| | Erythromycin ethylsuccinate | 17 | 1.7 | 1 | 5.9 | 16 | 1.7 | 13 | 81.3 |
| | Aminophylline hydrate | 16 | 1.6 | 1 | 6.3 | 16 | 1.7 | 10 | 62.5 |
| | Ceftriaxone sodium hydrate | 15 | 1.5 | 0 | 0.0 | 15 | 1.6 | 9 | 60.0 |
| | Benidipine hydrochloride | 14 | 1.4 | 0 | 0.0 | 12 | 1.3 | 10 | 83.3 |
| | Methylprednisolone | 14 | 1.4 | 1 | 7.1 | 13 | 1.4 | 11 | 84.6 |
| | Eldecalcitol | 14 | 1.4 | 0 | 0.0 | 12 | 1.3 | 11 | 91.7 |
| | Metformin hydrochloride | 14 | 1.4 | 0 | 0.0 | 12 | 1.3 | 11 | 91.7 |
| | Furosemide | 13 | 1.3 | 0 | 0.0 | 10 | 1.0 | 8 | 80.0 |
| | Pitavastatin calcium | 13 | 1.3 | 1 | 7.7 | 11 | 1.1 | 9 | 81.8 |
| | Betamethasone | 13 | 1.3 | 0 | 0.0 | 12 | 1.3 | 11 | 91.7 |
| | Mecobalamin | 13 | 1.3 | 2 | 15.4 | 10 | 1.0 | 8 | 80.0 |
| | Sodium risedronate hydrate | 13 | 1.3 | 0 | 0.0 | 12 | 1.3 | 12 | 100.0 |
| | Loxoprofen sodium hydrate | 12 | 1.2 | 0 | 0.0 | 10 | 1.0 | 9 | 90.0 |
| | Bisoprolol fumarate | 12 | 1.2 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Beclometasone dipropionate | 12 | 1.2 | 1 | 8.3 | 12 | 1.3 | 11 | 91.7 |
| | Desloratadine | 12 | 1.2 | 2 | 16.7 | 11 | 1.1 | 8 | 72.7 |
| | Levofloxacin hydrate | 12 | 1.2 | 0 | 0.0 | 11 | 1.1 | 11 | 100.0 |
| | Betamethasone sodium phosphate | 11 | 1.1 | 1 | 9.1 | 11 | 1.1 | 9 | 81.8 |
| | Umeclidinium bromide | 11 | 1.1 | 1 | 9.1 | 11 | 1.1 | 8 | 72.7 |
| | Sennoside | 11 | 1.1 | 0 | 0.0 | 11 | 1.1 | 8 | 72.7 |
| | Aspirin | 11 | 1.1 | 1 | 9.1 | 10 | 1.0 | 9 | 90.0 |
| | Loratadine | 11 | 1.1 | 0 | 0.0 | 9 | 0.9 | 9 | 100.0 |
| | Azithromycin hydrate | 11 | 1.1 | 1 | 9.1 | 10 | 1.0 | 8 | 80.0 |
| | Non-pyrine cold remedy (4) | 10 | 1.0 | 0 | 0.0 | 10 | 1.0 | 10 | 100.0 |
| | Azilsartan | 10 | 1.0 | 1 | 10.0 | 7 | 0.7 | 6 | 85.7 |
| | Fluticasone furoate | 10 | 1.0 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Teprenone | 10 | 1.0 | 0 | 0.0 | 10 | 1.0 | 8 | 80.0 |
| | Betamethasone/d-chlorpheniramine maleate | 10 | 1.0 | 0 | 0.0 | 10 | 1.0 | 9 | 90.0 |
| | Tamsulosin hydrochloride | 10 | 1.0 | 0 | 0.0 | 10 | 1.0 | 8 | 80.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Clopidogrel sulfate | 10 | 1.0 | 0 | 0.0 | 8 | 0.8 | 7 | 87.5 |
| | Allopurinol | 10 | 1.0 | 0 | 0.0 | 10 | 1.0 | 8 | 80.0 |
| | Etizolam | 9 | 0.9 | 1 | 11.1 | 9 | 0.9 | 7 | 77.8 |
| | Pregabalin | 9 | 0.9 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Suvorexant | 9 | 0.9 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Valsartan | 9 | 0.9 | 1 | 11.1 | 9 | 0.9 | 6 | 66.7 |
| | Sodium cromoglicate | 9 | 0.9 | 0 | 0.0 | 9 | 0.9 | 8 | 88.9 |
| | Fluticasone furoate/umeclidinium bromide/vilanterol trifenatate | 9 | 0.9 | 1 | 11.1 | 9 | 0.9 | 7 | 77.8 |
| | Clostridium butyricum preparation | 9 | 0.9 | 3 | 33.3 | 8 | 0.8 | 3 | 37.5 |
| | Mosapride citrate hydrate | 9 | 0.9 | 2 | 22.2 | 7 | 0.7 | 5 | 71.4 |
| | Loxoprofen sodium hydrate | 9 | 0.9 | 0 | 0.0 | 8 | 0.8 | 7 | 87.5 |
| | Zopiclone | 8 | 0.8 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Dexamethasone cipecilate | 8 | 0.8 | 1 | 12.5 | 6 | 0.6 | 6 | 100.0 |
| | Pravastatin sodium | 8 | 0.8 | 0 | 0.0 | 8 | 0.8 | 7 | 87.5 |
| | Ezetimibe | 8 | 0.8 | 0 | 0.0 | 7 | 0.7 | 5 | 71.4 |
| | Glycopyrronium bromide | 8 | 0.8 | 0 | 0.0 | 8 | 0.8 | 7 | 87.5 |
| | Fluticasone propionate | 8 | 0.8 | 0 | 0.0 | 7 | 0.7 | 7 | 100.0 |
| | Dexamethasone sodium phosphate | 8 | 0.8 | 1 | 12.5 | 7 | 0.7 | 6 | 85.7 |
| | Tranexamic acid | 8 | 0.8 | 0 | 0.0 | 8 | 0.8 | 6 | 75.0 |
| | Edoxaban tosilate hydrate | 8 | 0.8 | 1 | 12.5 | 6 | 0.6 | 6 | 100.0 |
| | Minodronic acid hydrate | 8 | 0.8 | 1 | 12.5 | 8 | 0.8 | 6 | 75.0 |
| | Mequitazine | 8 | 0.8 | 0 | 0.0 | 7 | 0.7 | 7 | 100.0 |
| | Bepotastine besilate | 8 | 0.8 | 1 | 12.5 | 7 | 0.7 | 6 | 85.7 |
| | Triazolam | 7 | 0.7 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Eszopiclone | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Tramadol hydrochloride/acetaminophen combination | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Olopatadine hydrochloride | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Spironolactone | 7 | 0.7 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Losartan potassium | 7 | 0.7 | 1 | 14.3 | 7 | 0.7 | 6 | 85.7 |
| | Candesartan cilexetil | 7 | 0.7 | 0 | 0.0 | 6 | 0.6 | 6 | 100.0 |
| | Fudosteine | 7 | 0.7 | 1 | 14.3 | 6 | 0.6 | 6 | 100.0 |
| | Umeclidinium bromide/vilanterol trifenatate | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Tiotropium bromide hydrate/olodaterol hydrochloride | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 5 | 71.4 |
| | Lubiprostone | 7 | 0.7 | 1 | 14.3 | 7 | 0.7 | 5 | 71.4 |
| | Ursodeoxycholic acid | 7 | 0.7 | 1 | 14.3 | 7 | 0.7 | 7 | 100.0 |
| | Insulin lispro (genetical recombination) | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 5 | 71.4 |
| | Fursultiamine | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 7 | 100.0 |
| | Warfarin potassium | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Linagliptin | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 5 | 71.4 |
| | Kakkonto | 7 | 0.7 | 2 | 28.6 | 6 | 0.6 | 5 | 83.3 |
| | Sho-seiryu-to | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 4 | 57.1 |
| | Bakumondo-to | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Ampicillin sodium/sulbactam sodium | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 5 | 71.4 |
| | Garenoxacin mesilate hydrate | 7 | 0.7 | 0 | 0.0 | 7 | 0.7 | 6 | 85.7 |
| | Itraconazole | 7 | 0.7 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Ramelteon | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Fluticasone propionate | 6 | 0.6 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Azosemide | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Telmisartan/amlodipine besilate combination | 6 | 0.6 | 1 | 16.7 | 6 | 0.6 | 5 | 83.3 |
| | Diltiazem hydrochloride | 6 | 0.6 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Bezafibrate | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Antitussive combination (1) | 6 | 0.6 | 1 | 16.7 | 4 | 0.4 | 4 | 100.0 |
| | Antibiotics-resistant lactic acid bacteriae preparation (3) | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 4 | 66.7 |
| | Polaprezinc | 6 | 0.6 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Hydrocortisone sodium phosphate | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 5 | 83.3 |
| | Prednisolone sodium succinate | 6 | 0.6 | 0 | 0.0 | 5 | 0.5 | 3 | 60.0 |
| | Benzbromarone | 6 | 0.6 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Meropenem hydrate | 6 | 0.6 | 0 | 0.0 | 6 | 0.6 | 6 | 100.0 |
| | Tazobactam sodium/piperacillin sodium | 6 | 0.6 | 1 | 16.7 | 6 | 0.6 | 3 | 50.0 |
| | Sodium valproate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Celecoxib | 5 | 0.5 | 1 | 20.0 | 2 | 0.2 | 1 | 50.0 |
| | Duloxetine hydrochloride | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Donepezil hydrochloride | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Doxazosin mesilate | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Irbesartan | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Tocopherol nicotinate | 5 | 0.5 | 1 | 20.0 | 4 | 0.4 | 4 | 100.0 |
| | Bromhexine hydrochloride | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Procaterol hydrochloride hydrate | 5 | 0.5 | 1 | 20.0 | 4 | 0.4 | 3 | 75.0 |
| | Clenbuterol hydrochloride | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Salmeterol xinafoate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Mometasone furoate | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Omeprazole | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Domperidone | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Hydrocortisone sodium succinate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Insulin glargine (genetical recombination) | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Silodosin | 5 | 0.5 | 1 | 20.0 | 5 | 0.5 | 4 | 80.0 |
| | Solifenacin succinate | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Mirabegron | 5 | 0.5 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Ketoprofen | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 3 | 60.0 |
| | Ascorbic acid/calcium pantothenate (1) | 5 | 0.5 | 1 | 20.0 | 4 | 0.4 | 4 | 100.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Sodium ferrous citrate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Apixaban | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 3 | 60.0 |
| | Limaprost alfadex | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Ethyl Icosapentate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Glimepiride | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 5 | 100.0 |
| | Rupatadine fumarate | 5 | 0.5 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Shakuyakukanzoto | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Peramivir hydrate | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 3 | 60.0 |
| | An extract from inflamed cutaneous tissue of rabbits inoculated with vaccinia virus | 4 | 0.4 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Ketoprofen | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Trazodone hydrochloride | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Quetiapine fumarate | 4 | 0.4 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Mirtazapine | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 3 | 75.0 |
| | Fluorometholone | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 3 | 75.0 |
| | Epinastine hydrochloride | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Tramazoline hydrochloride | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Diphenhydramine salicylate/diprophylline | 4 | 0.4 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Trichlormethiazide | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Verapamil hydrochloride | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 3 | 75.0 |
| | Fenofibrate | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Indacaterol maleate/glycopyrronium bromide | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Budesonide/glycopyrronium bromide/formoterol fumarate hydrate | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Sodium picosulfate hydrate | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 3 | 75.0 |
| | Senna leaf/senna pods | 4 | 0.4 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Insulin aspart (genetical recombination) | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Insulin degludec (genetical recombination) | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Dulaglutide (genetical recombination) | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Betamethasone butyrate propionate | 4 | 0.4 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Dried ferrous sulfate (3) | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 3 | 75.0 |
| | Vildagliptin | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 3 | 75.0 |
| | Amoxicillin hydrate | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 2 | 50.0 |
| | Cefditoren pivoxil | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 4 | 100.0 |
| | Amoxicillin hydrate/potassium clavulanate | 4 | 0.4 | 1 | 25.0 | 4 | 0.4 | 1 | 25.0 |
| | Salazosulfapyridine | 4 | 0.4 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Oseltamivir phosphate | 4 | 0.4 | 0 | 0.0 | 4 | 0.4 | 2 | 50.0 |
| | Flunitrazepam | 3 | 0.3 | 1 | 33.3 | 2 | 0.2 | 2 | 100.0 |
| | Rilmazafone hydrochloride hydrate | 3 | 0.3 | 1 | 33.3 | 3 | 0.3 | 1 | 33.3 |
| | Carbamazepine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Betahistine mesilate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Metildigoxin | 3 | 0.3 | 1 | 33.3 | 3 | 0.3 | 1 | 33.3 |
| | Cibenzoline succinate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Imidapril hydrochloride | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Cilnidipine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Irbesartan/amlodipine besilate combination | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Nicorandil | 3 | 0.3 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Isosorbide mononitrate | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Isosorbide dinitrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Simvastatin | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Precipitated calcium carbonate | 3 | 0.3 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Dimemorfan phosphate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Acetylcysteine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Fenoterol hydrobromide | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Bifidobacterium preparation (4) | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Ranitidine hydrochloride | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Lafutidine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Miconazole nitrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Diphenhydramine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Difluprednate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Felbinac | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Heparinoid | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 2 | 66.7 |
| | Cilostazol | 3 | 0.3 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Potassium citrate/sodium citrate hydrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Saxagliptin hydrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Ebastine | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Cetirizine hydrochloride | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Fexofenadine hydrochloride/pseudoephedrine hydrochloride combination | 3 | 0.3 | 1 | 33.3 | 3 | 0.3 | 2 | 66.7 |
| | Hange-kobokuto | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Cefepime dihydrochloride hydrate | 3 | 0.3 | 1 | 33.3 | 3 | 0.3 | 1 | 33.3 |
| | Erythromycin | 3 | 0.3 | 1 | 33.3 | 2 | 0.2 | 2 | 100.0 |
| | Levofloxacin hydrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Codeine phosphate hydrate | 3 | 0.3 | 0 | 0.0 | 3 | 0.3 | 3 | 100.0 |
| | Estazolam | 2 | 0.2 | 1 | 50.0 | 1 | 0.1 | 1 | 100.0 |
| | Lorazepam | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Alprazolam | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 2 | 100.0 |
| | Phenobarbital | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Tiaramide hydrochloride | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Tramadol hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Amitriptyline hydrochloride | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Clotiazepam | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Sulpiride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Escitalopram oxalate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Pyridostigmine bromide | 2 | 0.2 | 1 | 50.0 | 1 | 0.1 | 1 | 100.0 |
| | Purified sodium hyaluronate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Levocabastine hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Diquafosol sodium | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Brimonidine tartrate | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Ofloxacin | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 1 | 50.0 |
| | Digoxin | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Atenolol | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pilsicainide hydrochloride hydrate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Torasemide | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Tolvaptan | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Enalapril maleate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Carvedilol | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Azelnidipine | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Eplerenone | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Losartan potassium/hydrochlorothiazide combination | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Telmisartan/hydrochlorothiazide combination | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Sumatriptan succinate | 2 | 0.2 | 1 | 50.0 | 1 | 0.1 | 1 | 100.0 |
| | Omega-3 acid ethyl esters | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Calcium polystyrene sulfonate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Respiratory drugs | 2 | 0.2 | 1 | 50.0 | 1 | 0.1 | 1 | 100.0 |
| | Cloperastine fendizoate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Benproperine phosphate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Tulobuterol hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Aclidinium bromide | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 2 | 100.0 |
| | Omalizumab (genetical recombination) | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Famotidine | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Trimebutine maleate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Linaclotide | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Metoclopramide hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Fradiomycin/gramicidin S | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Dried thyroid | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Teriparatide (genetical recombination) | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dexamethasone | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Triamcinolone | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Insulin human (genetical recombination) | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Leuprorelin acetate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Amphotericin B | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Propiverine hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | White petrolatum | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Clobetasol propionate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Betamethasone valerate/gentamicin sulfate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Crotamiton | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Benzethonium chloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Fursultiamine/B2/B6/B12 combination (1) | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Benfotiamine/B6/B12 combination (1) | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Precipitated calcium carbonate/cholecalciferol/magnesium carbonate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Potassium L-aspartate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Glucose and electrolytes solution (3) | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Rivaroxaban | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Heparinoid | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Ticlopidine hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Sarpogrelate hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Aspirin/dialuminate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Aspirin/lansoprazole combination | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Monoammonium glycyrrhizinate/glycine/DL-methionine combination | 2 | 0.2 | 1 | 50.0 | 1 | 0.1 | 1 | 100.0 |
| | Topiroxostat | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Mitiglinide calcium hydrate | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Alogliptin benzoate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Ipragliflozin/L-proline | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Dapagliflozin propylene glycolate hydrate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Vildagliptin/metformin hydrochloride combination | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Camostat mesilate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Tacrolimus hydrate | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 2 | 100.0 |
| | Ketotifen fumarate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Azelastine hydrochloride | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Saibokuto | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 1 | 50.0 |
| | Bofutsushosan | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Yokukansan | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Rikkunshi-to | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Cefcapene/pivoxil hydrochloride hydrate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Cefoperazone sodium/sulbactam sodium | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Erythromycin stearate | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Rifampicin | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 1 | 50.0 |
| | Amphotericin B | 2 | 0.2 | 1 | 50.0 | 2 | 0.2 | 2 | 100.0 |
| | Sitafloxacin hydrate | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Valaciclovir hydrochloride | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Influenza vaccine | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Nitrazepam | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Lormetazepam | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diazepam | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bromazepam | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Flutoprazepam | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Phenytoin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Topiramate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Acetaminophen | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diclofenac sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bucolome | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pentazocine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pentazocine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Droxidopa | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Chlorpromazine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Levomepromazine maleate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Hydroxyzine pamoate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Haloperidol | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Risperidone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Fluvoxamine maleate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Aripiprazole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Sertraline hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Haloperidol | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Memantine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Galantamine hydrobromide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Mirogabalin besylate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Rivastigmine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Magnesium sulfate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Eperisone hydrochloride | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 1 | 100.0 |
| | Oxybuprocaine hydrochloride | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Dexamethasone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dexamethasone metasulfobenzoate sodium | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Gentamicin sulfate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Sodium gualenate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pirenoxine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ofloxacin | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Ketotifen fumarate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dorzolamide hydrochloride | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Latanoprost | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Levofloxacin hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Acitazanolast hydrate | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 1 | 100.0 |
| | Moxifloxacin hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bimatoprost | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Rebamipide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ripasudil hydrochloride hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Oxytetracycline hydrochloride/hydrocortisone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Fradiomycin sulfate/methylprednisolone | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 1 | 100.0 |
| | Boric acid/inorganic salt combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Brinzolamide/timolol maleate | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Carteolol hydrochloride/latanoprost | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Fosfomycin sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ubidecarenone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Amiodarone hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Acetazolamide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Furosemide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Lisinopril hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Perindopril erbumine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Tripamide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Indapamide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Urapidil | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Manidipine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Valsartan/amlodipine besilate combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Olmesartan medoxomil/azelnidipine combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Candesartan cilexetil/amlodipine besilate combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Azilsartan/amlodipine besilate combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Midodrine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Zolmitriptan | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Naratriptan hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dipyridamole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Isosorbide dinitrate | 1 | 0.1 | 1 | 100.0 | 0 | 0.0 | 0 | - |
| | Sodium polystyrene sulfonate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Romerizine hydrochloride | 1 | 0.1 | 1 | 100.0 | 0 | 0.0 | 0 | - |
| | Lanthanum carbonate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Amlodipine besylate/atorvastatin calcium hydrate combination (1) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Citicoline | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Clofedanol hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diprophylline/dihydrocodeine combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ethyl L-cysteine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Bromhexine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cherry bark extract | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Codeine phosphate hydrate (not more than 1%) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Eprazinone hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Tipepidine hibenzate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Formoterol fumarate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Sodium gualenate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Povidone-iodine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Benralizumab (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Indacaterol acetate/glycopyrronium bromide/mometasone furoate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Antibiotics-resistant lactic acid bacteriae preparation (1) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bifidobacterium combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Lactomin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dimeticone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cimetidine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Irsogladine maleate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Propantheline bromide/chlorophyll combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dicyclomine/aluminum hydroxide gel combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Sodium gualenate hydrate/L-glutamine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Omeprazole sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Lansoprazole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pancrelipase | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pancreatic digestive enzyme combination (2) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Powdered glycyrrhiza combination (1) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Sodium bicarbonate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Aluminum hydroxide gel/magnesium hydroxide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Elobixibat hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Macrogol 4000/sodium chloride/sodium bicarbonate/potassium chloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Granisetron hydrochloride | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Metoclopramide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Itopride hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Polycarbophil calcium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dequalinium chloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Propylthiouracil | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Noradrenaline | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dexamethasone acetate | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Prednisolone acetate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Estradiol | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Dydrogesterone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Kallidinogenase | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Insulin glulisine (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Insulin degludec (genetical recombination)/insulin aspart (genetical recombination) combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dutasteride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Semaglutide (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Flavoxate hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Naftopidil | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Imidafenacin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Fesoterodine fumarate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Chimaphila umbellata extract/populus extract combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Gentamicin sulfate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ozenoxacin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diphenhydramine laurylsulfate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diflucortolone valerate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Betamethasone valerate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Hydrocortisone butyrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Prednisolone valerate acetate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Clobetasone butyrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Diclofenac sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Luliconazole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Terbinafine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Maxacalcitol | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Flavin adenine dinucleotide sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Folic acid | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Octotiamine/B2/B6/B12 combination | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 1 | 100.0 |
| | Thiamine disulfide/B6/B12 combination | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ferrous fumarate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ferric pyrophosphate, soluble | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Potassium gluconate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Isoleucine/leucine/valine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Amino acid preparations for hepatic failure (1) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Physiological saline | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Lactated Ringer's solution | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Carbazochrome sodium sulfonate hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Dabigatran etexilate methanesulfonate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Beraprost sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Spherical adsorptive carbon | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Sodium bicarbonate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Gliclazide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Acarbose | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Voglibose | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Nateglinide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Repaglinide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Anagliptin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Canagliflozin hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |

