

**Adverse Events by System Organ Class and Preferred Term  
(Safety Analysis Set)**

| <b>System Organ Class<br/>Preferred Term</b> | <b>Placebo<br/>(N=86)</b> | <b>Xanomeline Low<br/>Dose<br/>(N=84)</b> | <b>Xanomeline High<br/>Dose<br/>(N=84)</b> |
|--|---------------------------|---|--|
| Participants in population                   | 86                        | 84  | 84   |
| Cardiac Disorders                            |                           |   |  |
| Atrial Fibrillation                          | 1                         | 1   | 3  |
| Atrial Flutter                               | 0                         | 1   | 1  |
| Atrial Hypertrophy                           | 1                         | 0   | 0  |
| Atrioventricular Block First Degree          | 1                         | 1   | 0  |
| Atrioventricular Block Second Degree         | 2                         | 0   | 3  |
| Bradycardia                                  | 1                         | 0   | 0  |
| Bundle Branch Block Left                     | 1                         | 0   | 0  |
| Bundle Branch Block Right                    | 1                         | 1   | 0  |
| Cardiac Disorder                             | 0                         | 0   | 1  |
| Cardiac Failure Congestive                   | 1                         | 0   | 0  |
| Myocardial Infarction                        | 4                         | 2   | 4  |
| Palpitations                                 | 0                         | 2   | 0  |
| Sinus Arrhythmia                             | 1                         | 0   | 0  |
| Sinus Bradycardia                            | 2                         | 7   | 8  |
| Supraventricular Extrasystoles               | 1                         | 1   | 1  |
| Supraventricular Tachycardia                 | 0                         | 1   | 0  |
| Tachycardia                                  | 1                         | 0   | 0  |
| Ventricular Extrasystoles                    | 0                         | 2   | 1  |
| Ventricular Hypertrophy                      | 1                         | 0   | 0  |
| Wolff-Parkinson-White Syndrome               | 0                         | 1   | 0  |
| Congenital, Familial And Genetic Disorders   |                           |   |  |
| Ventricular Septal Defect                    | 0                         | 1   | 2  |
| Ear And Labyrinth Disorders                  |                           |   |  |
| Cerumen Impaction                            | 0                         | 1   | 0  |
| Ear Pain                                     | 1                         | 0   | 0  |
| Tinnitus                                     | 0                         | 1   | 0  |
| Vertigo                                      | 0                         | 1   | 1  |
| Eye Disorders                                |                           |   |  |
| Conjunctival Haemorrhage                     | 0                         | 1   | 0  |
| Conjunctivitis                               | 2                         | 0   | 0  |
| Eye Allergy                                  | 1                         | 0   | 0  |
| Eye Pruritus                                 | 1                         | 0   | 0  |
| Eye Swelling                                 | 1                         | 0   | 0  |
| Glaucoma                                     | 1                         | 0   | 0  |

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|--|---------------------------|---|--|
| Vision Blurred                                       | 0                         | 1   | 1  |
| Gastrointestinal Disorders                           |                           |   |  |
| Abdominal Discomfort                                 | 0                         | 0   | 1  |
| Abdominal Pain                                       | 1                         | 3   | 1  |
| Constipation   | 1                         | 0   | 0  |
| Diarrhoea  | 9                         | 5   | 4  |
| Dyspepsia  | 1                         | 1   | 1  |
| Dysphagia  | 0                         | 1   | 0  |
| Flatulence   | 1                         | 0   | 0  |
| Gastrointestinal Haemorrhage                         | 0                         | 0   | 1  |
| Gastrooesophageal Reflux Disease                     | 1                         | 0   | 0  |
| Glossitis  | 1                         | 0   | 0  |
| Hiatus Hernia  | 1                         | 0   | 0  |
| Nausea   | 3                         | 3   | 6  |
| Rectal Haemorrhage                                   | 0                         | 1   | 0  |
| Salivary Hypersecretion                              | 0                         | 0   | 4  |
| Stomach Discomfort                                   | 0                         | 0   | 1  |
| Vomiting   | 3                         | 3   | 7  |
| General Disorders And Administration Site Conditions |                           |   |  |
| Application Site Bleeding                            | 0                         | 1   | 0  |
| Application Site Dermatitis                          | 5                         | 9   | 7  |
| Application Site Desquamation                        | 0                         | 1   | 0  |
| Application Site Discharge                           | 0                         | 0   | 1  |
| Application Site Discolouration                      | 0                         | 1   | 0  |
| Application Site Erythema                            | 3                         | 12  | 15   |
| Application Site Induration                          | 1                         | 0   | 0  |
| Application Site Irritation                          | 3                         | 9   | 9  |
| Application Site Pain                                | 0                         | 0   | 2  |
| Application Site Perspiration                        | 0                         | 0   | 2  |
| Application Site Pruritus                            | 6                         | 22  | 22   |
| Application Site Reaction                            | 1                         | 0   | 1  |
| Application Site Swelling                            | 0                         | 1   | 2  |
| Application Site Urticaria                           | 0                         | 2   | 1  |
| Application Site Vesicles                            | 1                         | 4   | 6  |
| Application Site Warmth                              | 0                         | 1   | 0  |
| Asthenia   | 1                         | 0   | 1  |
| Chest Discomfort                                     | 0                         | 0   | 2  |

