**TABLE, SUPPLEMENTAL DIGITAL CONTENT 1.** Incidence of Ocular and Nonocular TEAEs: Safety Population

| **System Organ Class Preferred Term, n (%)** | **Placebo****n = 111** | **Lifitegrast****n = 220** | **All Participants****n = 331** |
| --- | --- | --- | --- |
| **Participants with ≥1 ocular TEAE** | 38 (34.2) | 118 (53.6) | 156 (47.1) |
| Eye disorders | 33 (29.7) | 82 (37.3) | 115 (34.7) |
| Visual acuity reduced | 7 (6.3) | 25 (11.4) | 32 (9.7) |
| Vision blurred | 4 (3.6) | 9 (4.1) | 13 (3.9) |
| Conjunctival hyperemia | 4 (3.6) | 6 (2.7) | 10 (3.0) |
| Dry eye | 6 (5.4) | 4 (1.8%) | 10 (3.0) |
| Eye pruritus | 2 (1.8) | 8 (3.6) | 10 (3.0) |
| Lacrimation increased | 2 (1.8) | 8 (3.6) | 10 (3.0) |
| Eye irritation | 1 (0.9) | 8 (3.6) | 9 (2.7) |
| Eye pain | 0 | 7 (3.2%) | 7 (2.1) |
| Eye discharge | 1 (0.9) | 4 (1.8) | 5 (1.5) |
| Ocular hyperemia | 0 | 4 (1.8) | 4 (1.2) |
| Cataract | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Chalazion | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Conjunctival cyst | 2 (1.8) | 1 (0.5) | 3 (0.9) |
| Corneal erosion | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Eyelid Edema | 2 (1.8) | 1 (0.5) | 3 (0.9) |
| Vitreous detachment | 0 | 3 (1.4) | 3 (0.9) |
| Blepharitis | 0 | 2 (0.9) | 2 (0.6) |
| Cataract nuclear | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Cataract subcapsular | 0 | 2 (0.9) | 2 (0.6) |
| Conjunctival hemorrhage | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Conjunctivitis | 2 (1.8) | 0 | 2 (0.6) |
| Conjunctivitis allergic | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Dacryostenosis acquired | 2 (1.8) | 0 | 2 (0.6) |
| Foreign body sensation in eyes | 0 | 2 (0.9) | 2 (0.6) |
| Meibomian gland dysfunction | 1 (0.9) | 1 (0.5) | 2 (0.6%) |
| Punctate keratitis | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Abnormal sensation in eye | 0 | 1 (0.5) | 1 (0.3) |
| Amaurosis | 1 (0.9) | 0 | 1 (0.3) |
| Blepharal papilloma | 0 | 1 (0.5) | 1 (0.3) |
| Conjunctival primary acquired melanosis | 0 | 1 (0.5) | 1 (0.3) |
| Corneal dystrophy | 0 | 1 (0.5) | 1 (0.3) |
| Corneal endothelial cell loss | 0 | 1 (0.5) | 1 (0.3) |
| Dellen | 0 | 1 (0.5) | 1 (0.3) |
| Erythema of eyelid | 1 (0.9) | 0 | 1 (0.3) |
| Eyelid margin crusting | 1 (0.9) | 0 | 1 (0.3) |
| Eyelid pain | 0 | 1 (0.5) | 1 (0.3) |
| Glaucoma | 0 | 1 (0.5) | 1 (0.3) |
| Halo vision | 0 | 1 (0.5) | 1 (0.3) |
| Hordeolum | 1 (0.9) | 0 | 1 (0.3) |
| IVth nerve paralysis | 1 (0.9) | 0 | 1 (0.3) |
| Keratitis | 0 | 1 (0.5) | 1 (0.3) |
| Lenticular opacities | 1 (0.9) | 0 | 1 (0.3) |
| Metamorphopsia | 0 | 1 (0.5) | 1 (0.3) |
| Photophobia | 0 | 1 (0.5) | 1 (0.3) |