Table 5 Subject characteristics (concomitant medications and therapies)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| | Empagliflozin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Lactulose | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cyclosporine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Methotrexate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Raloxifene hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bazedoxifene acetate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Iguratimod | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Levocarnitine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Gabexate mesilate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ulinastatin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Golimumab (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Denosumab (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Tegafur/gimeracil/oteracil potassium combination | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Bicalutamide | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Anastrozole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Nilotinib hydrochloride hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Oxaliplatin | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Pembrolizumab (genetical recombination) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Promethazine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | d-chlorpheniramine maleate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Clemastine fumarate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Bucillamine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Other antiallergic drugs | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ozagrel hydrochloride hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ramatroban | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Standardized cedar pollen extract | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Emedastine fumarate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Kakkon-to-ka-senkyu-sin'i | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Kikyoto | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Goshajinkigan | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Koso-san | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Goreisan | 1 | 0.1 | 1 | 100.0 | 1 | 0.1 | 0 | 0.0 |
| | Shin'iseihaito | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Shimpito | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Daikenchuto | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Chorei-to | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Tokaku-joki-to | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ninjin-to | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Hachimi-jio-gan | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Hochuekkito | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Maoto | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Maobushisaishinto | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Mashiningan | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Coix seed extract | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cefalexin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cefmetazole sodium | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Cefozopran hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Roxithromycin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Azithromycin hydrate | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Minocycline hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Minocycline hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Amphotericin B | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Rifaximin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Vonoprazan fumarate/amoxicillin hydrate/metronidazole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ethambutol hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Moxifloxacin hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Linezolid | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Amenamevir | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Baloxavir marboxil | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Glecaprevir hydrate/pibrentasvir | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Ganciclovir | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Terbinafine hydrochloride | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Atovaquone | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Efinaconazole | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Pneumococcal vaccine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Virus vaccines | 1 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | - |
| | Influenza HA vaccine | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Freeze-dried polyethylene glycol treated human normal immunoglobulin | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| Concomitant therapies | Home oxygen therapy | 5 | 0.5 | 0 | 0.0 | 5 | 0.5 | 4 | 80.0 |
| | Oxygen therapy | 3 | 0.3 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Respiratory rehabilitation | 2 | 0.2 | 0 | 0.0 | 2 | 0.2 | 2 | 100.0 |
| | Bronchial thermoplasty | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Respiratory rehabilitation | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Home oxygen | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| | Long-term oxygen supplementation therapy | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Immunotherapy (mites) | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |

Table 6 Subject characteristics (administration status)

As of September 27, 2023

Subjects included in safety analysis, Subjects included in effectiveness analysis

| Item/Category | | Subjects included in safety analysis | | | | Subjects included in effectiveness analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Number of subjects | Usage ratio (%) | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Number of subjects | Usage ratio (%) | Number of responders | Rate of responders (%) |
| Daily dose [mg](at the start of administration) | 100 | 1026 | 99.9 | 42 | 4.1 | 958 | 99.9 | 865 | 90.3 |
| | 100< | 1 | 0.1 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| Total number of doses [dose] | <1 | 0 | 0.0 | 0 | - | 0 | 0.0 | 0 | - |
| Number of subjects: 1027/959 | 1≤ to <3 | 153 | 14.9 | 14 | 9.2 | 117 | 12.2 | 97 | 82.9 |
| Mean ± SD: 9.4±5.2/9.8±5.0 | 3≤ to <6 | 141 | 13.7 | 12 | 8.5 | 121 | 12.6 | 84 | 69.4 |
| Minimum: 1/1 | 6≤ to <9 | 118 | 11.5 | 5 | 4.2 | 112 | 11.7 | 96 | 85.7 |
| Median: 11.0/11.0 | 9≤ to <13 | 221 | 21.5 | 9 | 4.1 | 218 | 22.7 | 204 | 93.6 |
| Maximum: 20/20 | 13≤ | 394 | 38.4 | 2 | 0.5 | 391 | 40.8 | 385 | 98.5 |
| Total dose [mg] | <100 | 0 | 0.0 | 0 | - | 0 | 0.0 | 0 | - |
| Number of subjects: 1027/959 | 100≤ to <300 | 153 | 14.9 | 14 | 9.2 | 117 | 12.2 | 97 | 82.9 |
| Mean ± SD: 941.4±528.1/984.2±513.1 | 300≤ to <600 | 141 | 13.7 | 12 | 8.5 | 121 | 12.6 | 84 | 69.4 |
| Minimum: 100/100 | 600≤ to <900 | 118 | 11.5 | 5 | 4.2 | 112 | 11.7 | 96 | 85.7 |
| Median: 1100.0/1100.0 | 900≤ to <1300 | 221 | 21.5 | 9 | 4.1 | 218 | 22.7 | 204 | 93.6 |
| Maximum: 4500/4500 | 1300≤ | 394 | 38.4 | 2 | 0.5 | 391 | 40.8 | 385 | 98.5 |
| Duration of administration of this drug [days] | <28 | 96 | 9.3 | 7 | 7.3 | 73 | 7.6 | 61 | 83.6 |
| Number of subjects: 1027/959 | 28≤ to <84 | 101 | 9.8 | 9 | 8.9 | 74 | 7.7 | 55 | 74.3 |
| Mean ± SD: 272.6±163.0/286.4±157.3 | 84≤ to <168 | 109 | 10.6 | 11 | 10.1 | 100 | 10.4 | 72 | 72.0 |
| Minimum: 1/1 | 168≤ to <252 | 75 | 7.3 | 4 | 5.3 | 73 | 7.6 | 58 | 79.5 |
| Median: 344.0/355.0 | 252≤ to <365 | 218 | 21.2 | 6 | 2.8 | 215 | 22.4 | 203 | 94.4 |
| Maximum: 1418/1418 | 365≤ | 428 | 41.7 | 5 | 1.2 | 424 | 44.2 | 417 | 98.3 |
| Administration of the drug at the end of the observation period | Treatment continued | 559 | 54.4 | 5 | 0.9 | 553 | 57.7 | 543 | 98.2 |
| (Reasons for discontinuation: duplicates included) | Discontinuation/termination of administration | 468 | 45.6 | 37 | 7.9 | 406 | 42.3 | 323 | 79.6 |
| | Onset of adverse events | 54 | 5.3 | 28 | 51.9 | 41 | 4.3 | 31 | 75.6 |
| | Pregnancy | 2 | 0.2 | 0 | 0.0 | 1 | 0.1 | 1 | 100.0 |
| | Factors associated with effectiveness | 146 | 14.2 | 7 | 4.8 | 143 | 14.9 | 76 | 53.1 |
| | Financial reasons | 59 | 5.7 | 3 | 5.1 | 45 | 4.7 | 40 | 88.9 |
| | No revisit after the first prescription date | 0 | 0.0 | 0 | - | 0 | 0.0 | 0 | - |
| | No revisit in the middle of the study | 45 | 4.4 | 1 | 2.2 | 33 | 3.4 | 32 | 97.0 |
| | Patient's inconvenience other than the above mentioned | 115 | 11.2 | 0 | 0.0 | 97 | 10.1 | 93 | 95.9 |
| | Physician's judgment other than the above mentioned | 41 | 4.0 | 1 | 2.4 | 34 | 3.5 | 33 | 97.1 |
| | Unknown | 37 | 3.6 | 1 | 2.7 | 37 | 3.9 | 37 | 100.0 |

The "mean ± SD," "minimum," "median," and "maximum" for each item are presented in the order of "safety analysis set" / "effectiveness analysis set."

Table 7 Duration of administration of this drug by reason for Ddscontinuation/termination of administration

As of September 27, 2023

Subjects included in safety analysis

| | | Duration of administration of this drug until discontinuation/termination [days] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | <28 | 28≤ to <84 | 84≤ to <168 | 168≤ to <252 | 252≤ to <365 | Unknown | Total number of subjects (%) | |
| Number of subjects who discontinued/ terminated administration | | 96 | 101 | 109 | 75 | 87 | 0 | 468 | (45.6) |
| Reason for discontinuation/ termination of administration* | Onset of adverse events | 11 | 15 | 12 | 6 | 10 | 0 | 54 | (5.3) |
| | Pregnancy | 0 | 1 | 0 | 0 | 1 | 0 | 2 | (0.2) |
| | Factors related to effectiveness | 32 | 30 | 39 | 23 | 22 | 0 | 146 | (14.2) |
| | Economic reasons | 16 | 21 | 9 | 8 | 5 | 0 | 59 | (5.7) |
| | No revisit after the first prescription date | 0 | 0 | 0 | 0 | 0 | 0 | 0 | (0.0) |
| | No revisit in the middle of the study | 9 | 10 | 11 | 5 | 10 | 0 | 45 | (4.4) |
| | Patient's convenience other than the above | 13 | 25 | 34 | 26 | 17 | 0 | 115 | (11.2) |
| | Physician's judgment other than the above | 11 | 4 | 9 | 10 | 7 | 0 | 41 | (4.0) |
| | Unknown | 11 | 3 | 1 | 3 | 19 | 0 | 37 | (3.6) |

*: Duplicates included

Table 8 Incidence of adverse drug reactions by seriousness

As of September 27, 2023

Subjects included in safety analysis

| | Total | | Serious | |
|---|---|---|---|---|
| Number of subjects studied | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 42 | | 9 | |
| Incidence of adverse drug reactions, etc. (%) | 4.1 | | 0.9 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | |
| Respiratory, thoracic and mediastinal disorders | 12 | (1.2) | 3 | (0.3) |
| Asthma | 7 | (0.7) | 2 | (0.2) |
| Chronic eosinophilic rhinosinusitis | 4 | (0.4) | 1 | (0.1) |
| Upper respiratory tract inflammation | 1 | (0.1) | 0 | (0.0) |
| Skin and subcutaneous tissue disorders | 10 | (1.0) | 1 | (0.1) |
| Urticaria | 4 | (0.4) | 0 | (0.0) |
| Pruritus | 2 | (0.2) | 0 | (0.0) |
| Rash | 2 | (0.2) | 0 | (0.0) |
| Alopecia | 1 | (0.1) | 0 | (0.0) |
| Angioedema | 1 | (0.1) | 1 | (0.1) |
| Eczema | 1 | (0.1) | 0 | (0.0) |
| General disorders and administration site conditions | 9 | (0.9) | 1 | (0.1) |
| Condition aggravated | 4 | (0.4) | 1 | (0.1) |
| Malaise | 2 | (0.2) | 0 | (0.0) |
| Oedema peripheral | 1 | (0.1) | 0 | (0.0) |
| Pain | 1 | (0.1) | 0 | (0.0) |
| Pyrexia | 1 | (0.1) | 0 | (0.0) |
| Infections and infestations | 3 | (0.3) | 1 | (0.1) |
| Bronchitis | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 1 | (0.1) | 1 | (0.1) |
| Nervous system disorders | 3 | (0.3) | 1 | (0.1) |
| Headache | 2 | (0.2) | 0 | (0.0) |
| Myasthenia gravis | 1 | (0.1) | 1 | (0.1) |
| Musculoskeletal and connective tissue disorders | 3 | (0.3) | 0 | (0.0) |
| Back pain | 2 | (0.2) | 0 | (0.0) |
| Arthralgia | 1 | (0.1) | 0 | (0.0) |
| Pain in extremity | 1 | (0.1) | 0 | (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 2 | (0.2) | 2 | (0.2) |
| Gastric cancer | 1 | (0.1) | 1 | (0.1) |
| Intraductal papillary-mucinous carcinoma of pancreas | 1 | (0.1) | 1 | (0.1) |
| Cardiac disorders | 2 | (0.2) | 0 | (0.0) |
| Palpitations | 2 | (0.2) | 0 | (0.0) |
| Gastrointestinal disorders | 2 | (0.2) | 0 | (0.0) |
| Nausea | 2 | (0.2) | 0 | (0.0) |
| Vomiting | 1 | (0.1) | 0 | (0.0) |
| Hepatobiliary disorders | 2 | (0.2) | 0 | (0.0) |
| Hepatic function abnormal | 2 | (0.2) | 0 | (0.0) |

Table 8 Incidence of adverse drug reactions by seriousness

As of September 27, 2023

Subjects included in safety analysis

| | Total | | Serious | |
|---|---|---|---|---|
| Number of subjects studied | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 42 | | 9 | |
| Incidence of adverse drug reactions, etc. (%) | 4.1 | | 0.9 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | |
| Eye disorders | 1 | (0.1) | 1 | (0.1) |
| Optic neuropathy | 1 | (0.1) | 1 | (0.1) |
| Ear and labyrinth disorders | 1 | (0.1) | 1 | (0.1) |
| Vertigo positional | 1 | (0.1) | 1 | (0.1) |
| Investigations | 1 | (0.1) | 0 | (0.0) |
| Eosinophil count increased | 1 | (0.1) | 0 | (0.0) |

MedDRA/J (26.0)

Table 9 Outcome of adverse drug reactions by seriousness (by event)

As of September 27, 2023

Subjects included in safety analysis

| | Serious | | | | | | | | | | | | Non-serious | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 1027 | | | | | | | | | | | | 1027 | | | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 3 | | 0 | | 0 | | 2 | | 4 | | 0 | | 0 | | 0 | | 0 | | 12 | | 20 | | 1 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | |
| Infections and infestations | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Bronchitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Gastric cancer | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Intraductal papillary-mucinous carcinoma of pancreas | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Nervous system disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Headache | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Myasthenia gravis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Eye disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Optic neuropathy | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Ear and labyrinth disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Vertigo positional | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Cardiac disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Palpitations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Respiratory, thoracic and mediastinal disorders | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 6 | (0.6) | 3 | (0.3) | 0 | (0.0) |
| Asthma | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 2 | (0.2) | 0 | (0.0) |
| Upper respiratory tract inflammation | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Chronic eosinophilic rhinosinusitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) |
| Gastrointestinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Nausea | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Vomiting | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Hepatobiliary disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Hepatic function abnormal | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Skin and subcutaneous tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 8 | (0.8) | 0 | (0.0) |
| Alopecia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Angioedema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Eczema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pruritus | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Rash | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Urticaria | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) |
| Musculoskeletal and connective tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) |
| Arthralgia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Back pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Pain in extremity | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| General disorders and administration site conditions | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 1 | (0.1) | 0 | (0.0) |
| Condition aggravated | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) |
| Malaise | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) |
| Oedema peripheral | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pyrexia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Investigations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Eosinophil count increased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

Table 10 Listing of occurrence status of adverse drug reactions by subject characteristics

As of September 27, 2023

Subjects included in safety analysis

| Subject characteristics | | Number of subjects studied | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower limit | Upper limit |
| Total | | 1027 | 42 | 4.1 | 3.0 | 5.5 |
| Gender | Male | 386 | 13 | 3.4 | 1.8 | 5.7 |
| | Female | 641 | 29 | 4.5 | 3.1 | 6.4 |
| Pregnancy status "Female only" | No | 623 | 29 | 4.7 | 3.1 | 6.6 |
| | Yes | 2 | 0 | 0.0 | 0.0 | 84.2 |
| | Unknown | 16 | 0 | 0.0 | 0.0 | 20.6 |
| Age 1 [years] | <15 | 11 | 0 | 0.0 | 0.0 | 28.5 |
| Mean ± SD: 62.7±16.1 | 15≤ to <65 | 461 | 17 | 3.7 | 2.2 | 5.8 |
| Minimum: 12 | 65≤ to <75 | 280 | 14 | 5.0 | 2.8 | 8.2 |
| Median: 66.0 | 75≤ | 275 | 11 | 4.0 | 2.0 | 7.0 |
| Maximum: 93 | | | | | | |
| Age 2 [years] | <65 | 472 | 17 | 3.6 | 2.1 | 5.7 |
| | 65≤ | 555 | 25 | 4.5 | 2.9 | 6.6 |
| Hospitalization status | Inpatient | 59 | 3 | 5.1 | 1.1 | 14.1 |
| | Outpatient | 968 | 39 | 4.0 | 2.9 | 5.5 |
| Reason for use of this drug | Bronchial asthma | 1024 | 42 | 4.1 | 3.0 | 5.5 |
| | Other | 3 | 0 | 0.0 | 0.0 | 70.8 |
| Breakdown of other reasons for use of this drug (name of disease)(multiple reasons) | Bronchiectasis | 1 | 0 | 0.0 | 0.0 | 97.5 |
| | Bronchiolitis | 1 | 0 | 0.0 | 0.0 | 97.5 |
| | Eosinophilic granulomatosis with polyangiitis | 1 | 0 | 0.0 | 0.0 | 97.5 |
| Comorbidity | No | 290 | 5 | 1.7 | 0.6 | 4.0 |
| | Yes | 737 | 37 | 5.0 | 3.6 | 6.9 |
| Comorbidity (renal impairment) | No | 1002 | 41 | 4.1 | 3.0 | 5.5 |
| | Yes | 25 | 1 | 4.0 | 0.1 | 20.4 |
| Comorbidity (hepatic function disorder) | No | 997 | 40 | 4.0 | 2.9 | 5.4 |
| | Yes | 30 | 2 | 6.7 | 0.8 | 22.1 |
| Comorbidities (allergies) | No | 625 | 17 | 2.7 | 1.6 | 4.3 |
| | Yes | 402 | 25 | 6.2 | 4.1 | 9.0 |
| Comorbidities (other conditions) | No | 411 | 14 | 3.4 | 1.9 | 5.6 |
| | Yes | 616 | 28 | 4.5 | 3.0 | 6.5 |
| Smoking history | Never-smoker | 702 | 29 | 4.1 | 2.8 | 5.9 |
| | Ex-smoker | 289 | 13 | 4.5 | 2.4 | 7.6 |
| | Current-smoker | 36 | 0 | 0.0 | 0.0 | 9.7 |
| Primary disease (disease duration [years]) | ≤2 | 33 | 1 | 3.0 | 0.1 | 15.8 |
| | 2< to ≤5 | 68 | 5 | 7.4 | 2.4 | 16.3 |
| | 5< to ≤10 | 143 | 5 | 3.5 | 1.1 | 8.0 |
| | 10< | 638 | 28 | 4.4 | 2.9 | 6.3 |
| | Unknown | 145 | 3 | 2.1 | 0.4 | 5.9 |
| Primary disease (severity before administration) | Mild intermittent | 0 | 0 | - | - | - |
| | Mild persistent | 2 | 0 | 0.0 | 0.0 | 84.2 |
| | Moderate persistent | 30 | 3 | 10.0 | 2.1 | 26.5 |
| | Severe persistent | 688 | 23 | 3.3 | 2.1 | 5.0 |
| | Most severe persistent | 307 | 16 | 5.2 | 3.0 | 8.3 |
| Primary disease (disease type) | Atopic | 532 | 23 | 4.3 | 2.8 | 6.4 |
| | Non-atopic | 382 | 13 | 3.4 | 1.8 | 5.7 |
| | Unknown | 113 | 6 | 5.3 | 2.0 | 11.2 |
| Blood eosinophil count (9 to 52 weeks before start of administration of this drug)[/μL] | <150 | 110 | 8 | 7.3 | 3.2 | 13.8 |
| Mean ± SD: 701.0±935.1 | 150≤ to <300 | 95 | 1 | 1.1 | 0.0 | 5.7 |
| Minimum: 0 | 300≤ to <500 | 143 | 6 | 4.2 | 1.6 | 8.9 |
| Median: 460.0 | 500≤ | 308 | 15 | 4.9 | 2.8 | 7.9 |
| Maximum: 9999 | Unknown | 371 | 12 | 3.2 | 1.7 | 5.6 |
| Blood eosinophil count (baseline)[/μL] | <150 | 163 | 6 | 3.7 | 1.4 | 7.8 |
| Mean± SD: 641.5±822.9 | 150≤ to <300 | 110 | 5 | 4.5 | 1.5 | 10.3 |
| Minimum: 0 | 300≤ to <500 | 196 | 9 | 4.6 | 2.1 | 8.5 |
| Median: 418.0 | 500≤ | 350 | 19 | 5.4 | 3.3 | 8.3 |
| Maximum: 7500 | Unknown | 208 | 3 | 1.4 | 0.3 | 4.2 |
| History of omalizumab use | No | 871 | 32 | 3.7 | 2.5 | 5.1 |
| | Yes | 156 | 10 | 6.4 | 3.1 | 11.5 |
| Prior medications for bronchial asthma | No | 7 | 0 | 0.0 | 0.0 | 41.0 |
| | Yes | 1020 | 42 | 4.1 | 3.0 | 5.5 |
| Concomitant medications | No | 75 | 2 | 2.7 | 0.3 | 9.3 |
| | Yes | 952 | 40 | 4.2 | 3.0 | 5.7 |
| Concomitant therapies for bronchial asthma (other than drug therapy) | No | 1013 | 42 | 4.1 | 3.0 | 5.6 |
| | Yes | 14 | 0 | 0.0 | 0.0 | 23.2 |