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|--|---------------------------|---|--|
|  |                           |   |  |
| Chest Pain                                   | 0                         | 0   | 2  |
| Chills                                       | 1                         | 1   | 1  |
| Cyst   | 0                         | 1   | 0  |
| Fatigue                                      | 1                         | 5   | 5  |
| Feeling Abnormal                             | 0                         | 0   | 1  |
| Feeling Cold                                 | 0                         | 0   | 1  |
| Inflammation                                 | 0                         | 1   | 0  |
| Malaise                                      | 0                         | 1   | 2  |
| Oedema                                       | 0                         | 2   | 0  |
| Oedema Peripheral                            | 2                         | 1   | 2  |
| Pain   | 0                         | 1   | 1  |
| Pyrexia                                      | 2                         | 0   | 1  |
| Secretion Discharge                          | 0                         | 1   | 0  |
| Sudden Death                                 | 0                         | 1   | 0  |
| Swelling                                     | 0                         | 1   | 0  |
| Ulcer  | 0                         | 1   | 0  |
| Hepatobiliary Disorders                      |                           |   |  |
| Hyperbilirubinaemia                          | 1                         | 0   | 0  |
| Immune System Disorders                      |                           |   |  |
| Hypersensitivity                             | 0                         | 1   | 0  |
| Seasonal Allergy                             | 0                         | 0   | 1  |
| Infections And Infestations                  |                           |   |  |
| Bronchitis                                   | 1                         | 0   | 0  |
| Cellulitis                                   | 0                         | 1   | 0  |
| Cervicitis                                   | 1                         | 0   | 0  |
| Cystitis                                     | 1                         | 0   | 1  |
| Ear Infection                                | 2                         | 0   | 0  |
| Gastroenteritis Viral                        | 1                         | 0   | 0  |
| Hordeolum                                    | 0                         | 0   | 1  |
| Influenza                                    | 1                         | 1   | 1  |
| Localised Infection                          | 1                         | 1   | 0  |
| Lower Respiratory Tract Infection            | 0                         | 0   | 1  |
| Nasopharyngitis                              | 2                         | 4   | 6  |
| Onychomycosis                                | 0                         | 1   | 0  |
| Pneumonia                                    | 0                         | 1   | 0  |
| Rhinitis                                     | 0                         | 0   | 1  |
| Upper Respiratory Tract Infection            | 6                         | 1   | 3  |

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|--|---------------------------|---|--|
| Urinary Tract Infection                        | 2                         | 0   | 1  |
| Vaginal Mycosis                                | 1                         | 0   | 0  |
| Viral Infection                                | 0                         | 1   | 0  |
| Injury, Poisoning And Procedural Complications |                           |   |  |
| Contusion                                      | 1                         | 1   | 2  |
| Excoriation                                    | 2                         | 1   | 1  |
| Facial Bones Fracture                          | 0                         | 0   | 1  |
| Fall   | 1                         | 2   | 1  |
| Hip Fracture                                   | 1                         | 0   | 2  |
| Joint Dislocation                              | 0                         | 1   | 0  |
| Skin Laceration                                | 1                         | 2   | 0  |
| Wound  | 0                         | 1   | 0  |
| Investigations                                 |                           |   |  |
| Biopsy   | 0                         | 0   | 1  |
| Biopsy Prostate                                | 0                         | 0   | 1  |
| Blood Alkaline Phosphatase Increased           | 1                         | 0   | 0  |
| Blood Cholesterol Increased                    | 0                         | 0   | 1  |
| Blood Creatine Phosphokinase Increased         | 1                         | 0   | 0  |
| Blood Glucose Increased                        | 0                         | 1   | 1  |
| Blood Urine Present                            | 1                         | 0   | 0  |
| Body Temperature Increased                     | 0                         | 1   | 0  |
| Cystoscopy                                     | 1                         | 0   | 0  |
| Electrocardiogram St Segment Depression        | 4                         | 1   | 0  |
| Electrocardiogram T Wave Amplitude Decreased   | 1                         | 1   | 0  |
| Electrocardiogram T Wave Inversion             | 2                         | 1   | 1  |
| Heart Rate Increased                           | 1                         | 0   | 0  |
| Heart Rate Irregular                           | 1                         | 0   | 0  |
| Nasal Mucosa Biopsy                            | 0                         | 1   | 0  |
| Neutrophil Count Increased                     | 0                         | 1   | 0  |
| Urine Analysis Abnormal                        | 0                         | 1   | 0  |
| Weight Decreased                               | 0                         | 0   | 1  |
| White Blood Cell Count Increased               | 0                         | 1   | 0  |
| Metabolism And Nutrition Disorders             |                           |   |  |
| Decreased Appetite                             | 1                         | 0   | 1  |
| Dehydration                                    | 1                         | 0   | 0  |
| Diabetes Mellitus                              | 1                         | 0   | 0  |
| Food Craving                                   | 1                         | 1   | 0  |