| Presbyopia | 1 (0.9) | 0 | 1 (0.3) |
| Vitreous floaters | 1 (0.9) | 0 | 1 (0.3) |
| General disorders and administration site conditions | 7 (6.3) | 51 (23.2) | 58 (17.5) |
| Instillation site irritation | 5 (4.5) | 33 (15.0) | 38 (11.5) |
| Instillation site reaction | 2 (1.8) | 29 (13.2) | 31 (9.4) |
| Instillation site pain | 2 (1.8) | 7 (3.2) | 9 (2.7) |
| Instillation site foreign body sensation | 0 | 6 (2.7) | 6 (1.8) |
| Instillation site pruritus | 1 (0.9) | 5 (2.3) | 6 (1.8) |
| Instillation site lacrimation | 1 (0.9) | 3 (1.4) | 4 (1.2) |
| Instillation site discomfort | 0 | 1 (0.5) | 1 (0.3) |
| Immune system disorders | 0 | 3 (1.4) | 3 (0.9) |
| Seasonal allergy | 0 | 3 (1.4) | 3 (0.9) |
| Infections and infestations | 0 | 2 (0.9) | 2 (0.6) |
| Conjunctivitis bacterial | 0 | 1 (0.5) | 1 (0.3) |
| Dacryocystitis | 0 | 1 (0.5) | 1 (0.3) |
| Injury, poisoning, and procedural complications | 0 | 2 (0.9) | 2 (0.6) |
| Corneal abrasion | 0 | 2 (0.9) | 2 (0.6) |
| Nervous system disorders | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Migraine with aura | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Skin and subcutaneous tissue disorders | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Actinic keratosis | 1 (0.9) | 0 | 1 (0.3) |
| Skin fissures | 0 | 1 (0.5) | 1 (0.3) |
| Endocrine disorders | 1 (0.9) | 0 | 1 (0.3) |
| Diabetic retinopathy | 1 (0.9) | 0 | 1 (0.3) |
| Investigations | 0 | 1 (0.5) | 1 (0.3) |
| Visual acuity tests abnormal | 0 | 1 (0.5) | 1 (0.3) |
| **Participants with ≥1 nonocular TEAE** | 40 (36.0) | 104 (47.3) | 144 (43.5) |
| Nervous system disorders | 5 (4.5) | 49 (22.3) | 54 (16.3) |
| Dysgeusia | 2 (1.8) | 36 (16.4) | 38 (11.5) |
| Headache | 0 | 9 (4.1) | 9 (2.7) |
| Restless legs syndrome | 0 | 3 (1.4) | 3 (0.9) |
| Neuropathy peripheral | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Cerebral atrophy | 0 | 1 (0.5) | 1 (0.3) |
| Dizziness | 1 (0.9) | 0 | 1 (0.3) |
| Hypoesthesia | 0 | 1 (0.5) | 1 (0.3) |
| Insomnia | 0 | 1 (0.5) | 1 (0.3) |
| Nerve compression | 0 | 1 (0.5) | 1 (0.3) |
| Neuralgia | 0 | 1 (0.5) | 1 (0.3) |
| Paresthesia | 0 | 1 (0.5) | 1 (0.3) |
| Sinus headache | 0 | 1 (0.5) | 1 (0.3) |
| Syncope | 0 | 1 (0.5) | 1 (0.3) |
| Tremor | 1 (0.9) | 0 | 1 (0.3) |
| Infections and infestations | 17 (15.3) | 28 (12.7) | 45 (13.6) |
| Sinusitis | 2 (1.8) | 7 (3.2) | 9 (2.7) |
| Nasopharyngitis | 2 (1.8) | 6 (2.7) | 8 (2.4) |
| Urinary tract infection | 3 (2.7) | 4 (1.8) | 7 (2.1) |
| Upper respiratory tract infection | 2 (1.8) | 3 (1.4) | 5 (1.5) |
| Influenza | 2 (1.8) | 2 (0.9) | 4 (1.2) |
| Bronchitis | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Pneumonia | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Ear infection | 0 | 2 (0.9) | 2 (0.6) |