Table 11 Multivariate logistic regression analysis (Safety)

As of September 27, 2023

Subjects included in safety analysis

Odds ratio estimated by multivariate logistic regression

| Item/Category | | Number of subjects studied | Number of subjects with adverse drug reactions | Incidence of adverse drug reactions (%) | Adjusted odds ratio | | |
|---|---|---|---|---|---|---|---|
| | | | | | Point estimation | 95% confidence | |
| | | | | | | Lower limit | Upper limit |
| Total | | 1027 | 42 | 4.1 | - | - | - |
| Comorbidities (allergies) | No * | 625 | 17 | 2.7 | - | - | - |
| | Yes | 402 | 25 | 6.2 | 1.864 | 0.951 | 3.655 |

*: Criteria

Table 12 Time to onset of adverse drug reactions

As of September 27, 2023

Subjects included in safety analysis

| | Time to onset of adverse drug reactions [days][*1] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | <28 | 28≤ to <84 | 84≤ to <168 | 168≤ to <252 | 252≤ to <365 | 365≤ | Unknown[*2] | Total number of subjects with adverse drug reactions (%)[*3] | |
| Safety Analysis Set | 1027 | 931 | 830 | 721 | 646 | 428 | 0 | 1027 | - |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions by type | | | | | | | | |
| Respiratory, thoracic and mediastinal disorders | 1 | 4 | 1 | 1 | 4 | 1 | 0 | 12 | (1.2) |
| Asthma | 1 | 3 | 0 | 1 | 1 | 1 | 0 | 7 | (0.7) |
| Chronic eosinophilic rhinosinusitis | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 4 | (0.4) |
| Upper respiratory tract inflammation | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Skin and subcutaneous tissue disorders | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 10 | (1.0) |
| Urticaria | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 4 | (0.4) |
| Pruritus | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Rash | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Alopecia | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Angioedema | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Eczema | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| General disorders and administration site conditions | 2 | 1 | 2 | 1 | 3 | 0 | 0 | 9 | (0.9) |
| Condition aggravated | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 4 | (0.4) |
| Malaise | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Oedema peripheral | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | (0.1) |
| Pain | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Pyrexia | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Infections and infestations | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 3 | (0.3) |
| Bronchitis | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Nasopharyngitis | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Pharyngitis | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Pneumonia | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Nervous system disorders | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 3 | (0.3) |
| Headache | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Myasthenia gravis | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | (0.1) |

Table 12 Time to onset of adverse drug reactions

As of September 27, 2023

Subjects included in safety analysis

| | Time to onset of adverse drug reactions [days][*1] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | <28 | 28≤ to <84 | 84≤ to <168 | 168≤ to <252 | 252≤ to <365 | 365≤ | Unknown[*2] | Total number of subjects with adverse drug reactions (%)[*3] | |
| Safety Analysis Set | 1027 | 931 | 830 | 721 | 646 | 428 | 0 | 1027 | - |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions by type | | | | | | | | |
| Musculoskeletal and connective tissue disorders | 0 | 0 | 2 | 0 | 1 | 0 | 0 | 3 | (0.3) |
| Back pain | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Arthralgia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | (0.1) |
| Pain in extremity | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | (0.1) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 2 | (0.2) |
| Gastric cancer | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | (0.1) |
| Intraductal papillary-mucinous carcinoma of pancreas | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | (0.1) |
| Cardiac disorders | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Palpitations | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Gastrointestinal disorders | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Nausea | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | (0.2) |
| Vomiting | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | (0.1) |
| Hepatobiliary disorders | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | (0.2) |
| Hepatic function abnormal | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | (0.2) |
| Eye disorders | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | (0.1) |
| Optic neuropathy | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | (0.1) |
| Ear and labyrinth disorders | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | (0.1) |
| Vertigo positional | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | (0.1) |
| Investigations | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | (0.1) |
| Eosinophil count increased | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | (0.1) |
| Number of subjects with adverse drug reactions | 12 | 11 | 8 | 3 | 6 | 2 | 0 | 42 | (4.1) |
| (%)[*4] | (28.6) | (26.2) | (19.0) | (7.1) | (14.3) | (4.8) | (0.0) | - | - |
| Cumulative number of subjects with adverse drug reactions | 12 | 23 | 31 | 34 | 40 | 42 | 0 | - | - |
| (%)[*5] | (28.6) | (54.8) | (73.8) | (81.0) | (95.2) | (100.0) | (0.0) | - | - |

*1: When multiple adverse drug reactions under the same system organ class (SOC) and preferred term (PT) occurred in the same subject, the adverse drug reactions which occurred for the first time under the SOC and PT were tabulated. MedDRA/J (26.0)

*2: Subjects with unknown date of onset of adverse drug reactions were tabulated as those with unknown time to onset of adverse drug reactions.

*3: Overlapping cases in each administration category and type of adverse drug reactions were excluded. The percentage was calculated as (number of subjects with adverse drug reactions/safety analysis set)*100.

*4: (Number of subjects with adverse drug reactions/Total number of subjects with adverse drug reactions)*100

*5: (Cumulative number of subjects with adverse drug reactions/Total number of subjects with adverse drug reactions)*100

Table 13　List of MedDRA codes for safety specification

As of September 27, 2023

Subjects included in safety analysis

| Special Interest AE Group | SMQ, HLGT, HLT, SOC, PT or LLT | Code | Term (Japanese) |
|---|---|---|---|
| Hypersensitivity reactions including anaphylaxis | SMQ | 20000021 | Anaphylactic reaction (narrow) |
| Hypersensitivity reactions including anaphylaxis | SMQ | 20000214 | Hypersensitivity (narrow) |
| Infections | SOC | 10021881 | Infections and infestations |
| Malignant tumor | SMQ | 20000227 | Malignant tumor (narrow) |
| Malignant tumor | SMQ | 20000228 | Malignant tumor (narrow) |
| Malignant tumor | SMQ | 20000215 | Malignant lymphoma (narrow) |

Table 14 Occurrence status of adverse drug reactions by safety specification (hypersensitivity reactions including anaphylaxis)

As of September 27, 2023

Subjects included in safety analysis

| | Total | | Serious | |
|---|---|---|---|---|
| Number of subjects studied | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 12 | | 2 | |
| Incidence of adverse drug reactions, etc. (%) | 1.2 | | 0.2 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | |
| Skin and subcutaneous tissue disorders | 8 | (0.8) | 1 | (0.1) |
| Urticaria | 4 | (0.4) | 0 | (0.0) |
| Rash | 2 | (0.2) | 0 | (0.0) |
| Angioedema | 1 | (0.1) | 1 | (0.1) |
| Eczema | 1 | (0.1) | 0 | (0.0) |
| Respiratory, thoracic and mediastinal disorders | 4 | (0.4) | 1 | (0.1) |
| Chronic eosinophilic rhinosinusitis | 4 | (0.4) | 1 | (0.1) |

MedDRA/J (26.0)

Table 15　Outcome of adverse drug reactions by safety specification (by events) （hypersensitivity reactions including anaphylaxis）

As of September 27, 2023

Subjects included in safety analysis

| | Serious | | | | | | | | | | | | Non-serious | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 1027 | | | | | | | | | | | | 1027 | | | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 0 | | 0 | | 0 | | 1 | | 1 | | 0 | | 0 | | 0 | | 0 | | 3 | | 7 | | 0 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number oNumber of subjects with adverse drug reactions (%) | | | | | | | | | | | |
| Respiratory, thoracic and mediastinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) |
| Chronic eosinophilic rhinosinusitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) |
| Skin and subcutaneous tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 0 | (0.0) |
| Angioedema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Eczema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Rash | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Urticaria | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > not recovered > unknown.

Table 16 Occurrence status of adverse drug reactions by safety specification (infections)

As of September 27, 2023

Subjects included in safety analysis

| | Total | | Serious | |
|---|---|---|---|---|
| Number of subjects studied | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 3 | | 1 | |
| Incidence of adverse drug reactions, etc. (%) | 0.3 | | 0.1 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | |
| Infections and infestations | 3 | (0.3) | 1 | (0.1) |
| Bronchitis | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 1 | (0.1) | 1 | (0.1) |

MedDRA/J (26.0)

Table 17　Outcome of adverse drug reactions by safety specification (by events) （infections）

As of September 27, 2023

Subjects included in safety analysis

| | Serious | | | | | | | | | | | | Non-serious | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 1027 | | | | | | | | | | | | 1027 | | | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 1 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | | 2 | | 0 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number oNumber of subjects with adverse drug reactions (%) | | | | | | | | | | | |
| Infections and infestations | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Bronchitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

Table 18 Occurrence status of adverse drug reactions by safety specification (malignant tumor)

As of September 27, 2023

Subjects included in safety analysis (malignant tumor)

| | Total | | Serious | |
|---|---|---|---|---|
| Number of subjects studied | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 2 | | 2 | |
| Incidence of adverse drug reactions, etc. (%) | 0.2 | | 0.2 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 2 | (0.2) | 2 | (0.2) |
| Gastric cancer | 1 | (0.1) | 1 | (0.1) |
| Intraductal papillary-mucinous carcinoma of pancreas | 1 | (0.1) | 1 | (0.1) |

MedDRA/J (26.0)

Table 19 Outcome of adverse drug reactions by safety specification (by events) (malignant tumor)

As of September 27, 2023

Subjects included in safety analysis

| | Serious | | | | | | | | | | | | Non-serious | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 1027 | | | | | | | | | | | | 1027 | | | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 1 | | 0 | | 0 | | 0 | | 1 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Gastric cancer | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Intraductal papillary-mucinous carcinoma of pancreas | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

Table 20 Summary statistics of blood eosinophil count

As of September 27, 2023

Subjects included in safety analysis

| Item/Category | | Blood eosinophil count [/μL] |
|---|---|---|
| Subjects included in analysis | | 1027 |
| 9 to 52 weeks before the initiation of Nucala treatment | Number of subjects | 656 |
| | Mean ± standard deviation | 701.0±935.1 |
| | Minimum | 0 |
| | 25% point | 225.0 |
| | Median | 460.0 |
| | 75% point | 828.0 |
| | Maximum | 9999 |
| Baseline (0 to 8 weeks before the initiation of Nucala treatment) | Number of subjects | 819 |
| | Mean ± standard deviation | 641.5±822.9 |
| | Minimum | 0 |
| | 25% point | 200.0 |
| | Median | 418.0 |
| | 75% point | 784.0 |
| | Maximum | 7500 |
| 12 weeks after the initiation of Nucala treatment | Number of subjects | 555 |
| | Mean ± standard deviation | 124.5±503.5 |
| | Minimum | 0 |
| | 25% point | 20.0 |
| | Median | 50.0 |
| | 75% point | 100.0 |
| | Maximum | 8210 |
| 24 weeks after the initiation of Nucala treatment | Number of subjects | 416 |
| | Mean ± standard deviation | 129.9±446.6 |
| | Minimum | 0 |
| | 25% point | 20.0 |
| | Median | 50.0 |
| | 75% point | 90.5 |
| | Maximum | 4807 |
| 52 weeks after the initiation of Nucala treatment or at the time of discontinuation/termination | Number of subjects | 578 |
| | Mean ± standard deviation | 128.7±421.2 |
| | Minimum | 0 |
| | 25% point | 21.0 |
| | Median | 50.0 |
| | 75% point | 90.0 |
| | Maximum | 5050 |

Table 21 Summary statistics of blood eosinophil count (subjects who continued treatment for 52 weeks)

As of September 27, 2023

Subjects included in safety analysis

| Item/Category | | Blood eosinophil count [/μL] |
|---|---|---|
| Subjects included in analysis | | 559 |
| 9 to 52 weeks before the initiation of Nucala treatment | Number of subjects | 383 |
| | Mean ± standard deviation | 711.2±869.1 |
| | Minimum | 0 |
| | 25% point | 251.0 |
| | Median | 492.0 |
| | 75% point | 863.0 |
| | Maximum | 7192 |
| Baseline (0 to 8 weeks before the initiation of Nucala treatment) | Number of subjects | 455 |
| | Mean ± standard deviation | 618.0±658.5 |
| | Minimum | 0 |
| | 25% point | 205.0 |
| | Median | 432.0 |
| | 75% point | 811.0 |
| | Maximum | 5550 |
| 12 weeks after the initiation of Nucala treatment | Number of subjects | 348 |
| | Mean ± standard deviation | 125.8±562.7 |
| | Minimum | 0 |
| | 25% point | 20.0 |
| | Median | 50.0 |
| | 75% point | 98.5 |
| | Maximum | 8210 |
| 24 weeks after the initiation of Nucala treatment | Number of subjects | 312 |
| | Mean ± standard deviation | 105.7±333.9 |
| | Minimum | 0 |
| | 25% point | 20.0 |
| | Median | 48.5 |
| | 75% point | 89.0 |
| | Maximum | 3870 |
| 52 weeks after the initiation of Nucala treatment | Number of subjects | 303 |
| | Mean ± standard deviation | 118.9±410.2 |
| | Minimum | 0 |
| | 25% point | 22.0 |
| | Median | 53.0 |
| | 75% point | 88.0 |
| | Maximum | 5050 |

Table 22 IgE concentration by presence/absence of history of omalizumab use

As of September 27, 2023

Subjects included in safety analysis

| Item/Category | | History of omalizumab use | | | |
|---|---|---|---|---|---|
| | | No | Yes | Unknown | Total |
| Subjects included in analysis | | 871 | 156 | 0 | 1027 |
| Serum total IgE concentration [IU/mL] | Number of subjects | 545 | 132 | 0 | 677 |
| | Mean ± standard deviation | 798.5±1421.6 | 546.9±1037.2 | - | 749.5±1358.2 |
| | Minimum | 1 | 4 | - | 1 |
| | 25% point | 85.0 | 112.5 | - | 95.0 |
| | Median | 269.0 | 281.5 | - | 269.0 |
| | 75% point | 772.0 | 638.0 | - | 745.0 |
| | Maximum | 9999 | 9999 | - | 9999 |

Table 23 Rate of responders by subject characteristics

As of September 27, 2023

Subjects included in effectiveness analysis

| Subject characteristics | | Number of subjects studied | Number of responders | Number of non-responders | Rate of responders (%) | 95% confidence interval | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower limit | Upper limit |
| Total | | 959 | 866 | 93 | 90.3 | 88.3 | 92.1 |
| Gender | Male | 355 | 317 | 38 | 89.3 | 85.6 | 92.3 |
| | Female | 604 | 549 | 55 | 90.9 | 88.3 | 93.1 |
| Pregnancy status "Female only" | No | 589 | 536 | 53 | 91.0 | 88.4 | 93.2 |
| | Yes | 1 | 1 | 0 | 100.0 | 2.5 | 100.0 |
| | Unknown | 14 | 12 | 2 | 85.7 | 57.2 | 98.2 |
| Age 1 [years] | <15 | 11 | 9 | 2 | 81.8 | 48.2 | 97.7 |
| Mean ± SD: 62.6±16.1 | 15≤ to <65 | 431 | 387 | 44 | 89.8 | 86.5 | 92.5 |
| Minimum: 12 | 65≤ to <75 | 257 | 236 | 21 | 91.8 | 87.8 | 94.9 |
| Median: 66.0 | 75≤ | 260 | 234 | 26 | 90.0 | 85.7 | 93.4 |
| Maximum: 93 | | | | | | | |
| Age 2 [years] | <65 | 442 | 396 | 46 | 89.6 | 86.4 | 92.3 |
| | 65≤ | 517 | 470 | 47 | 90.9 | 88.1 | 93.2 |
| Hospitalization status | Inpatient | 50 | 46 | 4 | 92.0 | 80.8 | 97.8 |
| | Outpatient | 909 | 820 | 89 | 90.2 | 88.1 | 92.1 |
| Reason for use of this drug | Bronchial asthma | 959 | 866 | 93 | 90.3 | 88.3 | 92.1 |
| | Other | 0 | 0 | 0 | - | - | - |
| Comorbidity | No | 280 | 262 | 18 | 93.6 | 90.0 | 96.1 |
| | Yes | 679 | 604 | 75 | 89.0 | 86.4 | 91.2 |
| Comorbidity (renal impairment) | No | 938 | 847 | 91 | 90.3 | 88.2 | 92.1 |
| | Yes | 21 | 19 | 2 | 90.5 | 69.6 | 98.8 |
| Comorbidity (hepatic function disorder) | No | 931 | 841 | 90 | 90.3 | 88.3 | 92.2 |
| | Yes | 28 | 25 | 3 | 89.3 | 71.8 | 97.7 |
| Comorbidities (allergies) | No | 592 | 544 | 48 | 91.9 | 89.4 | 94.0 |
| | Yes | 367 | 322 | 45 | 87.7 | 83.9 | 90.9 |
| Comorbidities (other conditions) | No | 392 | 362 | 30 | 92.3 | 89.3 | 94.8 |
| | Yes | 567 | 504 | 63 | 88.9 | 86.0 | 91.4 |
| Smoking history | Never-smoker | 668 | 612 | 56 | 91.6 | 89.3 | 93.6 |
| | Ex-smoker | 260 | 229 | 31 | 88.1 | 83.5 | 91.8 |
| | Current-smoker | 31 | 25 | 6 | 80.6 | 62.5 | 92.5 |
| Primary disease (disease duration [years]) | ≤2 | 29 | 29 | 0 | 100.0 | 88.1 | 100.0 |
| | 2< to ≤5 | 60 | 55 | 5 | 91.7 | 81.6 | 97.2 |
| | 5< to ≤10 | 137 | 120 | 17 | 87.6 | 80.9 | 92.6 |
| | 10< | 589 | 530 | 59 | 90.0 | 87.3 | 92.3 |
| | Unknown | 144 | 132 | 12 | 91.7 | 85.9 | 95.6 |
| Primary disease (severity before administration) | Mild intermittent | 0 | 0 | 0 | - | - | - |
| | Mild persistent | 2 | 2 | 0 | 100.0 | 15.8 | 100.0 |
| | Moderate persistent | 29 | 27 | 2 | 93.1 | 77.2 | 99.2 |
| | Severe persistent | 642 | 592 | 50 | 92.2 | 89.9 | 94.2 |
| | Most severe persistent | 286 | 245 | 41 | 85.7 | 81.1 | 89.5 |
| Primary disease (disease type) | Atopic | 485 | 433 | 52 | 89.3 | 86.2 | 91.9 |
| | Non-atopic | 364 | 336 | 28 | 92.3 | 89.1 | 94.8 |
| | Unknown | 110 | 97 | 13 | 88.2 | 80.6 | 93.6 |
| Blood eosinophil count ( 9 to 52 weeks before start of administration of this drug)[/μL] | <150 | 97 | 88 | 9 | 90.7 | 83.1 | 95.7 |
| Mean ±SD: 708.1±938.0 | 150≤ to <300 | 93 | 68 | 25 | 73.1 | 62.9 | 81.8 |
| Minimum: 0 | 300≤ to <500 | 134 | 120 | 14 | 89.6 | 83.1 | 94.2 |
| Median: 466.0 | 500≤ | 290 | 265 | 25 | 91.4 | 87.5 | 94.3 |
| Maximum: 9999 | Unknown | 345 | 325 | 20 | 94.2 | 91.2 | 96.4 |
| Blood eosinophil count (baseline)[/μL] | <150 | 150 | 132 | 18 | 88.0 | 81.7 | 92.7 |
| Mean ± SD: 634.7±813.8 | 150≤ to <300 | 103 | 86 | 17 | 83.5 | 74.9 | 90.1 |
| Minimum: 0 | 300≤ to <500 | 182 | 169 | 13 | 92.9 | 88.1 | 96.1 |
| Median: 409.0 | 500≤ | 325 | 300 | 25 | 92.3 | 88.9 | 95.0 |
| Maximum: 7500 | Unknown | 199 | 179 | 20 | 89.9 | 84.9 | 93.8 |
| History of omalizumab use | No | 813 | 748 | 65 | 92.0 | 89.9 | 93.8 |
| | Yes | 146 | 118 | 28 | 80.8 | 73.5 | 86.9 |
| Prior medications for bronchial asthma | No | 7 | 7 | 0 | 100.0 | 59.0 | 100.0 |
| | Yes | 952 | 859 | 93 | 90.2 | 88.2 | 92.0 |
| Concomitant medications | No | 69 | 59 | 10 | 85.5 | 75.0 | 92.8 |
| | Yes | 890 | 807 | 83 | 90.7 | 88.6 | 92.5 |
| Concomitant therapies for bronchial asthma (other than drug therapy) | No | 946 | 855 | 91 | 90.4 | 88.3 | 92.2 |
| | Yes | 13 | 11 | 2 | 84.6 | 54.6 | 98.1 |