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|---|---------------------------|---|--|
| Hypercholesterolaemia   | 0                         | 0   | 1  |
| Hyponatraemia   | 1                         | 0   | 0  |
| Increased Appetite  | 1                         | 0   | 1  |
| Musculoskeletal And Connective Tissue Disorders                     |                           |   |  |
| Arthralgia  | 1                         | 2   | 1  |
| Arthritis   | 1                         | 0   | 1  |
| Back Pain   | 1                         | 1   | 3  |
| Flank Pain  | 0                         | 0   | 2  |
| Muscle Spasms   | 0                         | 1   | 1  |
| Muscular Weakness   | 0                         | 1   | 0  |
| Myalgia   | 0                         | 0   | 1  |
| Pain In Extremity   | 1                         | 0   | 0  |
| Shoulder Pain   | 1                         | 2   | 0  |
| Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps) |                           |   |  |
| Colon Cancer  | 0                         | 1   | 0  |
| Malignant Fibrous Histiocytoma                                      | 0                         | 1   | 0  |
| Prostate Cancer   | 0                         | 0   | 1  |
| Nervous System Disorders  |                           |   |  |
| Amnesia   | 0                         | 0   | 1  |
| Balance Disorder  | 0                         | 1   | 0  |
| Burning Sensation   | 0                         | 0   | 2  |
| Cognitive Disorder  | 0                         | 0   | 1  |
| Complex Partial Seizures  | 0                         | 1   | 0  |
| Coordination Abnormal   | 0                         | 1   | 0  |
| Dizziness   | 2                         | 8   | 12   |
| Headache  | 7                         | 3   | 6  |
| Hemianopia Homonymous   | 0                         | 1   | 0  |
| Hypersomnia   | 0                         | 0   | 1  |
| Lethargy  | 0                         | 1   | 1  |
| Paraesthesia  | 0                         | 0   | 1  |
| Paraesthesia Oral   | 0                         | 1   | 0  |
| Parkinson'S Disease   | 1                         | 0   | 0  |
| Parosmia  | 0                         | 0   | 1  |
| Partial Seizures With Secondary Generalisation                      | 0                         | 0   | 1  |
| Psychomotor Hyperactivity   | 1                         | 0   | 0  |
| Somnolence  | 2                         | 3   | 1  |