| Laryngitis | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Cystitis | 1 (0.9) | 0 | 1 (0.3) |
| Diverticulitis | 0 | 1 (0.5) | 1 (0.3) |
| Kidney infection | 0 | 1 (0.5) | 1 (0.3) |
| Prostate infection | 0 | 1 (0.5) | 1 (0.3) |
| Rhinitis | 0 | 1 (0.5) | 1 (0.3) |
| Rhinovirus infection | 1 (0.9) | 0 | 1 (0.3) |
| Sialadenitis | 0 | 1 (0.5) | 1 (0.3) |
| Skin bacterial infection | 0 | 1 (0.5) | 1 (0.3) |
| Skin infection | 1 (0.9) | 0 | 1 (0.3) |
| Staphylococcal skin infection | 0 | 1 (0.5) | 1 (0.3) |
| Musculoskeletal and connective tissue disorders | 11 (9.9) | 17 (7.7) | 28 (8.5) |
| Arthralgia | 0 | 5 (2.3) | 5 (1.5) |
| Osteoarthritis | 2 (1.8) | 3 (1.4) | 5 (1.5) |
| Back pain | 2 (1.8) | 2 (0.9) | 4 (1.2) |
| Intervertebral disc protrusion | 1 (0.9) | 3 (1.4) | 4 (1.2) |
| Arthritis | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Intervertebral disc degeneration | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Neck pain | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Pain in extremity | 0 | 2 (0.9) | 2 (0.6) |
| Rheumatoid arthritis | 0 | 2 (0.9) | 2 (0.6) |
| Fibromyalgia | 0 | 1 (0.5) | 1 (0.3) |
| Muscle spasms | 1 (0.9) | 0 | 1 (0.3) |
| Muscular weakness | 0 | 1 (0.5) | 1 (0.3) |
| Rotator cuff syndrome | 0 | 1 (0.5) | 1 (0.3) |
| Sjögren's syndrome | 1 (0.9) | 0 | 1 (0.3) |
| Spinal column stenosis | 0 | 1 (0.5) | 1 (0.3) |
| Synovial cyst | 1 (0.9) | 0 | 1 (0.3) |
| Respiratory, thoracic, and mediastinal disorders | 6 (5.4) | 16 (7.3) | 22 (6.6) |
| Chronic obstructive pulmonary disease | 2 (1.8) | 2 (0.9) | 4 (1.2) |
| Asthma | 0 | 3 (1.4) | 3 (0.9) |
| Cough | 3 (2.7) | 0 | 3 (0.9) |
| Dyspnea | 0 | 3 (1.4) | 3 (0.9) |
| Oropharyngeal pain | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Sinus congestion | 0 | 3 (1.4) | 3 (0.9) |
| Nasal congestion | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Rhinorrhea | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Upper airway cough syndrome | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Epistaxis | 1 (0.9) | 0 | 1 (0.3) |
| Pulmonary fibrosis | 0 | 1 (0.5) | 1 (0.3) |
| Rhinitis allergic | 1 (0.9) | 0 | 1 (0.3) |
| Sinus disorder | 0 | 1 (0.5) | 1 (0.3) |
| Upper respiratory tract congestion | 0 | 1 (0.5) | 1 (0.3) |
| Gastrointestinal disorders | 5 (4.5) | 11 (5.0) | 16 (4.8) |
| Gastroesophageal reflux disease | 0 | 3 (1.4) | 3 (0.9) |
| Abdominal discomfort | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Dry mouth | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Abdominal pain | 1 (0.9) | 0 | 1 (0.3) |
| Diarrhea | 0 | 1 (0.5) | 1 (0.3) |