Table 24 Multivariate logistic regression analysis (effectiveness)

As of September 27, 2023

Subjects included in effectiveness analysis

Odds ratio estimated by multivariate logistic regression

| Item/Category | | Number of subjects studied | Number of responders | Rate of responders (%) | Adjusted odds ratio | | |
|---|---|---|---|---|---|---|---|
| | | | | | Point estimation | 95% confidence | |
| | | | | | | Lower limit | Upper limit |
| Total | | 959 | 866 | 90.3 | - | - | - |
| Comorbidity | No * | 280 | 262 | 93.6 | - | - | - |
| | Yes | 679 | 604 | 89.0 | 0.476 | 0.217 | 1.044 |
| Blood eosinophil count (baseline)[/μL] | <150 * | 150 | 132 | 88.0 | - | - | - |
| | 150≤ to <300 | 103 | 86 | 83.5 | 0.768 | 0.360 | 1.639 |
| | 300≤ to <500 | 182 | 169 | 92.9 | 1.888 | 0.837 | 4.259 |
| | 500≤ | 325 | 300 | 92.3 | 1.898 | 0.974 | 3.699 |

*: Criteria

Table 25 Exacerbation of bronchial asthma

As of September 27, 2023

Subjects included in effectiveness analysis

| Exacerbation of bronchial asthma | Period | Number of subjects | Total person-year [*1] | Number of exacerbation/ number of days | Rate [*2] | Number of subjects with events | Minimum [*3] | Median [*3] | Maximum [*3] | Rate Ratio [*4] | 95% CI [*4] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| The frequency of all bronchial asthma exacerbations | 52 weeks before the initiation of Nucala treatment | 943 | 943.0 | 3537 | 3.8 | 707 | 1 | 3.0 | 170 | - | - |
| | Week 52 of treatment or at the time of treatment discontinuation | 959 | 736.8 | 708 | 1.0 | 219 | 1 | 2.0 | 73 | 0.32 | 0.27-0.38 |
| The frequency of exacerbations requiring hospitalization | 52 weeks before the initiation of Nucala treatment | 956 | 956.0 | 414 | 0.4 | 195 | 1 | 1.0 | 99 | - | - |
| | Week 52 of treatment or at the time of treatment discontinuation | 959 | 736.8 | 90 | 0.1 | 63 | 1 | 1.0 | 4 | 0.32 | 0.23-0.45 |
| The frequency of exacerbations requiring emergency department visits | 52 weeks before the initiation of Nucala treatment | 943 | 943.0 | 892 | 0.9 | 260 | 1 | 2.0 | 99 | - | - |
| | Week 52 of treatment or at the time of treatment discontinuation | 959 | 736.8 | 170 | 0.2 | 81 | 1 | 1.0 | 12 | 0.27 | 0.20-0.37 |
| The frequency of exacerbations requiring the use of systemic corticosteroid | 52 weeks before the initiation of Nucala treatment | 956 | 956.0 | 3017 | 3.2 | 674 | 1 | 3.0 | 156 | - | - |
| | Week 52 of treatment or at the time of treatment discontinuation | 959 | 736.8 | 523 | 0.7 | 183 | 1 | 2.0 | 68 | 0.26 | 0.22-0.31 |
| Bronchial asthma exacerbations requiring hospitalization (number of days of hospitalization) | 52 weeks before the initiation of Nucala treatment | 956 | 956.0 | 3879 | 4.1 | 192 | 1 | 11.5 | 131 | - | - |
| | Week 52 of treatment or at the time of treatment discontinuation | 959 | 736.8 | 1597 | 2.2 | 63 | 1 | 12.0 | 233 | 0.89 | 0.54-1.48 |

*1: 52 weeks were converted to 1 year

*2: Number of exacerbation/number of days / total person-year

*3: Subjects with events were included

*4: Negative binomial regression model using administration period as an explanatory variable and observation period (log) as an offset variable

Table 26 Respiratory function test values

As of September 27, 2023

Subjects included in effectiveness analysis

| Item/Category | Peak Flow (PEF) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | 12 weeks after the initiation of Nucala treatment | | 24 weeks after the initiation of Nucala treatment | | 52 weeks after the initiation of Nucala treatment | | At the time of treatment discontinuation/termination | |
| | Number of subjects (%)/ summary statistics | | Number of subjects (%)/ summary statistics | | Number of subjects (%)/ summary statistics | | Number of subjects (%)/ summary statistics | | Number of subjects (%)/ summary statistics | |
| Subjects included in analysis | 120 | (12.5) | 78 | (8.1) | 51 | (5.3) | 45 | (4.7) | 43 | (4.5) |
| Number of subjects | 120 | | 78 | | 51 | | 45 | | 43 | |
| Mean ± standard deviation | 304.4±146.8 | | 333.7±150.5 | | 334.2±138.7 | | 358.9±129.8 | | 349.5±134.7 | |
| Minimum | 66 | | 55 | | 130 | | 54 | | 54 | |
| Median | 281.0 | | 310.0 | | 305.0 | | 340.0 | | 320.0 | |
| Maximum | 869 | | 999 | | 913 | | 620 | | 620 | |

Table 27 ACT score (all subjects)

As of September 27, 2023

Subjects included in effectiveness analysis

| Item/Category | | ACT score | |
|---|---|---|---|
| Subjects included in effectiveness analysis | | 959 | |
| Subjects included in ACT analysis | | 352 | |
| Baseline | Number of subjects | 352 | |
| | Mean ± standard deviation | 16.2±4.9 | |
| | Minimum | 5 | |
| | 25% point | 13.0 | |
| | Median | 17.0 | |
| | 75% point | 20.0 | |
| | Maximum | 25 | |
| 12 weeks after the initiation of Nucala treatment | Number of subjects | 317 | |
| | Mean ± standard deviation | 20.5±4.3 | |
| | Minimum | 7 | |
| | 25% point | 19.0 | |
| | Median | 22.0 | |
| | 75% point | 24.0 | |
| | Maximum | 25 | |
| 24 weeks after the initiation of Nucala treatment | Number of subjects | 261 | |
| | Mean ± standard deviation | 20.9±4.2 | |
| | Minimum | 5 | |
| | 25% point | 19.0 | |
| | Median | 22.0 | |
| | 75% point | 24.0 | |
| | Maximum | 25 | |
| 52 weeks after the initiation of Nucala treatment | Number of subjects | 221 | |
| | Mean ± standard deviation | 21.4±4.0 | |
| | Minimum | 6 | |
| | 25% point | 20.0 | |
| | Median | 23.0 | |
| | 75% point | 25.0 | |
| | Maximum | 25 | |
| ACT score (12 weeks after the initiation of Nucala treatment - at the initiation of Nucala treatment) ≥3 | Number of subjects | 208 | (65.6) |
| ACT score (24 weeks after the initiation of Nucala treatment - at the initiation of Nucala treatment) ≥3 | Number of subjects | 180 | (69.0) |
| ACT score (52 weeks after the initiation of Nucala treatment - at the initiation of Nucala treatment) ≥3 | Number of subjects | 163 | (73.8) |

Table 28 Occurrence status of adverse drug reactions in patients with specific backgrounds (elderly)

As of September 27, 2023

Subjects included in safety analysis

| | Elderly | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 65≤ | | | | <65 | | | | Total | | | |
| | Total | | Serious | | Total | | Serious | | Total | | Serious | |
| Number of subjects studied | 555 | | | | 472 | | | | 1027 | | | |
| Number of subjects with adverse drug reactions, etc. | 25 | | 6 | | 17 | | 3 | | 42 | | 9 | |
| Incidence of adverse drug reactions, etc. (%) | 4.5 | | 1.1 | | 3.6 | | 0.6 | | 4.1 | | 0.9 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | Number of subjects with adverse drug reactions (%) | | | | Number of subjects with adverse drug reactions (%) | | | |
| Respiratory, thoracic and mediastinal disorders | 5 | (0.9) | 1 | (0.2) | 7 | (1.5) | 2 | (0.4) | 12 | (1.2) | 3 | (0.3) |
| Asthma | 3 | (0.5) | 1 | (0.2) | 4 | (0.8) | 1 | (0.2) | 7 | (0.7) | 2 | (0.2) |
| Chronic eosinophilic rhinosinusitis | 1 | (0.2) | 0 | (0.0) | 3 | (0.6) | 1 | (0.2) | 4 | (0.4) | 1 | (0.1) |
| Upper respiratory tract inflammation | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Skin and subcutaneous tissue disorders | 6 | (1.1) | 1 | (0.2) | 4 | (0.8) | 0 | (0.0) | 10 | (1.0) | 1 | (0.1) |
| Urticaria | 2 | (0.4) | 0 | (0.0) | 2 | (0.4) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) |
| Pruritus | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Rash | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Alopecia | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Angioedema | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Eczema | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| General disorders and administration site conditions | 4 | (0.7) | 0 | (0.0) | 5 | (1.1) | 1 | (0.2) | 9 | (0.9) | 1 | (0.1) |
| Condition aggravated | 1 | (0.2) | 0 | (0.0) | 3 | (0.6) | 1 | (0.2) | 4 | (0.4) | 1 | (0.1) |
| Malaise | 0 | (0.0) | 0 | (0.0) | 2 | (0.4) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Oedema peripheral | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pain | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pyrexia | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Infections and infestations | 2 | (0.4) | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 3 | (0.3) | 1 | (0.1) |
| Bronchitis | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Nervous system disorders | 2 | (0.4) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 3 | (0.3) | 1 | (0.1) |
| Headache | 2 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Myasthenia gravis | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 1 | (0.1) | 1 | (0.1) |
| Musculoskeletal and connective tissue disorders | 3 | (0.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) |
| Back pain | 2 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Arthralgia | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pain in extremity | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 2 | (0.4) | 2 | (0.4) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 2 | (0.2) |
| Gastric cancer | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Intraductal papillary-mucinous carcinoma of pancreas | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Cardiac disorders | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Palpitations | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Gastrointestinal disorders | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Nausea | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Vomiting | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Hepatobiliary disorders | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Hepatic function abnormal | 1 | (0.2) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Eye disorders | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 1 | (0.1) | 1 | (0.1) |
| Optic neuropathy | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 1 | (0.1) | 1 | (0.1) |
| Ear and labyrinth disorders | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Vertigo positional | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Investigations | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Eosinophil count increased | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |

MedDRA/J (26.0)

Table 29　Outcome of adverse dOutcome of adverse drug reactions in patients with specific backgrounds（elderly）

As of Sentember 27, 2023

Subjects included in safety analysis

| | elderly | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ≧65 | | | | | | < 65 | | | | | | Total | | | | | |
| | Death | Recovered with sequelae | Not recovered | Recovering | Recovered | Unknown | Death | Recovered with sequelae | Not recovered | Recovering | Recovered | Unknown | Death | Recovered with sequelae | Not recovered | Recovering | Recovered | Unknown |
| Number of subjects studied | 555 | | | | | | 472 | | | | | | 1027 | | | | | |
| Number of subjects with adverse drug reactions. etc. | 3 | 0 | 0 | 7 | 15 | 0 | 0 | 0 | 0 | 8 | 9 | 1 | 3 | 0 | 0 | 15 | 24 | 1 |
| Types of adverse drug reactions, etc. | Number oNumber of subjects with adverse drug reactions (%) | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | Number of subjects with adverse drug reactions (%) | | | | | |
| Infections and infestations | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Bronchitis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Nasopharyngitis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Pharyngitis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Pneumonia | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Gastric cancer | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Intraductal nanillary-mucinous carcinoma of nancreas | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Nervous system disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Headache | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| MyasthMyasthenia gravis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Eye disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Optic neuropathy | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Ear and labyrinth disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Vertigo nositional | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Cardiac disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Palpitations | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Respiratory, thoracic and mediastinal disorders | 1 (0.2) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 2 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 5 (1.1) | 2 (0.4) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 7 (0.7) | 4 (0.4) | 0 (0.0) |
| Asthma | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 2 (0.4) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 3 (0.3) | 3 (0.3) | 0 (0.0) |
| Upper respiratory tract inflammation | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Chronic eosinophilic rhinosinusitis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4 (0.4) | 0 (0.0) | 0 (0.0) |
| Gastrointestinal disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Nausea | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Vomiting | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Hepatobiliary disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Hepatic function abnormal | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Skin and subcutaneous tissue disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 5 (0.9) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4 (0.8) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 9 (0.9) | 0 (0.0) |
| Alopecia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Anuioedema | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Eczema | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Pruritus | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) | 0 (0.0) |
| Rash | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Urticaria | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4 (0.4) | 0 (0.0) |
| Musculoskeletal and connective tissue disorders | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.3) | 0 (0.0) |
| Arthralgia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Back nain | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Pain in extremity | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| General disorders and administration site conditions | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.5) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 5 (1.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 8 (0.8) | 1 (0.1) | 0 (0.0) |
| Condition aggravated | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4 (0.4) | 0 (0.0) | 0 (0.0) |
| Malaise | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (0.2) | 0 (0.0) | 0 (0.0) |
| Oedema peripheral | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Pain | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Pyrexia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) |
| Investigations | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |
| Eosinonhil count increased | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

Table 30 Outcome of adverse drug reactions in patients with specific backgrounds (renal impairment)

As of September 27, 2023

Subjects included in safety analysis

| | Renal impairment | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | | | | | | | | | | | | No | | | | | | | | | | Total | | | | | | | | | |
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequel | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 25 | | | | | | | | | | | | 1002 | | | | | | | | | | | 1027 | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 0 | | 0 | | 0 | | 1 | | 0 | | 0 | | 3 | | 0 | | 0 | | 14 | | 24 | | 1 | | 3 | | 0 | | 0 | | 15 | | 24 | | 1 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | |
| Infections and infestations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Bronchitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 0 | (0.0) | 0 | (0.0) | 1 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Gastric cancer | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Intraductal papillary-mucinous carcinoma of pancreas | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nervous system disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (4.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 1 | (0.1) | 0 | (0.0) |
| Headache | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Myasthenia gravis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (4.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Eye disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Optic neuropathy | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Ear and labyrinth disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Vertigo positional | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Cardiac disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Palpitations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Respiratory, thoracic and mediastinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 4 | (0.4) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 4 | (0.4) | 0 | (0.0) |
| Asthma | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 3 | (0.3) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 3 | (0.3) | 0 | (0.0) |
| Upper respiratory tract inflammation | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Chronic eosinophilic rhinosinusitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) |
| Gastrointestinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Nausea | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Vomiting | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Hepatobiliary disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Hepatic function abnormal | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Skin and subcutaneous tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 9 | (0.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 9 | (0.9) | 0 | (0.0) |
| Alopecia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Angioedema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Eczema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pruritus | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Rash | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Urticaria | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) |
| Musculoskeletal and connective tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) |
| Arthralgia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Back pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Pain in extremity | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| General disorders and administration site conditions | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 8 | (0.8) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 8 | (0.8) | 1 | (0.1) | 0 | (0.0) |
| Condition aggravated | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) |
| Malaise | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) |
| Oedema peripheral | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pyrexia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Investigations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Eosinophil count increased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

Table 31 Outcome of adverse drug reactions in patients with specific backgrounds (hepatic impairment)

As of September 27, 2023

Subjects included in safety analysis

| | Hepatic impairment | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | | | | | | | | | | | | No | | | | | | | | | | | | Total | | | | | | | | | |
| | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | | Death | | Recovered with sequelae | | Not recovered | | Recovering | | Recovered | | Unknown | |
| Number of subjects studied | 30 | | | | | | | | | | | | 997 | | | | | | | | | | | | 1027 | | | | | | | | | | |
| Number of subjects with adverse drug reactions, etc. | 0 | | 0 | | 0 | | 0 | | 2 | | 0 | | 3 | | 0 | | 0 | | 15 | | 22 | | 1 | | 3 | | 0 | | 0 | | 15 | | 24 | | 1 | |
| Types of adverse drug reactions, etc. | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | | | Number of subjects with adverse drug reactions (%) | | | | | | | | | | |
| Infections and infestations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Bronchitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nasopharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pharyngitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pneumonia | 0 | (0.0) | 0 | (0.0) | 1 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Gastric cancer | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Intraductal papillary-mucinous carcinoma of pancreas | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Nervous system disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 1 | (0.1) | 0 | (0.0) |
| Headache | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Myasthenia gravis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Eye disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Optic neuropathy | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Ear and labyrinth disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Vertigo positional | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Cardiac disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Palpitations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Respiratory, thoracic and mediastinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 4 | (0.4) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 7 | (0.7) | 4 | (0.4) | 0 | (0.0) |
| Asthma | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 3 | (0.3) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 3 | (0.3) | 0 | (0.0) |
| Upper respiratory tract inflammation | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Chronic eosinophilic rhinosinusitis | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) |
| Gastrointestinal disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Nausea | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Vomiting | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Hepatobiliary disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Hepatic function abnormal | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) |
| Skin and subcutaneous tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 8 | (0.8) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 9 | (0.9) | 0 | (0.0) |
| Alopecia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Angioedema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Eczema | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Pruritus | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 1 | (0.1) | 0 | (0.0) |
| Rash | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Urticaria | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) |
| Musculoskeletal and connective tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (0.3) | 0 | (0.0) |
| Arthralgia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Back pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) |
| Pain in extremity | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| General disorders and administration site conditions | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 8 | (0.8) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 8 | (0.8) | 1 | (0.1) | 0 | (0.0) |
| Condition aggravated | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.4) | 0 | (0.0) | 0 | (0.0) |
| Malaise | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.2) | 0 | (0.0) | 0 | (0.0) |
| Oedema peripheral | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Pyrexia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) |
| Investigations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Eosinophil count increased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |

MedDRA/J (26.0)

If multiple events under the same SOC and PT occurred in the same subject, they were tabulated for each SOC and PT in the order of priority of (1) serious > non-serious, (2) death > recovered with sequelae > not recovered > recovering > recovered > unknown.

# Nucala® Subcutaneous Injection
# Special Drug Use Investigation
# (Long-Term)

# Protocol

## GlaxoSmithKline K.K.

Revised: 8 December 2022 (Vers.3.1)

## <Contents>

## 1. Objectives

The objective of the study is to collect and assess information regarding the safety and effectiveness of long term use of Nucala® for subcutaneous injection (hereinafter referred to as "Nucala") in asthma patients in daily clinical practice.

## 2. Safety Specification

In the study, the occurrence of safety specification and the priority investigation matter will be monitored. They will be defined as follows;

- Hypersensitivity reaction including anaphylaxis
- Infections
- Malignant tumour

## 3. Target Population

The study will include patients receiving Nucala for the first time for treatment of bronchial asthma (a refractory asthma whose symptoms are inadequately controlled despite receiving standard asthma medications), for which Nucala is indicated.

## 4. Target Sample Size and Rationale

1) Target number of subjects : 1,000 subjects (as enrolled subjects)
2) Rationale :

In the Phase III Global Trial (385 subjects), the incidence of adverse drug reactions (ADRs) occurring in one patient was 0.26%. Since 885 subjects are required to detect an ADRs including unexpected ADRs occurring at an incidence of ≧0.26% in at least one patient with a probability of 90%, the target number of subjects was set at 1,000 in consideration of withdrawal and dropouts.

In addition, in the placebo-controlled trial targeting severe asthma patients, the incidence of "allergic reaction/hypersensitivity", one of the "hypersensitivity reaction including anaphylaxis" defined as the important potential risk, was 1.14% (3/263 subjects). On the assumption that the incidence used as a threshold is assumed to be 1.2%, to confirm the incidence in the post-marketing surveillance with the estimation accuracy which detects the 1.2% of threshold with a statistical power of ≧80% when the real risk exists two times or more of the threshold, 827 subjects are required as a safety analysis set. Accordingly, it is thought to be possible to examine the incidence in the study with 1,000 subjects.

## 5. Planned Number of Medical Institutions by Department

Approximately 200, mainly the departments of respiratory medicine

## 6. Study Period

1. Study conduct

Study period : January 2017 - September 2023

Observation period: The observation period per subject will be 1 year (52 weeks) from the initiation of Nucala treatment.