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|---|---------------------------|---|--|
| Stupor  | 0                         | 1   | 0  |
| Syncope   | 0                         | 4   | 3  |
| Syncope Vasovagal                               | 0                         | 0   | 1  |
| Transient Ischaemic Attack                      | 0                         | 2   | 1  |
| Psychiatric Disorders                           |                           |   |  |
| Agitation                                       | 2                         | 2   | 1  |
| Anxiety   | 1                         | 3   | 0  |
| Completed Suicide                               | 1                         | 0   | 0  |
| Confusional State                               | 2                         | 3   | 1  |
| Delirium  | 0                         | 0   | 1  |
| Delusion  | 1                         | 0   | 1  |
| Depressed Mood                                  | 0                         | 1   | 1  |
| Disorientation                                  | 1                         | 0   | 0  |
| Hallucination                                   | 0                         | 0   | 1  |
| Hallucination, Visual                           | 0                         | 0   | 1  |
| Insomnia  | 2                         | 0   | 2  |
| Irritability                                    | 1                         | 1   | 0  |
| Libido Decreased                                | 0                         | 0   | 1  |
| Listless  | 0                         | 0   | 1  |
| Nightmare                                       | 0                         | 0   | 1  |
| Restlessness                                    | 0                         | 1   | 0  |
| Renal And Urinary Disorders                     |                           |   |  |
| Calculus Urethral                               | 0                         | 0   | 1  |
| Dysuria   | 1                         | 1   | 0  |
| Enuresis  | 0                         | 1   | 0  |
| Incontinence                                    | 0                         | 1   | 0  |
| Micturition Urgency                             | 1                         | 1   | 1  |
| Nephrolithiasis                                 | 1                         | 0   | 1  |
| Pollakiuria                                     | 1                         | 0   | 0  |
| Reproductive System And Breast Disorders        |                           |   |  |
| Benign Prostatic Hyperplasia                    | 1                         | 0   | 1  |
| Pelvic Pain                                     | 1                         | 0   | 0  |
| Respiratory, Thoracic And Mediastinal Disorders |                           |   |  |
| Allergic Granulomatous Angitis                  | 0                         | 0   | 1  |
| Cough   | 3                         | 6   | 5  |
| Dysphonia                                       | 0                         | 1   | 0  |
| Dyspnoea  | 1                         | 1   | 1  |

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|--|---------------------------|---|--|
| Emphysema                                    | 1                         | 0   | 0  |
| Epistaxis                                    | 0                         | 1   | 2  |
| Haemoptysis                                  | 1                         | 0   | 0  |
| Nasal Congestion                             | 3                         | 1   | 3  |
| Pharyngeal Erythema                          | 0                         | 0   | 1  |
| Pharyngolaryngeal Pain                       | 0                         | 1   | 1  |
| Postnasal Drip                               | 1                         | 0   | 0  |
| Productive Cough                             | 0                         | 0   | 1  |
| Rales  | 1                         | 0   | 0  |
| Respiratory Tract Congestion                 | 0                         | 0   | 1  |
| Rhinorrhoea                                  | 0                         | 1   | 1  |
| Skin And Subcutaneous Tissue Disorders       |                           |   |  |
| Actinic Keratosis                            | 0                         | 0   | 1  |
| Alopecia                                     | 1                         | 0   | 0  |
| Blister                                      | 0                         | 5   | 1  |
| Cold Sweat                                   | 1                         | 0   | 0  |
| Dermatitis Atopic                            | 1                         | 0   | 0  |
| Dermatitis Contact                           | 0                         | 1   | 0  |
| Drug Eruption                                | 1                         | 0   | 0  |
| Erythema                                     | 9                         | 15  | 14   |
| Hyperhidrosis                                | 2                         | 4   | 8  |
| Pruritus                                     | 8                         | 23  | 26   |
| Pruritus Generalised                         | 0                         | 1   | 1  |
| Rash   | 5                         | 13  | 11   |
| Rash Erythematous                            | 0                         | 2   | 0  |
| Rash Maculo-Papular                          | 0                         | 0   | 1  |
| Rash Papular                                 | 0                         | 0   | 1  |
| Rash Pruritic                                | 0                         | 1   | 2  |
| Skin Exfoliation                             | 0                         | 1   | 0  |
| Skin Irritation                              | 3                         | 6   | 5  |
| Skin Odour Abnormal                          | 0                         | 0   | 1  |
| Skin Ulcer                                   | 1                         | 0   | 0  |
| Urticaria                                    | 0                         | 1   | 1  |
| Social Circumstances                         |                           |   |  |
| Alcohol Use                                  | 0                         | 0   | 1  |
| Surgical And Medical Procedures              |                           |   |  |
| Acrochordon Excision                         | 0                         | 0   | 1  |

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|---|---------------------------|---|--|
| Cataract Operation  | 1                         | 1   | 0  |
| Eye Laser Surgery   | 1                         | 0   | 0  |
| Skin Lesion Excision  | 0                         | 0   | 1  |
| Vascular Disorders  |                           |   |  |
| Hot Flush   | 0                         | 1   | 0  |
| Hypertension  | 1                         | 1   | 1  |
| Hypotension   | 2                         | 1   | 0  |
| Orthostatic Hypotension   | 1                         | 0   | 0  |
| Wound Haemorrhage   | 0                         | 0   | 1  |
| MedDRA version 25.0.  |                           |   |  |
| Each participant is counted once within each preferred term and system organ class.               |                           |   |  |
| Participants with multiple events in the same preferred term are counted only once for that term. |                           |   |  |

Source: ADAE Analysis Dataset (Data cutoff: 01JAN2023)