| Diverticulum | 1 (0.9) | 0 | 1 (0.3) |
| Diverticulum intestinal | 0 | 1 (0.5) | 1 (0.3) |
| Gingivitis | 1 (0.9) | 0 | 1 (0.3) |
| Irritable bowel syndrome | 0 | 1 (0.5) | 1 (0.3) |
| Nausea | 0 | 1 (0.5) | 1 (0.3) |
| Esophageal irritation | 0 | 1 (0.5) | 1 (0.3) |
| Tooth disorder | 1 (0.9) | 0 | 1 (0.3) |
| Umbilical hernia | 1 (0.9) | 0 | 1 (0.3) |
| Vomiting | 0 | 1 (0.5) | 1 (0.3) |
| Injury, poisoning, and procedural complications | 5 (4.5) | 6 (2.7) | 11 (3.3) |
| Contusion | 2 (1.8) | 1 (0.5) | 3 (0.9) |
| Rib fracture | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Animal bite | 0 | 1 (0.5) | 1 (0.3) |
| Animal scratch | 0 | 1 (0.5) | 1 (0.3) |
| Arthropod bite | 1 (0.9) | 0 | 1 (0.3) |
| Foot fracture | 0 | 1 (0.5) | 1 (0.3) |
| Hand fracture | 0 | 1 (0.5) | 1 (0.3) |
| Hip fracture | 0 | 1 (0.5) | 1 (0.3) |
| Joint injury | 0 | 1 (0.5) | 1 (0.3) |
| Ligament rupture | 1 (0.9) | 0 | 1 (0.3) |
| Limb crushing injury | 0 | 1 (0.5) | 1 (0.3) |
| Muscle rupture | 1 (0.9) | 0 | 1 (0.3) |
| Spinal fracture | 1 (0.9) | 0 | 1 (0.3) |
| Wrist fracture | 0 | 1 (0.5) | 1 (0.3) |
| General disorders and administration site conditions | 4 (3.6) | 5 (2.3) | 9 (2.7) |
| Edema peripheral | 2 (1.8) | 1 (0.5) | 3 (0.9) |
| Procedural pain | 0 | 2 (0.9) | 2 (0.6) |
| Chest pain | 1 (0.9) | 0 | 1 (0.3) |
| Chills | 1 (0.9) | 0 | 1 (0.3) |
| Facial pain | 0 | 1 (0.5) | 1 (0.3) |
| Influenza-like illness | 0 | 1 (0.5) | 1 (0.3) |
| Pain | 1 (0.9) | 0 | 1 (0.3) |
| Immune system disorders | 4 (3.6) | 4 (1.8) | 8 (2.4) |
| Seasonal allergy | 2 (1.8) | 3 (1.4) | 5 (1.5) |
| Drug hypersensitivity | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Hypersensitivity | 1 (0.9) | 0 | 1 (0.3) |
| Skin and subcutaneous tissue disorders | 2 (1.8) | 6 (2.7) | 8 (2.4) |
| Rash | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Dermatitis contact | 0 | 2 (0.9) | 2 (0.6) |
| Basal cell carcinoma | 1 (0.9) | 0 | 1 (0.3) |
| Dermatitis | 0 | 1 (0.5) | 1 (0.3) |
| Skin Irritation | 0 | 1 (0.5) | 1 (0.3) |
| Investigations | 4 (3.6) | 3 (1.4) | 7 (2.1) |
| Blood pressure increased | 1 (0.9) | 0 | 1 (0.3) |
| *Helicobacter* test | 1 (0.9) | 0 | 1 (0.3) |
| Occult blood | 0 | 1 (0.5) | 1 (0.3) |
| Esophagogastroduodenoscopy | 0 | 1 (0.5) | 1 (0.3) |
| Pancreatic enzymes increased | 1 (0.9) | 0 | 1 (0.3) |
| Red blood cell count decreased | 1 (0.9) | 0 | 1 (0.3) |
| White blood cell count increased | 0 | 1 (0.5) | 1 (0.3) |
| Metabolism and nutrition disorders | 3 (2.7) | 4 (1.8) | 7 (2.1) |
| Diabetes mellitus | 2 (1.8) | 0 | 2 (0.6) |
| Abnormal loss of weight | 0 | 1 (0.5) | 1 (0.3) |
| Dehydration | 0 | 1 (0.5) | 1 (0.3) |