In addition, the follow-up investigation will be conducted for 2 years after the observation period (or after the withdrawal/termination, if a subject has withdrawn from/ terminated the administration of the drug) to examine the occurrence of malignant tumour.

Planned enrollment period : January 2017 - June 2020

However, if the number of enrolled subjects has reached the target sample size, enrollment may be terminated even before completing the above-mentioned planned enrollment period.

2. Study end

Completion of final analysis: January 2024

Completion of final report writing : June 2024

## 7. Study Methods

In the study, the electronic data capture (EDC) system will be used for case registration and data collection.

1) Request and contract for the study
   (1) The person in charge of the study (medical representative or monitoring outsourcee) will explain the objectives, target population, study items, study methods, etc. to the planned physicians for the study, etc. at the medical institutions where Nucala is adopted/delivered, and will request them to cooperate with the study.
   (2) If cooperation to the study has been obtained, the Written Contract should be concluded with the heads (e.g. directors, etc.) of the medical institutions before starting the study.
2) Enrollment of target population

   The study will be conducted using a central enrollment method.
   (1) The investigator will enter and enroll subject information, etc. in the EDC system within 14 days from the initiation of Nucala treatment regarding "3. Target Population" who started administration of Nucala after the conclusion of the contract (the start date of the administration will be regarded as Day 1).
   (2) If the number of enrolled subjects has reached the number of contracted subjects, enrollment into the study will be terminated.
3) Collection of data and entry in the EDC system
   (1) The investigator will confirm the study items, such as the characteristics of enrolled subjects.
   (2) If asthma control test (ACT) is conducted to an enrolled subject at the initiation of Nucala treatment, and at Week 12, 24 and 52 after the administration (or at the time point of withdrawal/termination if a subject has withdrawn from/terminated the administration), the investigator will check the content, and enter the test score in the EDC system.
   (3) During the observation period, the investigator will monitor the information regarding the safety and effectiveness, etc. If an enrolled subject does not visit the hospital/clinic during the observation period, the investigator will monitor the information regarding AEs and others by telephone, etc. as far as possible.
   (4) The investigator will enter the information of the enrolled subjects obtained at the end of the observation period, and send it.
   (5) During the follow-up period of 2 years after the observation period (or after the withdrawal/termination if a subject has withdrawn from/terminated the administration), the information regarding the onset of malignant tumour will be monitored. The investigator will enter the information of an enrolled subject obtained at the time point when the onset of malignant tumour has been monitored or at the end of the follow-up period in the EDC system, and send it.

In case other ADR (AE suspected of being related to Nucala), has been monitored, the investigator will contact the person in charge of the study. If an enrolled subject does not visit the hospital/clinic during the follow-up period, the investigator will confirm the presence/absence of onset of malignant tumour by telephone, etc. as far as possible.

## 8. Study Items

The investigator will collect the information regarding the following items, etc. as far as possible and enter it in the EDC system.

1) Information regarding medical institutions
   Name of medical institution, department, investigator
2) Subject characteristics (at the initiation of Nucala treatment)
   Identification number, gender, year of birth, start date of administration, hospitalization status, reason for use, presence/absence and name of complications (renal impairment, hepatic impairment, allergy, others), history of smoking, duration of asthma, pre-administration severity and type of asthma
   To protect the confidentiality regarding identification of an individual subject, the identification number should be a unique number assigned to an individual subject by the investigator, etc.
   In this study, any disease/symptom except for asthma which is present before the initiation of Nucala treatment will be handled as a “complication”.
3) Pretreatment medications for asthma (during 4 weeks prior to the initiation of Nucala treatment)
   Presence or absence of pretreatment medications for asthma during 4 weeks prior to the initiation of Nucala treatment, category and product name of medication, single dose and dose unit (as for inhaled steroids and oral steroids)
4) Administration status of Nucala
   Single dose and dose unit, daily dose frequency, date of administration
5) Concomitant medications
   Presence or absence of concomitant medications, name of medications, route of administration, reason for administration, single dose and dose unit of inhaled steroids and oral steroids during the observation period
6) Concomitant therapies for asthma (except for medications)
   Presence or absence of concomitant therapies for asthma, name of therapies during the observation period.
7) Blood test item
   Presence or absence of eosinophils count $\geqq 300/\mu L$ during 52 weeks prior to the Nucala treatment, eosinophils count and examination date at the initiation of Nucala treatment, at Week 12, 24 and 52 after the administration or at the time point of withdrawal/termination (only if examination is performed), administration history of Omalizumab, serum total IgE levels* and examination date
   * In subject with Omalizumab history, the serum total IgE levels measured before the treatment start of Omalizumab or, on and after 1 year post last dose will be entered.
8) Exacerbation of asthma
   Frequency of exacerbation of asthma from 52 weeks prior to the initiation of Nucala treatment to 52 weeks after the administration (or to the time point of withdrawal/termination), frequency of exacerbation of asthma and number of days of hospitalization from 52 weeks prior to the initiation of Nucala treatment to 52 weeks after

the administration (or to the time point of withdrawal/termination) which corresponds to the either types of exacerbation defined below;

・exacerbation of asthma which requires hospitalization

・exacerbation of asthma which requires emergency room visit

・exacerbation of asthma which requires usage of systemic steroids*

*The definitions for use of systemic steroids are as follows;

When administering steroids (e.g., prednisolone) orally and intravenously (or intramuscularly) for a total of ≧three days are required.

When in subject receiving the maintenance therapy of systemic steroids, who requires administering double the existing maintenance dose for≧three days.

Multiple exacerbation of asthma for which steroids are administered at a interval of ＜ seven days will be handled as continuation of exacerbation of the same asthma.

9) Respiratory Function Test (Peak Expiratory Flow (PEF))
Morning/evening PEF score measured at the nearest time point of 1 week before and after the initiation of Nucala treatment, and at Week12, 24, and 54 after the administration, or at the withdrawal/termination* (only if PEF is conducted), measurement date, measurement time of the day, presence and absence of use of short-acting beta 2 agonist (SABA) within 4 hours before measuring PEF score

* All PEF score obtained during this period will be entered in the EDC system

10) Asthma Control Test (ACT)
The information of ACT recorded by a subject at the initiation of Nucala treatment, at Week 12, 24 and 52 after the administration, or at the time point of withdrawal/termination if a subject has withdrawn from/terminated administration. (only if ACT is conducted)

11) Global assessment of effectiveness
Effectiveness will be comprehensively assessed by any of “effective” or “not effective” at 52 weeks after the initiation of Nucala treatment or at the time point of withdrawal from/termination of administration, based on the course of subjective symptoms, and course of clinical symptoms, etc. from the initiation of Nucala treatment to the end of the observation period. If effectiveness cannot be determined for some reasons, it should be assessed as “indeterminable”, and the reason should be entered in the EDC system.

12) Administration of the drug at the end of the observation period
Administration of the drug at the end of the observation period, the reason if a subject has withdrawn from/terminated administration

13) Occurrence of malignant tumour during 2 years after the observation period (follow-up investigation)
Presence or absence of onset of malignant tumour during 2 years after the observation period (or during 2 years after the withdrawal/termination if a subject has withdrawn from/terminated administration of the drug), diagnosis or symptoms, onset date, outcome of malignant tumour, outcome date, seriousness, relationship to Nucala and factors suspected of being related to AEs except for Nucala

14) Pregnancy
(For female subjects) whether or not the drug is administered to a pregnant woman, whether or not a subject is pregnant during the observation period and expected delivery date

In addition, the follow-up investigation should be conducted for a mother and her foetus as far as possible regarding the course of delivery, spontaneous abortion, elective abortion and AEs, etc.

15) Adverse Events (AEs)

Presence or absence of AEs after initiation of Nucala treatment, diagnosis or symptoms, onset date, outcome of AEs, outcome date, seriousness, reason for assessing as serious, relationship to the drug, factors suspected of being related to AEs except for Nucala

(1) In this study, the priority study matters are defined as follows;

- Hypersensitivity reaction including anaphylaxis, infections and malignant tumour

(2) To grasp the priority study matters and ADRs, the investigator will enter the information regarding all AEs (e.g., a disease, symptom, abnormal laboratory value) occurring after the initiation of Nucala treatment in the EDC system, regardless of whether or not the Nucala is related to an AE. Considering whether or not the possibility of a reasonable relationship to the drug is present, etc., the relationship to the drug will be assessed on a scale of two categories, any of "related" or "not related", and it will be entered in the EDC system.

(3) AEs assessed as "related" to Nucala will be handled as suspected "ADRs" that are caused by the product.

## 9. Analysis Items and Methods

1) Analysis items

(1) Subject disposition-related matters

① Number of enrolled subjects and number of subjects whose data is entered in the EDC system and fixed

② Number of subjects included in the safety and effectiveness analysis sets, number of subjects excluded from analysis and the reason for exclusion

③ Number of subjects included in the analysis sets regarding exacerbation of asthma, number of subjects excluded from the analysis sets and the reason for exclusion

④ Number of subjects included in the analysis sets regarding ACT, number of subjects excluded from the analysis sets and the reason for exclusion

(2) Safety-related matters

① Occurrence of ADRs and infections (type, severity and incidence of ADRs, etc.)

② Occurrence of events defined as a priority investigation matter

(3) Effectiveness-related matters

① Response rate based on the global assessment of effectiveness
The response rate is the proportion of subjects assessed as "effective".

② Frequency of exacerbation of asthma

③ Total score of ACT

④ PEF score

2) Analysis methods

(1) Safety

① The incidence of ADRs and 95% confidence interval will be calculated.

(2) Effectiveness

① The response rate and its 95% confidence interval will be calculated.

② For comparison of the scores, etc., the summary statistics for values at the time of measurement and changes from baseline will be calculated.

(3) Consideration of covariates

① The covariate that affects safety (incidence of ADRs) will be considered by calculating the odds ratio and its 95% confidence interval.
② The covariate that affects effectiveness (response rate) will be considered by calculating the odds ratio and its 95% confidence interval (It will be graphically presented using a forest plot, etc., as appropriate).

## 10. Organizational Structure

See Attachment 1.

## 11. Name, Address of the Outsourcees, and the Scope of Outsourced Operations

1) Enrollment
Outsourcee : CMIC Co., Ltd. (1-1-1, Shibaura, Minato-ku, Tokyo)
Scope : patient enrollment and other related operations
2) Data management
Outsourcee : CMIC Co., Ltd. (1-1-1, Shibaura, Minato-ku, Tokyo)
Scope : patient enrollment and other related operations
3) Statistical analysis
Outsourcee : CMIC Co., Ltd. (1-1-1, Shibaura, Minato-ku, Tokyo)
Scope : statistical analysis and other related operations
4) EDC system operarions
Outsourcee : FUJITSU FIP Corporation (1-2-1, Shibaura, Minato-ku, Tokyo)
Scope : development and operation of EDC system, and other related operations
5) Monitoring
Outsourcee: CMIC Co., Ltd.
Shibaura1-1-1, Minato-ku, Tokyo
Scope : contract with medical institutions, payment to medical institutions, promotion of enrolment and CRF collection, other related operations

## 12. Planned Timing to Be a Milestone for Assessing the Status and Results in the Study or Reporting to the Pharmaceuticals and Medical Devices Agency (PMDA) and Rationale

- At the time of Periodic Safety Reports: consideration will be comprehensively given to the safety and effectiveness information.
- At the time of re-examination application: the final report will be prepared/submitted, based on the results of tabular analysis obtained from the fixed data in the EDC.

## 13. Additional Measures that Have a Potential to Be Taken Depending on the Study Results and the Decision Criteria for the Start

The RMP including the following, will be reviewed at the timings to be a milestone.

- Regarding hypersensitivity including anaphylaxis, if the proportion, the peak onset period and risk factors become visible as an ADR caused by the drug, the necessity for revision to the Package Insert and study materials will be considered as appropriate.
- Including the presence or absence of a new issue in the safety specification, the necessity for changes in the content of plan in this study will be considered.

· The necessity for creation of Risk Minimization Plan for a new issue in the safety specification will be considered.

## 14. Publication of the Study Results

The information regarding the results of the study will be provided to clinical sites as an interim report and a final report as appropriate for the purpose of "proper use" and "safety assurance", considering a proper timing and the number of subjects whose data is collected, etc., by means of presentation at an academic conference and papers.

In addition, the summaries of plan and results in this study will be disclosed in GSK Clinical Study Register.

## 15. Other Requirements

1) Protocol Revision

The progress in the study, the number of subjects excluded from analysis, occurrence of unexpected/serious ADRs, large increase in occurrence of specific ADRs and validity of the study items, etc. will be timely grasped during the study period, and the Protocol will be reviewed and revised if required.

If the content of the Protocol in the study has been changed, the change notification should be submitted to the PMDA in advance, except for minor changes.

<Examples of minor changes>

(1) Change of the organization or the person in charge for the conduct of the study

(2) Change of the planned number of medical institutions (by department)

(3) EDC system

[1] Modifications to the layout of items (relocation of items, enlargement or reduction of sections)

[2] Change in the explanation of items

[3] Inclusion of additional examples of ADRs, in association with a revision of the Precautions or inclusion of noteworthy ADRs

(4) Addition, change, and deletion of items that have no impact on the entire study, particularly efficacy and safety analyses

(5) Study period

[1] Change of the start day of the study due to a delay in the product launch

[2] Prolongation of the study period to correspond to a short-term (within 3 months) prolongation, if necessary, of the registration period

[3] Reduction of the study period in case no change has been made to the planned sample size

2) Handling of problems or questions detected

If any problem is found during the study period or in the evaluation and analysis results, etc. after completion of the study, implementation of an additional special drug use investigation or post-marketing clinical study will be considered according to need.

## 16. Attachments

| | | |
|---|---|---|
| 5) | Nucala® for Subcutaneous Injection SDUI Case Report Form (CRF) | AT 5 |
| 6) | Nucala® for Subcutaneous Injection SDUI Asthma Control Test (ACT) | AT 6 |

# Nucala ® Subcutaneous Injection

# Drug Use Investigation

# (long-term)

# Statistical Analysis Plan

Title : Nucala Subcutaneous Injection Drug Use Investigation (Long-term)

Protocol No. :204524

Version :10.0

Date : 21/SEP/2023

Author : PPD

Study Accountable Person/ Non-Interventional Study Scientific Lead: PPD

Approved by : PPD

*Signature/Date*

PPD (Statistical) (based on GPSP-WI-P020-10)

Real World Data Analytics

Approved by : PPD

*Signature/Date*

Functional line manager of Study Accountable Person/ Non-Interventional Study Scientific Lead,(based on VQD-WI-048285(Link))

VEO Respiratory

Table of Contents

## 1. Purpose of Investigation

This survey was conducted to collect and evaluate the long-term safety and effectiveness of Nucala ® for Subcutaneous Injection (drug) in subjects with bronchial asthma.

## 2. Software and dictionary to be used

### 2.1. Statistical analysis and tabulation software

| | Software and Version |
|---|---|
| OS | Microsoft Windows 10<br>Or use a later version. |
| Statistical analysis software | SAS Ver.9.4<br>Or use a later version. |
| Tabulation software | Microsoft Excel 2016<br>Or use a later version. |

### 2.2. Dictionary to use

| Selected item | Dictionary name |
|---|---|
| Name of disease (complication), adverse event, and adverse reaction | Calculated based on the version of MedDRA/J used for coding in DM. *The version of MedDRA to be used will be discussed and determined by the team for each report. |
| Pharmaceutical name, drug name | Prescription Drug Names Data File (to be tabulated in the version used for coding in DM. *As a rule, the most recent version is used.) |

## 3. Defined Terms

| Term | Definitions |
|---|---|
| Date of initiation of drug treatment | The earliest date of medication in CRF [drug administration status].<br>However, the determination will be made based on the record that both "dose per dose [mg/dose]" and "number of doses per day [doses/day]" in CRF [drug administration status] are not missing. |
| Date of completion of drug administration | TCRF [Drug administration status] Among the dates listed on the drug administration date, the latest administration date excluding blank dates.<br>However, the judgment will be made based on records in which both the "dose [mg/dose]" and "number of doses per day [doses/day]" of CRF [drug administration] are not missing. |
| Date of discontinuation of drug | The end date of administration shall be the end date of administration for any case that is determined to be discontinued during the observation period in ``4.11 Handling of discontinued/completed cases and continued cases." |
| ACT | Asthma control test |
| IDSL | Integrated Data Standard Library |

| Term | Definitions |
|---|---|
| MedDRA/J | Medical Dictionary for Regulatory Activities Japanese version |
| LLT | Lower MedDRA/J term |
| PT | MedDRA/J preferred term |
| HLGT | MedDRA/J high-group term |
| SOC | System MedDRA/J Organ Class |
| SMQ | Standardised MedDRA queries |
| Ethical drug name data file | Drug data base provided by MT Council |
| Registration slip | Registry forms collected in EDC. |
| Case Report Form (CRF) | Case Report Form collected in EDC. |
| Re-examination period | March 28, 2016-March 27, 2024 |
| Data lock date | The last day of each investigation unit period is defined. |
| Observation period | One year (52 weeks) from the date of initiation of drug treatment. |
| Duration of follow-up | The annual will be 2 years (104 weeks) from the date of completion (discontinuation) of drug administration. |

# 4. Handling of cases and data

## 4.1. Number of subjects

✧ Number of subjects: Number of subjects who met the relevant conditions.

✧ Number of subjects with adverse events (adverse drug reactions):

An adverse event (adverse reaction) is considered an adverse event (adverse reaction) if it occurs in at least one case. When summarizing adverse events (adverse drug reactions) according to symptoms, the following procedures will be performed.

・For each SOC, the same SOC in the same case is counted as a single case.

・For each PT, the same PT in the same case is counted as a single case.

Adverse events occurring outside the investigation period or beyond the observation period for each patient are not included in this investigation.

## 4.2. Analysis set/site

| Selected item | Definitions |
|---|---|
| Enrolled sites | Sites for all enrolled subjects (eligible subjects).<br>Institutions with subjects with a registration date and before the data lock date<br>(excluding duplicate site codes). |
| Enrolled subjects | Subjects registered within the enrollment period specified in the protocol (January 1, 2017, to June 30, 2020) (enrolled eligible subjects).<br>Subjects with a registration date before the data lock date. |
| Sites that have obtained a CRF | All registry sites for which case report forms were collected.<br>"Case report form status" in the case report form information of PMS progress control system is one of the following: "This approval", "Survey sheet re-survey", "Content confirmation", "Content confirmation", "Re-entry", "Re-investigation after approval", and "Confirmation after approval"<br>Institutions with a value on the date of receipt of the survey form headquarters and a date prior to the data lock date |
| Subjects that have obtained a CRF | Among the enrolled subjects, all subjects for which a case report form was collected.<br>Case of the case report form recalled in the above-mentioned "case report form recalled site" |
| Sites that have fixed a CRF | Of the case report form collection sites, those where the case report form was approved.<br>Institutions where "case report form status" is "approved" in the case report form information of PMS progress control system.<br>Institutions with values on "the approval date of this case report form" and dated before the data lock date |
| Case that have fixed a CRF | Of the enrolled subjects, all subjects in which the case report form was retrieved and fixed.<br>Subjects in which PMS Progress Control System-based case report form information includes the date of recall, the date of completion of treatment, and the date of completion of treatment is before the date of data lock. |
| Sites for safety analysis | Of the CRF fixed sites, subjects that do not fall under the safety analysis exclusion subjects (see 4.3.1). |

| Selected item | Definitions |
|---|---|
| Safety analysis subjects | Of the subjects fixed in the CRF, subjects that do not fall under the safety analysis exclusion subjects (see 4.3.1). |
| Effectiveness analysis subjects | Of the subjects included in safety analysis, subjects that do not fall under the subjects excluded from efficacy analysis (see 4.3.2). |
| Follow-up analysis subjects | Of the subjects s included in safety analysis, subjects that a follow-up survey was conducted 52 weeks after the end of observation (or after discontinuation of administration if this drug was discontinued), and a questionnaire was collected. |
| ACT analysis subjects | Of the subjects s included in effectiveness analysis, Subjects that ACT scores were measured before and after starting administration of this drug |
| Asthma exacerbation analysis subjects | Of the subjects s included in effectiveness analysis, Subjects that asthma exacerbations were count before and after the start of administration of this drug. |

## 4.3. Analysis exclusion criteria

### 4.3.1. Subjects excluded from safety analysis

If the reasons for exclusion overlap and prioritize, the reasons for exclusion from safety analysis should be assigned according to the following ranking:

| Code | Safety Reasons for the exclusion from analyses | Priority Ranking | Condition of exclusion | Logic Judgement |
|---|---|---|---|---|
| S1 | Outside the period of investigation and registration | 1 | ・The date of commencement of drug administration or the date of completion of drug administration is outside the investigation period.<br>・The registration date is outside the registration period. | ○ |
| S2 | Outside the contract period | 2 | ・The date of commencement of drug administration or completion of drug administration is outside the contract period.<br>・The registration date is outside the contract period. | ○ |
| S3 | Violation of registration | 3 | Not registered within 14 days of the starting day of drug administration | ○ |
| S4 | Patients not treated | 4 | Subjects in which the administration status of drug is not described at all, or in which the description of all doses is 0 | ○ |
| S5 | No visit after the first administration date | 5 | [drug administration status at the completion of the run-in period]. The reason for discontinuation/completion of administration is "no visit after the first administration date" | ○ |
| S6 | Adverse event data unknown | 6 | The presence or absence of adverse events is blank, and there are no adverse event data. | ○ |
| S7 | Other (safety) | 7 | Subjects for whom the reasons for exclusion from the safety analysis were other than the above (S1～S6) | × |

#### 4.3.2. Effectiveness analysis excluded subjects

If the reasons for exclusion overlap and prioritize, the reasons for exclusion from effectiveness analysis will be assigned according to the following ranking:

| Code | Effectiveness Reasons for the exclusion from analyses | Priority Ranking | Condition of exclusion | Logic Judgement |
|---|---|---|---|---|
| E1 | Off-label use | 1 | If the reeasons for use is other than bronchial asthma. | × |
| E2 | Response not evaluable | 2 | [Overall effectiveness evaluation]. ""Undeterminable"." | ○ |
| E3 | Response evaluation not described | 3 | [Overall effectiveness evaluation]. There is no entry. | ○ |
| E4 | Other (effectiveness) | 4 | Subjects for whom the reason for exclusion from effectiveness analysis was other than the above (E1～E3) | × |

#### 4.3.3. Other subjects excluded from analysis

Not applicable in this survey.

### 4.4. Handling of missing data

#### 4.4.1. Data complement

Data imputation is not performed for missing data.

#### 4.4.2. Missing continuous quantities

Missing data from the tabulation of serial quantities are excluded from the tabulation. If there is a continuous volume of data at more than one time point, only missing time points are excluded. In classifying continuous quantities into categorical categories, follow 4.4.3 Categorical Data.

#### 4.4.3. Categorical data

✧ Handling of Unknown Categories

Depending on whether the category contains an unknown category, it should be labeled as follows:

- When the category includes unknown categories

  Missing or undescribed data are not distinguished, and if present in one case, they are labeled as "undescribed".

  When 0 subjects fall under "unknown" or "undescribed", the category is not labeled.

- If the category does not contain an unknown category

  Missing/unknown/undescribed subjects are not distinguished, and if relevant subjects exist, they are labeled as unknown.

  When 0 subjects fall under "unknown," the unknown category is not output.

✧ Missing data are included in the denominator of proportions.

✧ Exclude unknown categories when calculating tests and odds ratios

#### 4.4.4. Date variable

The imputation of date variables is addressed as follows.

<Date of completion of drug administration>

✧ If there is a deficiency date, it is not imputed and is considered unknown.

<Adverse events>

✧ If there is a defect on the date of onset or the date of outcome, it is not imputed and is considered unknown.

### 4.5. Handling of presence/absence

Whether or not such information is handled shall be as follows in principle.

| Description of the presence/absence column | Presence or absence of detail field records | Handling of presence/absence |
|---|---|---|
| Absence | Absence | "Absence" is set. |
| | Presence | "Presence" is defined. |
| Presence | Absence | "Unknown" is defined. |
| | Presence | "Presence" is defined. |
| Unknown/Not stated | Absence | "Unknown" is defined. |
| | Presence | "Presence" is defined. |

#### 4.5.1. Presence or absence of pregnancy

Regarding pregnancy status ,the decision is made as follows when the gender is "female".

✧ If you enter "Yes" in "Pregnancy" in CRF, it will be counted as "Pregnant".

✧ If you enter "no" in "pregnancy" in CRF, it will be counted as "no pregnancy".

✧ If "Pregnancy" in the CFR does not have "Yes" or "No" entered, it will be counted as "Unknown Pregnancy".

#### 4.5.2. Presence or absence of prior medication

All drugs entered on the page of the case report form [Pretreatment Drugs for Bronchial Asthma] are included.

✧ Determination of the presence

The presence or absence of the previous drug, the category of the drug, and the name of the product will be determined in the following order.

① When the item "Product name (only for the most recent use)" in the case report form [Pre-treatment drugs for bronchial asthma]

1. If the product name (only for the most recent use) in the [Pretreatment Drugs for Bronchial Asthma] in the case report form is entered, the product name is "present"
2. 1. If there is at least one entry in the product name (only for the most recent use) of the [Pretreatment Drugs for Bronchial Asthma] in the case report form, the drug category to which the product name is applicable is "present"
3. 1. Or product name or drug category not applicable in 2. shall be "nothing

② When there is no item in the product name (only the most recently used drug) of the case report form [Pre-treatment drug for bronchial asthma]

1. If the "Drug category (multiple choices) of the case report form [Pre-treatment Drugs for Bronchial Asthma] is entered, the corresponding

drug category is "presence"

2. 1. Drug categories not applicable are designated as "nothing

③ Determination of the presence or absence of pretreatment drugs

1. "Present" if one or more drug categories fall under ①-2 or ②-1

2. 1. When it does not correspond, it is considered as "nothing."

#### 4.5.3. Presence of concomitant medications

All drugs entered on the [Combination Drugs] page of the case report form are included.

✧ Determination of the presence

The presence or absence of concomitant medication will be determined as follows.

- If the "Drug name" in the [Combination Drug] section of the case report form is entered, it shall be "presence"
- In other subjects than the above, it is set to "nothing"

#### 4.5.4. Presence or absence of concomitant therapy

All therapies entered on the page of the case report form [Combination therapy for bronchial asthma (other than drugs)] are included.

✧ Determination of the presence

Concomitant therapy is assessed as follows.

- "Presence" is indicated in "Therapy name" in the survey form [Combination therapy for bronchial asthma (other than drugs)].
- In other subjects than the above, it is set to "nothing"

#### 4.5.5. Presence of complications

All events entered in the disease name of the complication on the [Patient Background] page of the case report form are included.

✧ Determination of the presence

The presence or absence of complications is determined as follows.

- "Presence" is indicated when the "disease name (including allergy history)" in the [Patient background] of the survey form is entered.
- In other subjects than the above, it is set to "nothing"

### 4.6. Calculation of days and age

✧ Days

The number of days based on the starting day of drug administration is calculated as follows, when the study day is before or after the starting day of drug administration.

・Date of first administration of drug < = date of study: date of subject-date of first administration of drug + 1

・Date of first administration of drug > target date: target date-drug starting date

※Days (days) after the initiation of drug treatment are labeled as 1 for the first day of drug treatment and-1 for the day before the initiation of drug treatment; 0 is not used.

Treat 1 week as 7 days.

The definition of each period shall be as follows.

| Selected item | Definitions |
|---|---|
| Duration of drug treatment (days) | Calculate using the following formula.<br>Calculation formula<br>Duration of drug treatment (days) = date of completion of drug treatment-date of initiation of drug treatment + 1 |
| Time to onset of adverse drug reactions (days) | Calculate using the following formula.<br>Calculation formula<br>Day of onset of adverse drug reaction-Day of first administration of drug + 1 |

✧ Age

Age [years] is calculated using the date at the beginning of drug treatment, complemented with June 30 in the birth year on the [cover] of the case report form.

① If the year (Taisho, Showa, and Heisei) is entered in the 'year of birth' on the [cover] of the case report form, it is converted to the western calendar and used to calculate the age.

If there is a western calendar entry in the 'year of birth' on the [cover] of the case report form, it will be used to calculate age as in.

② Determine the difference in the year of the date.

③ When the date of birth is before the date of birth, subtract 1 from the difference of the year to reach the age.

When the date is the same or later than the date of birth, the difference between the years is set as the full age.

### 4.7. Assessment window

#### 4.7.1. Adoption data for blood test items by assessment period

✧ Adoption data for the evaluation period of blood eosinophil count

Identify Adoption data in the following processing order:

① Laboratory data that are unknown or cannot be quantified are excluded.

② In accordance with the table below, the data for inclusion will be identified according to the time of evaluation.

| Time of evaluation | Adoption data |
|---|---|
| 9-52 weeks prior to initiation of drug | Blood eosinophil count [/μL] entered in the "9-52 weeks prior to drug administration" section of the case report form [blood test items-blood eosinophil count] |
| At the beginning of drug administration | Blood eosinophil count [/μL] entered in the entry column for drug administration (0-8 weeks prior to administration) in the [Blood test items-Blood eosinophil count] in the case report form |
| 12 weeks after initiation of drug | Blood eosinophil count [/μL] entered in the "12 weeks after the initiation of drug administration" section of the case report form [blood test items-blood eosinophil count] |
| 24 weeks after initiation of drug | Blood eosinophil count [/μL] entered in the "24 weeks after the start of drug administration" section of the case report form [blood test items-blood eosinophil count] |
| 52 weeks after the initiation of drug administration or at the time of discontinuation/completion of administration | Blood eosinophil count [/μL] entered in the "Week 52 after initiation of drug treatment or at the time of discontinuation/completion" section of the case report form [blood test items-blood eosinophil count]<br>However, if there is no entry in the "Week 52 after the start of drug administration or at the end of administration" section of the [Blood test items-Blood eosinophil count] of the case report form in subjects who discontinued/completed the study, the following adoption data will be specified.<br>Blood eosinophil counts [/μL] entered in the [blood test items-blood eosinophil counts] of the case report form after 12 weeks of drug administration, and the blood eosinophil counts [/μL] at the latest assessment period<br>※In subjects who continue for 52 weeks, the treatment will be handled as "52 weeks after the initiation of drug therapy." |

✧ Adoption data for evaluation time of serum total IgE concentration

Identify recruitment data in the following processing order:

① Laboratory data that are unknown or cannot be quantified are excluded.

② In accordance with the table below, the data for inclusion will be identified according to the time of evaluation.

| Time of evaluation | Adoption data |
|---|---|
| Prior to start of drug | Serum total IgE level entered in the "Prior to drug administration" section of the case report form [blood test item-serum total IgE level] [IU/mL] |

#### 4.7.2. Adoption data for effectiveness endpoints by time point

✧ Adoption data for the time of evaluation of exacerbations of asthma

Identify recruitment data in the following processing order:

① Exclude unknown or non-quantifiable input data.

② In accordance with the table below, the data for inclusion will be identified according to the time of evaluation.

| Time of evaluation | Adoption data |
|---|---|
| 52 weeks prior to initiation of drug | The data entered in the field "52 weeks prior to the initiation of drug administration" in the [Asthmatic exacerbation] of the case report form |
| 52 weeks after initiation of drug treatment or until discontinuation | Data entered in the field "52 weeks after initiation of drug treatment or until discontinuation of treatment" in the [Asthmatic exacerbation] of the case report form<br><br>**Entry items of interest**<br>・ Number of asthma exacerbations<br>・ Asthma exacerbations requiring hospitalization<br>・ Total hospital stay<br>・ Asthma exacerbations requiring emergency department visits<br>・ Asthma exacerbations requiring use of systemic corticosteroids |

✧ Range of adoption of evaluation time for respiratory function test (peak flow)

Data from each evaluation period will be collected from the range of inclusion specified in the table below. If observations or measurements have been performed more than once within the data range, the following procedures will be used to determine the data to be used.

① Adopt data in which "measurement time-period" and "short-acting $\beta_2$ stimulant use or not" with input to [respiratory function test (peak flow)] of the case report form are not missing, and the value of "peak flow (PEF)" can be quantified.

② Adoption of data corresponding to the inclusion range category at each evaluation period on the measurement date of the [respiratory function test (peak flow)] in the case report form.

③ For the data adopted in ②, the mean value of the [respiratory function test (peak flow)] peak flow (PEF) value of the case report form is calculated for each recruitment category and used for tabulation.

Mean values are calculated using the following equation.

Mean = total of the peak flow (PEF) values in each recruitment category

÷ Number of records corresponding to each adoption range category

| Time of evaluation | Category of scope of adoption |
|---|---|
| At the beginning of drug administration | Day of first drug dose ≦ ≦ drug Day 7 |
| 12 weeks after initiation of drug | Starting day of drug administration +77 days ≦ ≦ drug starting day +91 days |
| 24 weeks after initiation of drug | Day of first drug administration + 161 days ≦ ≦ drug day of first administration + 175 days |
| 52 weeks after initiation of drug | Day of first drug administration + 357 days ≦ ≦ drug day of first administration + 371 days |
| Discontinuation/completion of drug treatment | End of observation (Week 52)-Day 7 ≦ ≦ End of observation (Week 52) + Day 7 |

**e.g., calculation of the mean peak flow at the beginning of drug treatment**

Original data

| Case No. | Date of initiation of drug treatment | Days measured | Measurement Time of day | Peak flow (PEF | Use of short-acting $\beta_2$ agonists | Data Acceptance * |
|---|---|---|---|---|---|---|
| PPD | 2018/3/7 | 2018/2/10 | In the morning | 250 | With | Non-adoption |
| | | 2018/2/10 | At night | 270 | With | Non-adoption |
| | | 2018/3/4 | In the morning | 290 | With | Adoption |
| | | 2018/3/4 | At night | 300 | With | Adoption |
| | | | In the morning | 280 | None | Non-adoption |
| | | 2018/3/2 | | 280 | | Non-adoption |
| | | 2018/3/2 | At night | 300 | None | Adoption |
| | | 2018/3/7 | In the morning | 290 | None | Adoption |
| | | 2018/3/7 | At night | 350 | None | Adoption |

* "Respiratory function test (peak flow)" in the case report form is not missing for both "measurement time period" and "short-acting $\beta_2$ stimulant use" and the value of "peak flow (PEF)" can be quantified, and "measurement date" falls within the inclusion category for each assessment period.

Calculation of mean peak flow (PEF

Calculated by (290+300+300+290+350) ÷5.

✧ Adoption of the Asthma Control Test (ACT) at the time of assessment

Identify recruitment data in the following processing order:

① Total scores that are unknown or cannot be quantified are excluded.

② In accordance with the table below, the data for inclusion will be identified according to the time of evaluation.

| Time of evaluation | Adoption data |
|---|---|
| At the beginning of drug administration | Total scored [dots] entered in the entry column for "Initiation of drug administration" in the [Asthma Control Test (ACT)] of the case report form |
| 12 weeks after initiation of drug | Total scored [dots] entered in the "12 weeks after initiation of drug administration" field of the [Asthma Control Test (ACT)] in the case report form |
| 24 weeks after initiation of drug | Total scored [dots] entered in the field "24 weeks after starting drug administration" in the [Asthma Control Test (ACT)] of the case report form |
| 52 weeks after initiation of drug | Total scored [dots] entered in the field "52 weeks after starting drug administration" in the [Asthma Control Test (ACT)] of the case report form |
| Discontinuation/completion of administration | Total scored [points] entered in the entry column for "Discontinuation/End of Treatment" in the [Asthma Control Test (ACT)] of the case report form<br>However, if there is no entry in the "Discontinuation/End" section of the [Asthma Control Test (ACT)] of the case report form in subjects who discontinued/completed the study, the following inclusion data will be specified.<br>・ Within the total score [points] entered in the [Asthma Control Test (ACT)] of the case report form, the total score [points] of the latest assessment time among the data from 12 weeks after the initiation of drug treatment. |

### 4.8. Handling of transferred subjects

Not applicable in this survey.

### 4.9. Adverse events/adverse reactions

| Term | Definitions |
|---|---|
| Adverse Event | Events entered into Argus. |
| Side Effects | Adverse events other than "Determined causality" and "Reported causality" are "Unrelated" or "Can be denied." |
| Serious adverse events (adverse drug reactions) | Adverse events (adverse drug reactions) that are "serious." |
| First adverse event (adverse reaction) | Adverse events (adverse drug reactions) with the date of onset being the earliest event. However, when the onset date includes an unknown event, the following measures should be taken.<br><br>**When the decision is made in the same case and in the same event unit**<br>Records with unknown date of onset shall be adopted when there is a record containing unknown date of onset.<br><br>**When judging on a case basis**<br>When an event with an unknown onset date exists after the first adverse event (ADR) is determined in the same case and by the same event unit, the onset date of the first adverse event (ADR) in that patient is unknown. |
| Adverse reactions after completion of drug administration | Adverse drug reactions are defined as those that meet the following conditions.<br><br>**Judgment condition**<br>Date of completion (discontinuation) of drug administration < date of onset<br>However, when the date of onset is unknown, it is not subject to evaluation (not applicable) because the condition cannot be judged. |

**4.10. Safety Specification, Definition of Complications**

The following adverse events will be defined for the Safety Specification:

| Classification of Safety Specification | Definitions | Dictionary code |
|---|---|---|
| Hypersensitivity such as anaphylaxis | Anaphylactic response (SMQ, narrow zone) | 20000021(narrow area) |
| | Hypersensitivity (SMQ, narrow zone) | 20000214(narrow area) |
| Infectious Disease | Infectious diseases: Infectious and parasitic diseases (MedDRA/J SOC) | MedDRA/J SOC:10021881 |
| Malignant tumor | Malignancy (SMQ narrow zone) | 20000227(narrow area)<br>20000228(narrow area) |
| | Malignant lymphoma (narrow SMQ spectrum) | 20000215(narrow area) |

In the item of the case report form [patient background] Complications, it is classified according to the following dictionary code.

| Classification of complications | Definitions | Dictionary code |
|---|---|---|
| Kidney dysfunction | Nephropathy (HLGT) | MedDRA/J HLGT:10029149 |
| | Renal impairment (excl nephropathy) (HLGT) | MedDRA/J HLGT:10038430 |
| | ACUTE RENAL FAILURE (SMQ, broad/narrow spectrum) | 20000003(broad and narrow) |
| Liver dysfunction | SMQ level 1 PT included in "Hepatic disorders" minus SMQ level 3 PT included in "Coagulation and hemorrhage disorders related to the liver" | SMQ level-1 'hepatic impairment': (20000006,20000007,)20000008,20000009,20000010,20000011,20000012,20000013,20000014,(20000015,)20000016,20000017,20000018,20000208,20000209<br>SMQ Level-3 Coagulation and Hemorrhage Disorders Associated with the Liver:<br>20000015 |
| Allergy | Allergic diseases (HLGT) | MedDRA/J HLGT:10001708 |
| Other | An event that does not correspond to renal or hepatic dysfunction or allergy. | - |

### 4.11. Handling of Continued/Discontinuation・Completed Administration

Treat as follows:

| | | |
|---|---|---|
| Continuation of drug treatment (Case report form) | Date of completion of drug administration | Handling (Logic assessment of drug administration) |
| Continuation of treatment | Date of completion of drug administration-drug administration start day + 1 < 364-28 | Treat as discontinued or completed subjects<br>The reason for discontinuation/completion of administration is "unknown" |
| | Date of completion of drug administration-drug administration start day + 1 > = 364-28 | Continued administration (not changed) |
| Discontinuation/completion of administration | Date of completion of drug administration-drug administration start day + 1 < 364-28 | Discontinuation/completion of administration (no change) |
| | Date of completion of drug administration-drug administration start day + 1 > = 364-28 | Treatment is treated as a continuation case, and the reason for discontinuation/completion of treatment as described in the case report form is not used. |

✧ The end of observation (Week 52), start/end of follow-up, and last observation day shall be handled as shown below.

| Term | Definitions |
|---|---|
| End of observation (Week 52) | Calculate using the following formula.<br><br>・Day of completion of drug administration-drug day of initiation +1 > = 364<br>End of Observation (Week 52) = +364 on the starting day of drug administration.<br><br>・Date of completion of drug administration-drug administration start day + 1 < 364<br>End of Observation (Week 52) = end of drug administration + 28. However, when the day of completion of drug administration + 28 > drug administration start day + 364, the day of completion of drug administration observation = the day of initiation of drug administration + 364. |
| Start date of follow-up | ・ Date of completion of drug administration-drug administration start day + 1 > = 364<br>Starting day of follow-up = end of observation (week 52) + 1.<br><br>・ Date of completion of drug administration-drug administration start day + 1 < 364<br>The starting date of follow-up = the date of completion of drug administration + 1. |

| Term | Definitions |
|---|---|
| End of follow-up | The following is calculated using "Have you completed the follow-up survey" in the survey form [Confirmation of completion of the follow-up survey].<br><br>・If yes is selected<br>End of follow-up = start of follow-up day + 52 weeks (= 52 × 7 days) × 2-1<br><br>・If yes is not selected<br>① When the presence or absence of malignancy is "Present"<br>The date of the end of follow-up = the latest in the status of malignancy (follow-up) 2 years after the end of the observation period].<br>However, if the above date exceeds "the start date of follow-up + 52 weeks (= 52 × 7 days) × 2-1", then "the start date of follow-up + 52 weeks (= 52 × 7 days) × 2-1".<br>② When the presence or absence of malignancy is "none"<br>End of follow-up = end of drug treatment<br><br>If the follow-up form has not occurred, the date of completion of follow-up = starting date of follow-up. |
| Last day of observation | Define as below.<br>・When focusing on events other than malignancy<br>Final observation day = end of observation day (week 52).<br><br>・When focusing on malignancy<br>① Final observation day = end of follow-up day.<br>② If the follow-up form has not occurred, the date of last observation = end of observation (52 weeks). |

**4.12. Handling of subjects whose administration purpose has been changed**

The date of the last administration of drug for severe asthma is the date of completion of drug therapy for subjects who have been changed from severe asthma to eosinophilic polyangiitis granulomatosis (EGPA).