| Hypercholesterolemia | 0 | 1 (0.5) | 1 (0.3) |
| Hyperlipidemia | 0 | 1 (0.5) | 1 (0.3) |
| Hyponatremia | 1 (0.9) | 0 | 1 (0.3) |
| Overweight | 0 | 1 (0.5) | 1 (0.3) |
| Psychiatric disorders | 1 (0.9) | 6 (2.7) | 7 (2.1) |
| Depression | 1 (0.9) | 4 (1.8) | 5 (1.5) |
| Anxiety | 0 | 1 (0.5) | 1 (0.3) |
| Conversion disorder | 0 | 1 (0.5) | 1 (0.3) |
| Cardiac disorders | 2 (1.8) | 3 (1.4) | 5 (1.5) |
| Arrhythmia | 1 (0.9) | 0 | 1 (0.3) |
| Atrioventricular block | 0 | 1 (0.5) | 1 (0.3) |
| Bundle branch block right | 0 | 1 (0.5) | 1 (0.3) |
| Myocardial infarction | 0 | 1 (0.5) | 1 (0.3) |
| Tachycardia | 1 (0.9) | 0 | 1 (0.3) |
| Vascular disorders | 0 | 5 (2.3) | 5 (1.5) |
| Aortic calcification | 0 | 1 (0.5) | 1 (0.3) |
| Hypertension | 0 | 1 (0.5) | 1 (0.3) |
| Phlebitis superficial | 0 | 1 (0.5) | 1 (0.3) |
| Thrombosis | 0 | 1 (0.5) | 1 (0.3) |
| Transient ischemic attack | 0 | 1 (0.5) | 1 (0.3) |
| Neoplasms benign, malignant, and unspecified (including cysts and polyps) | 2 (1.8) | 2 (0.9) | 4 (1.2) |
| Benign breast neoplasm | 1 (0.9) | 0 | 1 (0.3) |
| Colonic polyp | 0 | 1 (0.5) | 1 (0.3) |
| Cyst | 1 (0.9) | 0 | 1 (0.3) |
| Metastases to peritoneum | 0 | 1 (0.5) | 1 (0.3) |
| Renal and urinary disorders | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Nephrolithiasis | 0 | 1 (0.5) | 1 (0.3) |
| Urinary incontinence | 1 (0.9) | 0 | 1 (0.3) |
| Urine flow decreased | 0 | 1 (0.5) | 1 (0.3) |
| Reproductive system and breast disorders | 1 (0.9) | 2 (0.9) | 3 (0.9) |
| Dysmenorrhea | 0 | 1 (0.5) | 1 (0.3) |
| Endometrial hypertrophy | 1 (0.9) | 0 | 1 (0.3) |
| Menorrhagia | 0 | 1 (0.5) | 1 (0.3) |
| Ovarian cyst | 0 | 1 (0.5) | 1 (0.3) |
| Ear and labyrinth disorders | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Vertigo | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Hepatobiliary disorders | 1 (0.9) | 1 (0.5) | 2 (0.6) |
| Cholelithiasis | 0 | 1 (0.5) | 1 (0.3) |
| Hepatitis | 1 (0.9) | 0 | 1 (0.3) |
| Surgical and medical procedures | 0 | 2 (0.9) | 2 (0.6) |
| Breast reconstruction | 0 | 1 (0.5) | 1 (0.3) |
| Carpal tunnel decompression | 0 | 1 (0.5) | 1 (0.3) |
| Blood and lymphatic system disorders | 0 | 1 (0.5) | 1 (0.3) |
| Splenic calcification | 0 | 1 (0.5) | 1 (0.3) |
| Endocrine disorders | 0 | 1 (0.5) | 1 (0.3) |
| Hypothyroidism | 0 | 1 (0.5) | 1 (0.3) |

Percentages are based on the number of participants in the safety population.

Adverse events are classified into System Organ Class and Preferred Term using version 14.1 of Medical Dictionary for Regulatory Activities.

TEAEs were defined as adverse events that occurred after the start of randomized treatment.

TEAE, treatment-emergent adverse event.