## 5. Items related to statistical processing

### 5.1. Summary statistics

The number of subjects, mean, standard deviation, minimum, 25% point, median, 75% point, and maximum are indicated.

### 5.2. Change, Percentage Change, and Percentage

Change from baseline, percentage change, and percentage change are calculated by the following equation.

- ✧ Change = Measured at each observation period-Baseline
- ✧ Percentage change (%) = (Change/ Baseline Measured) × 100
- ✧ Percentage (%) = (number of subjects included/number of subjects included in the analysis) × 100

### 5.3. Display of results

The labeling of the tabulated results is as follows.

| Classification | Labeled digit |
|---|---|
| Percentage change | The second decimal point is rounded and displayed up to the first rank. |
| Number of subjects | You display as an integer. |
| Mean, SD, 25 percentage points; Median, 75 percentage points; confidence interval of the mean | Rounded down to the nearest two digits of the original data and displayed down to the lowest one digit of the displayed digit. |
| Min, max | Rounded off one digit of the number of digits displayed on the original data and displayed up to the same number of digits as the number of digits displayed. |
| p value | The fourth decimal point is rounded and displayed up to the third decimal point. However, if the p-value before rounding is less than 0.001, it is labeled as uniformly "p<0.001". If p-value cannot be calculated, p-value shall be "-" (double-byte hyphen).<br><Example><br>Original value: 0.0098<br>Displayed: p = 0.010 |
| Odds ratio; confidence interval of odds ratio; correlation coefficient | The fourth decimal point is rounded and displayed up to the third decimal point. |

### 5.4. Exploratory analysis of influential factors

CCI

[redacted]

# 6. Primary analysis item

## 6.1. Case composition

### 6.1.1. Case Composition (Figure1.01)

Analyses included: -

Analysis content: The following numbers of subjects, the number of subjects excluded, and the reasons for exclusion are shown using a flow chart.

If there are multiple entries in the same case, the reasons for exclusion will be aggregated into high priority exclusion reasons.

The number of sites will be tabulated on a per-site basis, not considering clinical departments.

Figure1.01

- Enrolled sites
- Enrolled subjects
- Subjects that have not obtained a CRF
- Sites that have obtained a CRF
- Subjects that have obtained a CRF
- Subjects where CRF is not fixed
- Sites that have fixed a CRF
- Case that have fixed a CRF
- Subjects excluded from safety analysis and reasons for exclusion
- Number of sites
- Safety analysis subjects
- Effectiveness analysis excluded subjects and reasons for exclusion
- Effectiveness analysis subjects

Figure1.02

- Sites for follow-up
- Follow-up subjects
- Subjects with no follow-up form obtained
- Follow-up case report form collection site
- Follow-up form obtaineded subjects
- Unfixed follow-up form
- Follow-up form fixed site
- Follow-up form fixed subjects

## 6.2. Patient characteristics and baseline characteristics

### 6.2.1. Patient characteristics (Table1.01)

Analyses included: Safety analysis subject / Effectiveness analysis subjects

Analysis content: The number of subjects and percent and/or summary statistic will be calculated for each patient characteristics analysis.

The denominator of the constituent ratio (%) is the sum of the subjects included in the respective analyses, unless otherwise stated.

The 25% and 75% points of the summary statistics are not calculated.

Dose is defined as follows.

**Pretreatment**

1. Excluding missing or incompletely dated drug administration dates in the case report form [drug administration status].
2. The number of daily doses [times/day] in the case report form [drug administration status] excludes missing records.
3. The single dose [mg] of the case report form [drug administration status] excludes missing records.

| Selected item | Definitions |
|---|---|
| Total number of doses [times] | The total number of daily doses [times/day] is used. |
| Total dose [mg] | For each record of "dose per dose [mg] and "number of daily doses [times/day], the "dose per dose [mg] x "number of daily doses [times/day]" will be calculated, and the calculated data will be summated. |
| Duration of drug treatment [days] | Use "Duration (days) of drug" in "Calculation of 4.6 Days/Age". |
| (total) dose to onset of adverse reaction [mg] | For each record on the [drug dosing status] in the case report form that meets the criteria for the date of onset of adverse drug reactions ≧ drug dosing date, the "dose per dose [mg] × "number of daily doses [times/day]" is calculated, and the sum of these calculations is used. |
| Number of administrations until the onset of adverse drug reactions [times] | The sum of the number of daily doses [times/day] for each record on the [drug dosing status] of the case report form that meets the criteria for the date of onset of adverse drug reactions ≧ drug dosing date. |

Patient characteristics items: Table1.01.1:

- Gender: Male, Female, Unknown
- Presence of pregnancy "Women only": None, present, unknown
- Age 1 (years): <15, 15≦ to <65, 65≦ to <75, 75≦, unknown and summary statistics
- Age 2 (years): <65, 65≦, unknown

- Age 3 (years): <12, 12≦ to <18, 18≦, unknown
- Hospitalization/outpatient category: inpatient, outpatient, unknown
- Reasons for drug use: bronchial asthma. Otherwise unknown
- Reasons for drug use and breakdown (name of illness)
- Complications: None, Yes
- Complications (renal dysfunction, hepatic dysfunction, allergy, etc.): None, Yes
- Smoking history: no smoking history, current smoking, current smoking, unknown smoking history
- Primary disease (disease duration): ≦2, 2< to ≦5, 5< to ≦10, 10<, unknown
- Primary disease (severity before administration): mild intermittent, mild persistent, moderate persistent, severe persistent, and most severe persistent
- Primary disease (pathotype): atopic type, non-atopic type, unknown
- Blood eosinophil count (9-52 weeks prior to initiation of drug): <150, 150≦-<300, 300≦-<500, 500≦, unknown and summary statistic
- Blood eosinophil counts (start drug): <150, 150≦ to <300, 300≦ to <500, 500≦ and summary statistic
- History of omalizumab use: None, Yes
- Pretreatment Drugs for Bronchial Asthma: None, Yes
- Concomitant drugs: None, Yes
- Combination therapy (other than drugs) for bronchial asthma: None, Yes

Table 1.01.2: Miscellaneous Complications
Table1.01.3: Treatment Drugs
(The incidence of adverse reactions and the active proportion are also displayed.)
Table1.01.4: Concomitant Drugs and Therapies
(The incidence of adverse reactions and the active proportion are also displayed.)
Table1.01.5: Administration status
(The incidence of adverse reactions and the active proportion are also displayed.)

### 6.3. Safety evaluation

#### 6.3.1. Inventory of adverse drug reactions by patient characteristics (Table2.01)

Analyses included: Safety analysis subjects

Analysis content: The number of subjects surveyed, the number of subjects with adverse drug reactions, and the incidence proportion of adverse drug reactions and their 95% confidence intervals will be calculated for each patient characteristics.

The incidence of adverse reactions is calculated according to the following formula.

Incidence of adverse drug reactions = number of subjects with adverse drug reactions/number of subjects surveyed for each background item × 100

The number of subjects with adverse drug reactions is counted as 1 patient with at least 1 adverse drug reaction.

Patient characteristics items: Same section as "6.2.1 Patient characteristics (Table1.01)"

### 6.3.2. Time to onset of adverse drug reactions (Table2.02)

Analyses included: Safety analysis subjects

Analysis content: Regarding adverse reactions, the following items are calculated for each category of time to onset of adverse reactions and the total number of subjects.

- Number and percentage of subjects with adverse drug reactions
- Cumulative number of subjects with adverse drug reactions and the percentage

The denominator of the proportion of each item is as follows:

- Percentage of subjects with adverse drug reactions: Total number of subjects with adverse drug reactions
- Cumulative incidence of adverse drug reactions: total number of subjects with adverse drug reactions

However, the total number of subjects with adverse drug reactions should include "unknown" in the period to onset of adverse drug reactions.

The number of subjects with adverse reactions by SOC and PT will be summarized in terms of the time to onset by category and the total number of subjects.

For the total number of subjects, the percentage will be calculated.

The denominator of the proportion is the number of subjects included in the safety analysis.

**Time to onset of adverse reaction**

The tabulation of the time to onset of adverse drug reactions is as follows.

- In the tabulation of time to onset of adverse drug reactions by category, each time to onset of relevant adverse drug reactions is counted as one subject.

When the time to onset of adverse drug reactions cannot be calculated, it is counted as an unknown category.

For adverse events and adverse drug reactions, refer to "4.10 Adverse events and adverse drug reactions".

For the time to onset of adverse reactions, refer to "Calculate of the number of days and age" in 4.6.

The same case, the same SOC, and the same PT are processed as follows and used for tabulation.

For handling of adverse events and adverse reactions, refer to "4.10 Adverse events and adverse reactions".

**Time to onset of each adverse reaction category**

**<PT (preferred term)>**

The same case, the same SOC, and the same PT are summarized in the index case.

**<SOC (System Organ Class)>**

When the data are summarized according to the time of onset in the same case and in the same PT (preferred term) and the time to onset in the same case and in the same SOC (system organ class), the time to onset of adverse drug reactions is counted in each time category.

**<Adverse drug reaction subjects>**

The same case is counted as 1 case in the category of the time to onset of the relevant ADR in each case after being summarized in the index case.

Example :

Original data

| Case No. | SOC | PT | Date of onset | Time to onset of adverse drug reactions [days] |
|---|---|---|---|---|
| PPD | SOC1 | PT1 | 2017/01/01 | 1 |
| | SOC1 | PT1 | 2017/01/27 | 27 |
| | SOC1 | PT2 | 2017/01/27 | 27 |
| | SOC1 | PT3 | 2017/03/04 | 63 |

Identical subjects, identical SOC, and identical PT are summarized in the index case.

| Case No. | SOC | PT | Date of onset | Time to onset of adverse drug reactions [days] |
|---|---|---|---|---|
| PPD | SOC1 | PT1 | 2017/01/01 | 1 |
| | SOC1 | PT2 | 2017/01/27 | 27 |
| | SOC1 | PT3 | 2017/03/04 | 63 |

Tabulation results

| Time of onset | <28 | 28≦～<84 | 84≦～<168 | Unknown |
|---|---|---|---|---|
| SOC1 | 1 | 1 | 0 | 0 |
| PT1 | 1 | 0 | 0 | 0 |
| PT2 | 1 | 0 | 0 | 0 |
| PT3 | | 1 | 0 | 0 |
| Subjects with adverse reactions | 1 | 0 | 0 | 0 |
| Cumulative incidence of adverse reactions | 1 | 1 | 1 | 0 |

**Total number of subjects**

**<PT (preferred term)>**

The same case, the same SOC, and the same PT are summarized in one case regardless of the date of onset.

**<SOC (System Organ Class)>**

The same case and same SOC are summarized in one case regardless of the date of onset.

**<Adverse drug reaction subjects>**

The same case is summarized in one case regardless of the date of onset.

| | |
|---|---|
| Categorization of days to onset of adverse drug reactions: | <28、28≦～<84、84≦～<168、168≦～<252、252≦～<365、365≦、Unknown |
| Definition of time to onset of adverse drug reactions: | For the calculation of the time to onset of adverse reactions<br>See 4.6 Calculate of Days and Age.<br>However, the date of onset of adverse reaction is defined as the date of onset. |

**6.3.3. Total dose until onset of adverse reaction by type (Table2.03)**

| | |
|---|---|
| Analyses included: | Safety analysis subjects |
| Analysis content: | The total dose category and total dose of drug will be summarized in the same manner as in "6.3.2 Time to onset of adverse drug reactions (Table2.02)".<br>For the total dose of drug and the total dose of drug until the onset of adverse reactions, refer to "6.2.1 Patient characteristics (Table1.01)". |
| Total dose of drug to onset of side effects: | <100 mg, 100 mg≦～<300 mg, 300 mg≦～<600 mg, 600 mg≦～<900 mg, 900 mg≦～<1300 mg, 1300 mg≦, "unknown" |

**6.3.4. Incidence of reaction/event by seriousness (Table2.04～Table2.07)**

| | |
|---|---|
| Analyses included: | Safety analysis subjects |
| Analysis content: | For each reaction/event, the proportions by PT will be summarized by seriousness (total number/seriousness). The denominator of the ratio is the number of subjects included in the safety analysis. The output permutation is output in descending order of the number of SOC in the total number of columns, in descending order of the international consensus order of SOC, in descending order of the number of PT subjects, and in descending order of the number of PT subjects if there are no total number columns, in SOC international consensus order, and in PT coding order.<br>In addition, the number of subjects with ADRs/AEs and the proportion of ADRs/AEs will be summarized by outcome. The denominator of the percentage will be the number of subjects included in the safety analysis.<br><br>※If the same case and the same SOC, PT are present in the summary by outcome, the following priorities will be adopted and tabulated.<br>①Serious > non-serious; ② Fatal > Sequelae > Unrecovered > Remitted > Recovery > Unknown |

**6.3.5. Adverse reaction/event status (Table2.08～Table2.11) by safety considerations.**

| | |
|---|---|
| Analyses included: | Safety analysis subjects |
| Analysis content: | For adverse drug reactions/events, the proportions by PT will be summarized by seriousness (total number and seriousness) for each safety specification. The output order is output in descending order of the number of SOC in the total number of columns, SOC coding order, descending order of the number of PT subjects, and PT coding order.<br>The number of subjects with reaction/event and the proportion of subjects with reaction/event will be summarized by outcome for each safety consideration.<br>The denominator is the number of subjects included in the safety analysis. |

※If the same case and the same SOC, PT are present in the summary by outcome, the following priorities will be adopted and tabulated.

Death > Sequelae > Unresolved > Remitted > Recovery > Unknown

Table2.08.1～Table2.11.1: Hypersensitivity such as anaphylaxis

Table2.08.2～Table2.11.2: Infectious Disease

Table2.08.3～Table2.11.3: malignant tumor

### 6.3.6. Incidence of adverse reactions in subjects with special characteristics (Table2.12, Table2.13)

| | |
|---|---|
| Analyses included: | Safety analysis subjects |
| Analysis content: | The proportions of adverse drug reactions (total/serious) by PT will be tabulated for subjects with special patient characteristics. The denominator of the ratio is the number of subjects included in the safety analysis by patient characteristics. The output order is output in descending order of the number of SOC in the total number of columns, in international consensus order of SOC, in descending order of the number of PT, and in PT coding order. In addition, the number of subjects with adverse drug reactions and the incidence of adverse drug reactions will be tabulated according to the outcome. The denominator of the percentage will be the number of subjects included in the safety analysis by patient characteristics.<br>※If the same case and the same SOC, PT are present in the summary by outcome, the following priorities will be adopted and tabulated.<br>①Serious > non-serious; ② Fatal > Sequelae > Unrecovered > Remitted > Recovery > Unknown |
| Special patient characteristics: | Table2.12.1, Table2.13.1: Renal dysfunction<br>Table2.12.2, Table2.13.2: Hepatic dysfunction<br>Table2.12.3, Table2.13.3: Pediatric<br>Table2.12.4, Table2.13.4: Elderly<br>Table2.12.5, Table2.13.5: Pregnant women |

### 6.3.7. Duration of drug treatment by reason for discontinuation/completion of drug (Table2.23)

| | |
|---|---|
| Analyses included: | Safety analysis subjects |
| Analysis content: | The number of subjects who discontinued or completed drug treatment and the reason for discontinuation or completion of treatment will be summarized by the duration (days) of drug treatment until discontinuation or completion.<br>The reasons for discontinuation/completion of administration are duplicated. |
| Categories of drug treatment duration until discontinuation/comp | <28、28≦～<84、84≦～<168、168≦～<252、252≦～<365、Unknown |

letion of treatment:

Defining the duration (days) of drug treatment until discontinuation/completion of treatment: See "Calculation of the number of days and age" in "4.6 Calculation of drug duration of administration before discontinuation/completion of administration."
However, the target date is the date of completion of drug administration.

### 6.4. Evaluation of effectiveness

#### 6.4.1. Effectiveness proportion by patient characteristics (Table3.01)

Analyses included: Effectiveness analysis subjects

Analysis content: The number of subjects surveyed, effective subjects, ineffective subjects, and effective proportions with 95% confidence intervals will be calculated for each patient background item.

The active proportion is calculated using the following formula.

Effective proportion = number of effective subjects/number of investigated subjects for each background item × 100

Effectiveness is assessed as follows.

- "Effectiveness" in the [Overall Evaluation of Effectiveness] of the case report form is "effective" and "effective"
- If "Effectiveness" in the [Overall Evaluation of Effectiveness] of the case report form is "Ineffective", "Ineffective"
- When the "effectiveness" of the [Overall Effectiveness Evaluation] of the case report form has an input in "Undeterminable", it is set to "Undeterminable"
- If other than the above, indicate "unknown"

Patient characteristics items: Same section as "6.2.1 Patient characteristics (Table1.01)"

### 6.5. Listing

- ✧ Availability List for Review (Listing1)
- ✧ List of adverse events (Listing2)
- ✧ Case report form and List of Subjects (Lisiting3)
- ✧ List of Serious Adverse Drug Reactions (Listing5)
- ✧ List of Adverse Events by Safety Specification (All subjects) (Listing6.1)
- ✧ List of Adverse Events by Safety Specification (Serious subjects) (Listing6.2)
- ✧ Summary of fatal subjects (Listing7)
- ✧ List of adverse events in subjects excluded from safety analysis (Listing8)

- ✧ List of subjects for change in reason for use (Listing9)
- ✧ Incidence of adverse reactions/infectious diseases in the additional safety monitoring plan (Form 12)
- ✧ List of subjects surveyed (Format 16)

### 6.6. Exploratory analysis

CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

CCI

[redacted]

CCI

## 6.7. Proprietary form

### 6.7.1. Summarized statistic of blood eosinophil count. (Table2.21)

Analyses included: Safety analysis subjects

Analysis content: The number of all subjects or subjects who continued for 52 weeks will be tabulated for the analysis subjects.

In addition, for the blood eosinophil count, the summary statistics will be calculated for the analysis studies according to the time of evaluation.

The above analyses will be performed in all subjects and in subjects who continue for 52 weeks.

Table2.21.1: all subjects

Table2.22.2:52 Weeks Continued

Time of evaluation: See 4.8.1 "Recruitment Data by Time of Evaluation of Blood Test Items"

### 6.7.2. IgE levels in subjects with and without prior omalizumab use. (Table2.22)

Analyses included: Safety analysis subjects

Analysis content: Calculate the number of subjects according to the history of omalizumab use.

We will also calculate a summary statistic for total serum IgE levels by history of omalizumab use.

Definitions : See 4.8.1 "Recruitment data of blood test items by assessment period" for collection of data on total serum IgE levels.

### 6.7.3. Percentage of use of oral corticosteroids for bronchial asthma (Table2.24)

Analyses included: Safety analysis subjects

Analysis content: The presence and proportion of oral corticosteroids used in prior and concomitant medications will be tabulated.

However, in the case of concomitant medications, the indication is bronchial asthma for indication.

The denominator of the proportion is the number of subjects included in the safety analysis.

Definition of oral corticosteroids: Drugs listed in "Determination of the dose of oral corticosteroids used in Appendix B and concomitant medications."

### 6.7.4. Asthmatic exacerbation (Table3.05)

Analyses included: Effectiveness analysis subjects

Analysis content: The summary statistics and the incidence proportion per person-year are calculated for the breakdown of the following bronchial asthma exacerbations according to the time of evaluation.

① Number of bronchial asthma exacerbations

② Bronchial asthma exacerbations requiring hospitalization (number of times)

③ Bronchial asthma exacerbations requiring emergency department (number of times)

④ Bronchial asthma exacerbations requiring systemic steroid use (number of episodes)

⑤ Bronchial asthma exacerbations requiring hospitalization (days in hospital)

<Incidence>

The incidence proportion per person-year (IR: Incidence Rate) is calculated.

IR is calculated according to the following formula.

IR per capita year = “number of times/days”/T x 1

Here, T is the total of the observation period of the subjects /364 (52 weeks are converted to 1 year).

Time of evaluation: 52 weeks prior to initiation of drug

52 weeks after initiation of drug treatment or until discontinuation

**6.7.5. ACT score (Table3.07, Figure 3.07.1 (Fig. 1_Boxplot)).**

Analyses included: Effectiveness analysis subjects

Analysis content: The number of all subjects or subjects who continued for 52 weeks will be tabulated for the analysis subjects.

In addition, for ACT of the studies included in the analysis, the summarized statistic will be calculated according to the assessment period, and a Boxplot will be prepared.

The above analyses will be performed in all subjects and in subjects who continue for 52 weeks.

However, the evaluation time to calculate the summary statistics is as follows for all subjects and for subjects who continue for 52 weeks.

All subjects:

- ACT scored (at the beginning of drug treatment)
- ACT scored (12 weeks after initiation of drug treatment)
- ACT scored (24 weeks after initiation of drug treatment)
- ACT scored (52 weeks after initiation of drug treatment)
- ACT scored (12 weeks after initiation of drug treatment-at the beginning of drug treatment) ≧3
- ACT scored (24 weeks after initiation of drug treatment-at the initiation of drug treatment) ≧3
- ACT scored (52 weeks after initiation of drug treatment-at the start of drug treatment) ≧3

52-week continuation case:

- ACT scored (at the beginning of drug treatment)
- ACT scored (12 weeks after initiation of drug treatment)
- ACT scored (24 weeks after initiation of drug treatment)
- ACT scored (52 weeks after initiation of drug treatment)
- ACT scored (12 weeks after initiation of drug treatment-at the beginning of drug treatment) ≧3
- ACT scored (24 weeks after initiation of drug treatment-at the initiation of drug treatment) ≧3
- ACT scored (52 weeks after initiation of drug treatment-at the start of drug treatment) ≧3

Table3.07.1, Figure3.07.1: all subjects

Table3.07.2, Figure3.07.2: 52 Weeks Continued

### 6.7.6. Respiratory function tests (Table3.08)

Analyses included: Effectiveness analysis subjects

Analysis content: Calculate respiratory function test values (PEF) and calculate the proportion of the corresponding number of subjects by assessment period for the analysis subjects.

The denominator of the ratio is the number of subjects for analysis.

In addition, summary statistics of respiratory function test values will be calculated by assessment period. The 25% and 75% points of the summary statistics are not calculated.

### 6.7.7. The three items defined as clinically remission (Table3.09)

Analyses included: Effectiveness analysis subjects

Analysis content: The number of subjects who met the following conditions and the number of subjects who did not meet the following conditions for subjects who continued for 52 weeks will be tabulated for the analysis subjects.

① Subjects who did not experience exacerbation after treatment among those who had progression events prior to drug treatment

② Subjects who did not require oral corticosteroids to treat bronchial asthma prior to drug administration after administration.

③ Among subjects with ACT scores before and after drug treatment, those with ACT scores of 20 points or more after treatment were 23 points

④ ①~ Subjects meeting all of the conditions in ③ (only relevant subjects were tabulated)

## 7. ChangeLog

| Date | Version | Author | Description |
|---|---|---|---|
| 16-Mar-2018 | 1.0 | PPD | First edition |
| 20-Aug-2018 | 2.0 | PPD | The following items were modified according to the standard analysis plan:<br>・2.2 Dictionary to be used: The description of the lexicon name of the disease name was modified in the description to be decided after the study by the team.<br>・4.2 Analysis set and sites: Representation of the definitions of contract sites, enrollment sites, enrollment subjects, safety analysis sites, safety analysis subjects, effectiveness analysis subjects, asthma exacerbation analysis subjects, respiratory function test analysis subjects, and ACT analysis subjects were modified.<br>・4.9.2 Subjects continued for 52 weeks, subjects discontinued/completed: Added definition.<br>・4.11.1 Definition of adverse events/adverse drug reactions: The expression of the definitions of adverse events and serious adverse drug events (serious adverse drug reactions) was modified.<br>・4.15.2.3 The inclusion data for the assessment period of the Asthma Control Test (ACT) were added to the specification for the absence of data entry in "Discontinuation/End of Treatment".<br>・5.4.4 The indicated digits of the statistic:<br>①Proportions, proportions: The number of indicated digits was modified from decimal 2 to 1.<br>②p-value: The contents without "*" were corrected.<br>・5.5 Sample code: Wilcoxon signed rank test with additional sample codes for estimation of confidence intervals of means.<br>・6. Main analysis items:<br>①It was decided to output forms other than villa 1 and villa 11.<br>②Appendix 2: The title of "Case composition" was changed, and "Site" or "Number" was deleted from the display items. The form number was changed to Figure 1.<br>③Appendix 3: The title was changed to "Case composition ratio". And, the investigation form fixation case was removed from the analysis object.<br>④Appendix 4: The title was changed to "List of Incidence of Adverse Drug Reactions by Patient Background". The number of subjects with adverse drug reactions (%) was modified to the proportion of adverse drug reactions.<br>⑤Appendix 5, Appendix 6, Appendix 7, and Appendix 8: Percentages were standardized.<br>⑥Appendix 10: The title was revised to "Time to onset by type of adverse reaction." In addition, the tabulation of the number of subjects was deleted.<br>⑦Specifications for the following forms were added: |

| Date | Version | Author | Description |
|---|---|---|---|
| | | | -Appendix 13<br>-Appendix 14<br>-Appendix 15<br>-Appendix 16 |
| 20-Feb-2019 | 3.0 | PPD | Changes in chapter composition were made in line with the updated standard analysis plan.<br>3. The following definitions were added or modified by terminology:<br>・Modification of the Definition of "Date of Completion of drug Administration"<br>・Addition of definition of last observation day<br>4.2. Modification of the definition of exclusion conditions was performed in the analysis set and institutions.<br>4.7. In the calculation of days and age, the following definitions were added or deleted:<br>・Deletion of "Total number of days administered"<br>・Addition of the definition of "total observation period"<br>6.3.2. The following specifications were modified in the time to onset of adverse drug reactions:<br>・Total number of days administered was changed to the total observation period.<br>The following specifications for the sort order of forms were changed.<br>・6.6.4. Number of subjects according to complication symptoms<br>・6.6.5. Number of subjects by prior drug<br>Changes to the analysis set and modifications to the analysis content were performed in the following specification of each form:<br>・6.7.1. Exacerbation of asthma (number of asthma episodes)<br>・6.7.2. Asthma exacerbations (days in hospital)<br>・6.7.3.ACT score<br>・6.7.4. Respiratory function test values<br>Specifications for the following items were added as a unique form.<br>・6.3.3 Total dose until onset of adverse reaction by type<br>・6.7.5. Summary statistics of blood eosinophil count<br>・6.7.6. IgE levels in subjects with and without prior omalizumab use. |
| 18-Sep-2019 | 4.0 | PPD | In order to ensure consistency with the standard analysis plans and EGPA surveys for the Seventh Periodic Safety Report, and to make more appropriate expressions, the tabulation classification was reviewed as described below, and the target population was changed.<br>4.8.1. In the inclusion data for each time point for haematology parameters, it was added that subjects who discontinued the study should be enrolled in the imputation condition "Week 52 after the initiation of drug treatment or at the time of discontinuation/completion."<br>In addition, the definition of "52 weeks after the initiation of drug treatment or at the time |

| Date | Version | Author | Description |
|---|---|---|---|
| | | | of discontinuation/completion" was modified for the inclusion of haematology parameters by assessment period.<br>4.8.2. In the inclusion data for each time point for the effectiveness endpoint, it was added that subjects who discontinued the study should be enrolled in "Week 52 after the initiation of drug treatment or at the time of discontinuation/completion." In addition,<br>Adoption data by time point for effectiveness endpoints: "Discontinuation/End of Treatment" was modified from "Adoption data for Asthma Control Test (ACT)"<br>6.2.1. Patient characteristics (Table1.01): Additional definition total days of treatment<br>6.3.2. Time to onset of adverse drug reactions (Table2.02): Modification of classification<br>6.6.5. Number of subjects (Table2.18) by drug prior to treatment: Deletion of the following items<br>• Number of investigated subjects used for calculation<br>• Mean daily dose<br>6.7.1. Summary statistic for blood eosinophil count (Table2.21): Change in analysis set<br>6.7.3. Asthma exacerbations (number of asthma episodes) (Table3.05): Changes in the specification of the analysis set<br>6.7.4. Asthmatic exacerbations (days in hospital) (Table3.06): Change in specification of the analysis set 6.7.5. ACT Score (Table3.07): Change in analysis set<br>6.7.6. Respiratory function tests (Table3.08): Change in analysis set and modification of analysis text |
| 13-Mar-2020 | 5.0 | PPD | The following specifications were modified to ensure consistency with the standard analysis plan and to make the expressions more appropriate.<br>4.3.1. Subjects excluded from safety analysis: Modified definitions outside the contract period<br>4.11. Safety Specification, Definition of Complications: Added "Definition of Complications" to the item name.<br>6.1.1. Case Composition (Figure1.01): Additional Aggregation of Institutions<br>6.3.2. Time to onset of adverse drug reactions (Table2.02): Additional time to onset of adverse drug reactions<br>6.3.7. Duration of drug treatment by reason for discontinuation of drug (Table2.23): Additional specification of the new form<br>6.6.5. Number of subjects (Table2.18) by prior medication:<br>"Product name" was revised to "drug name" |
| 11-Sep-2020 | 6.0 | PPD | The following specifications were modified to ensure consistency with the standard analysis plan and to investigate the effectiveness.<br>6.1.1. Case composition (Figure1.01): Additional specification of case composition |

| Date | Version | Author | Description |
|---|---|---|---|
| | | | on the follow-up form<br>Specifications for the following items were added as a unique form.<br>6.7.3. Percentage of oral corticosteroids used (Table2.24): Adding the specification of a new form<br>6.7.4. Daily dose of oral corticosteroids (Table2.25): Additional specification of the new form |
| 22-Apr-2021 | 7.0 | PPD | 4.7 Calculate of days and age: "Duration of treatment (days) added to the definition of period)<br>6.2.1 Patient characteristics (Table1.01): The total number of days of administration [days] was deleted because it was equivalent to the total number of doses [times], the number of days of administration [days] was added, and the total observation period [days] was added. |
| 31-May-2022 | 8.0 | PPD | 4.1 Number of subjects with adverse events (adverse drug reactions): Additional handling of adverse events during the observation period<br>4.2 Analysis set/site: Subjects included in the follow-up analysis and subjects included in ACT analysis were added.<br>4.7 Calculation of days and age: The calculation formula was added to the definition column for the time to onset of adverse drug reactions, and the term "total observation period" was changed to the observation period.<br>6.2.1 Patient characteristics: The blood eosinophil count category was changed according to the package insert category, and Table1.01.6 (the effectiveness proportion in subjects who discontinued treatment or had completed the reason) was added.<br>6.3.5 Adverse reaction/event status by safety considerations: The text was interrupted, so it was added.<br>6.7.4 Daily dose of oral corticosteroids with additional definition of mean dose<br>The following forms were added to check OCS use before and after drug administration<br>Use of Pretreatment and Concomitant Medications (OCS) for Table2.26 Bronchial Asthma.<br>6.7.8 Added ACT Score: Boxplot and Bar Graph Creation. Additional number of subjects items with a score-difference of 3 or more before and after drug administration were added. |
| 02-Sep-2022 | 9.0 | PPD | 4.1 Number of subjects with adverse events (adverse drug reactions): Additional reference for definition of observation period<br>4.2 Analysis set/site: Additional asthma exacerbation analysis set<br>4.5 Date of completion of administration at the time of continuation of administration: Modified formula for calculation of date of completion of administration<br>4.7 Calculation of days and age: Deletion of description for 1 year<br>4.12 Addition of handling of continuation/discontinuation/completion of administration, deletion of existing descriptions due to changes in handling |

| Date | Version | Author | Description |
|---|---|---|---|
| | | | 5.4 Test: To confirm the signal of influential factors rather than the significance test, the name and content of the title are adjusted to the standard.<br>6.6.7 Incidence of ADRs in items with significant differences: To confirm the signal of influential factors rather than the significance test, the name and description are adjusted to the standard.<br>6.7.3 Percentage of use of oral corticosteroids: The word "for bronchial asthma" was added at the head of the item name, and the handling of the totaling study in the combined use medicine was added to the analysis content.<br>6.7.4 Daily dose of oral corticosteroids: Since calculation of the mean dose was a definition that cannot be handled by data collected on the case report form, it was deleted<br>6.7.6 Exacerbation of asthma (number of asthma): the number of asthma exacerbations was added because three categories were established |
| 21-Sep-2023 | 10.0 | PPD | Change signer based on amendment of procedure manual<br>3. Defining the terms: "date of last dose of drug" is set as "date of completion of drug administration" and improved. Last observation day was deleted because it was used as the "End of observation day (week 52)"<br>4.5. Date of completion of administration at the time of continuation of administration: 4.11. Deletion of this item to use handling of continuation of administration/discontinuation of administration/completion<br>4.5. Handling of presence/absence: Additional<br>4.6. Number of days: Calculation of age. "Observation period of drug" was changed to "administration period of drug"<br>4.11. Handling of continuation/discontinuation/completion of administration: The term "drug treatment observation date" was changed to "observation date (52 weeks)". The calculation formula was partially modified in order to revise the calculation method for the observation date (week 52). Addition of the definition of "the follow-up date"<br>4.12. Handling of subjects with a change in administration purpose:<br>6.2.1. Patient characteristics: "Age 3 (years)" was added to Table1.01.1 for EMA Article46 response. Table1.01.6 Delete<br>6.3.1. List of adverse reactions by patient characteristics: Added 95% confidence interval output for the incidence proportion of adverse reactions based on the protocol<br>6.4.1. Effective proportion by patient background: The 95% confidence interval output of the effective proportion was added based on the description in the protocol.<br>6.5. List: Added Listing9 (list of subjects for identification of subjects with change in reason for use)<br>6.6.1. Correlation of factors: Review of exploratory variables, deletion of "Age 2 (years),"" |

| Date | Version | Author | Description |
|---|---|---|---|
| | | | "Reason for drug use," addition of "Smoking history" and "Blood eosinophil count (at the start of drug administration)"<br>6.7.5. Use of pre-treatment and concomitant medication for bronchial asthma: Results of reconsideration not required and deleted<br>6.7.4. Exacerbation of asthma: change from exacerbation of asthma (number of asthma) to exacerbation of asthma. The content of the analysis was modified or changed with reference to the specification of EGPA survey. "Exacerbation of asthma (number of days in hospital)" was also tabulated in this section.<br>6.7.7 Three items defined as clinical remission were added to the secondary study of clinical remission. |

## Appendix A : How to identify Appendix A adverse events

Adverse events used in the analysis of this survey will be identified as follows:

◆ Prerequisite

Assessment of malignancy will be performed by SMQ coding as described in "4.11 Definitions of Safety/Complications" in SAP.

Adverse events other than malignancy occurring during follow-up will not be included in the analysis.

◆ Adverse events to be assessed

The following adverse events occur.

- Adverse events occurring by the end day of observation (Week 52)
- Adverse events occurring during follow-up (malignancy only)

| Dates of onset of adverse events | ※1 of the end-of-observation date (52 weeks) | Tracking Starting Date ※1 | Follow-up Ending Date ※1 | Judgement | | |
|---|---|---|---|---|---|---|
| | | | | Conditions | Subjects | |
| | | | | | Other than malignancy | Malignant tumor |
| Yes ※2 | Yes | - | - | <= Day of onset, end of observation (Week 52) | Applicable | Applicable |
| | | Yes | Yes | Start date of follow-up <= onset date <= end date of follow-up | Not applicable | Applicable |
| | Unknown | - | - | All relevant events are included in the analysis | Applicable | Applicable |
| Unknown | - | - | - | All relevant events are included in the analysis | Applicable | Applicable |

※1. See "Handling of Continuation/Discontinuation/Completion of Treatment" in 4.11"

※2. If only "Day" is unknown, judge using the following procedure

However, when the year or month is unknown, the date is treated as "unknown"

① Extract the date and month of the decision condition

② Compare the date and month of each decision condition to determine whether the decision condition is met

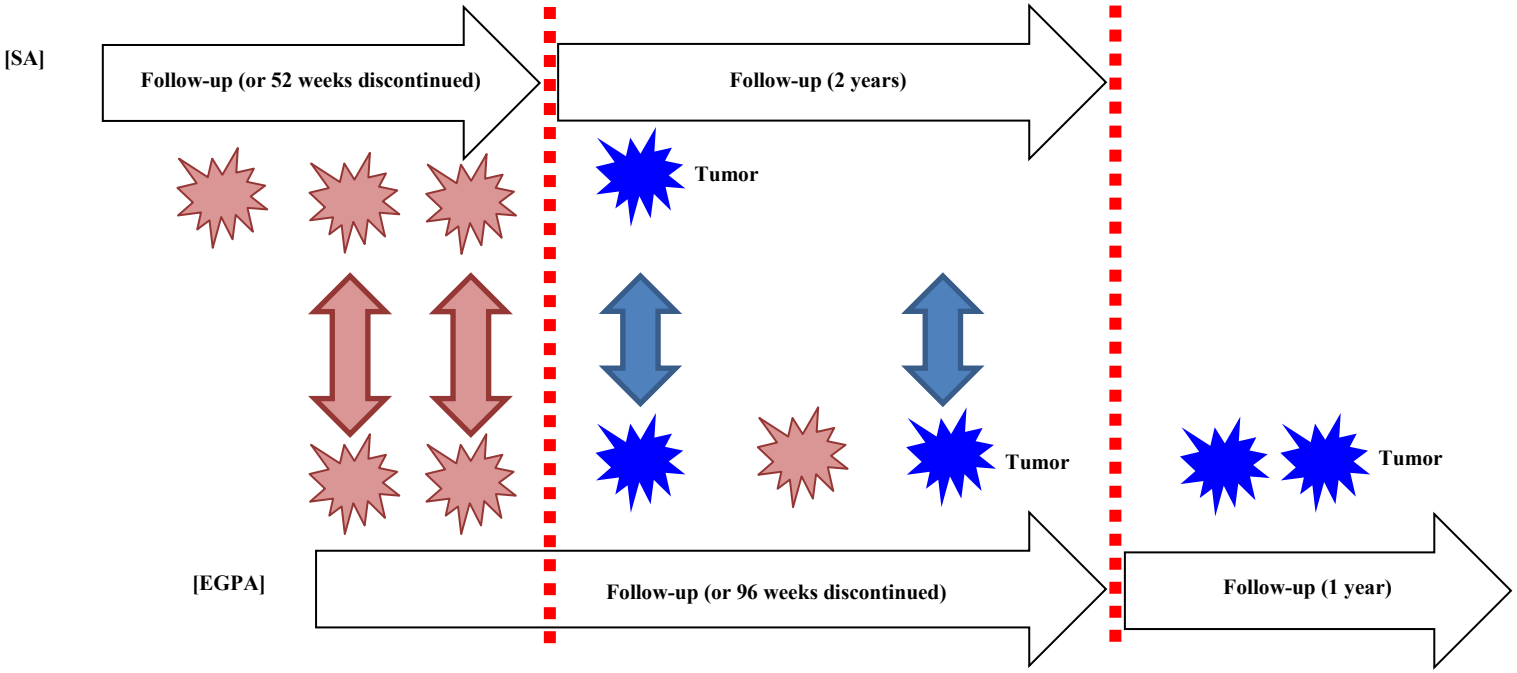
e.g., date of onset of adverse event, 2018/08; last observation day, 2018/11/20

① Day of onset of adverse event: 2018/08, last observation day: 2018/11

② Day of onset of adverse event (2018/08) < = last observation day (2018/11)

These adverse events will be included in the analysis.

Reference: Determination of adverse events of severe asthma (SA) and eosinophilic polyangiitis granulomatosis (EGPA)



**Appendix B : How to determine the dose of oral corticosteroids used in Appendix B treatment and concomitant medications**

Transform the unit of dose of oral corticosteroids as shown in the table below

List of unit transformations

| Classification of oral corticosteroids used in prior and concomitant medications | Units |
|---|---|
| Oral steroids | Mg |

*:Convert to prednisolone equivalent

List of coefficients of prednisolone equivalent

After converting to "μg" in units, calculate the dose by multiplying by the following factors.

| Generic name | Drug code (7 digits) | Product name | Clinical dose | Coefficient |
|---|---|---|---|---|
| Hydrocortisone | 2452002 | Cotolyl | 20 | 0.250 |
| Hydrocortisone Succinate | 2452400 | | 20 | 0.250 |
| Cortisone Acetate | 2452001 | Corton | 25 | 0.200 |
| Prednisone | | Unmarketed | 5 | 1.000 |
| Prednisolone | 2456002 | Predonine | 5 | 1.000 |
| Prednisolone succinate | 2456406 | | 5 | 1.000 |
| Methylprednisolone | 2456003 | Medrol | 4 | 1.250 |
| Methylprednisolone Succinate | 2456400 | | 4 | 1.250 |
| Triamcinolone | 2454003 | Redacoat | 4 | 1.250 |
| Triamcinolone acetonide | 2454402 | | 4 | 1.250 |
| Dexamethasone | 2454002 | Decadron | 0.75 | 6.667 |
| Dexamethasone phosphate | 2454405 | | 0.75 | 6.667 |
| Parametasone acetate | 2454001 | Parametasone | 2 | 2.500 |
| Betamethasone | 2454004 | Rinderon | 0.75 | 6.667 |
| Betamethasone phosphate | 2454005 | | 0.75 | 6.667 |