

Participants With Drug-Related Adverse Events
Weeks 0 to 12
All Participants as Treated

| | f | | | m | | | Total | | | | | | | | | | | |
|----------------------------------------------|----------|--------------|----------|--------------|----------|---------------|-----------|--------------|----------|--------------|-----------|--------------|----------|--------------|----------|--------------|----------|--------------|
| | Placebo | | Low Dose | Placebo | | Low Dose | High Dose | Placebo | | Low Dose | High Dose | | | | | | | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | | | | | | |
| Participants in population | 53 | | 50 | | 40 | | 33 | | 34 | | 44 | | 86 | | 84 | | 84 | |
| with one or more drug-related adverse events | 28 | (52.8) | 41 | (82.0) | 32 | (80.0) | 16 | (48.5) | 32 | (94.1) | 38 | (86.4) | 44 | (51.2) | 73 | (86.9) | 70 | (83.3) |
| with no drug-related adverse events | 25 | (47.2) | 9 | (18.0) | 8 | (20.0) | 17 | (51.5) | 2 | (5.9) | 6 | (13.6) | 42 | (48.8) | 11 | (13.1) | 14 | (16.7) |
| Cardiac disorders | 4 | (7.5) | 4 | (8.0) | 4 | (10.0) | 2 | (6.1) | 3 | (8.8) | 0 | (0.0) | 6 | (7.0) | 7 | (8.3) | 4 | (4.8) |
| Atrial fibrillation | 1 | (1.9) | 0 | (0.0) | 2 | (5.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 2 | (2.4) |
| Atrial flutter | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |

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|--------------------------------------|---------|-------|----------|-------|-----------|-------|---------|-------|----------|-------|-----------|-------|---------|-------|----------|-------|-----------|-------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Atrioventricular block first degree | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Atrioventricular block second degree | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Bradycardia | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Bundle branch block right | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Cardiac failure congestive | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Myocardial infarction | 2 | (3.8) | 1 | (2.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.3) | 1 | (1.2) | 1 | (1.2) |
| Palpitations | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Sinus arrhythmia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |

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|---------------------------------------------------|----------|--------------|----------|--------------|-----------|--------------|----------|--------------|----------|--------------|-----------|--------------|----------|--------------|----------|--------------|-----------|--------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Sinus bradycardia | 2 | (3.8) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 2 | (2.3) | 2 | (2.4) | 0 | (0.0) |
| Supraventricular extrasystoles | 0 | (0.0) | 1 | (2.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Ventricular extrasystoles | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Wolff-parkinson-white syndrome | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Congenital, familial and genetic disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Ventricular septal defect | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Ear and labyrinth disorders | 0 | (0.0) | 2 | (4.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 1 | (1.2) |
| Tinnitus | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Vertigo | 0 | (0.0) | 1 | (2.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |

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|-----------------------------------|----------|--------------|----------|---------------|-----------|--------------|----------|--------------|----------|--------------|-----------|---------------|----------|--------------|----------|--------------|-----------|---------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Eye disorders | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Vision blurred | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Gastrointestinal disorders | 1 | (1.9) | 6 | (12.0) | 3 | (7.5) | 3 | (9.1) | 2 | (5.9) | 7 | (15.9) | 4 | (4.7) | 8 | (9.5) | 10 | (11.9) |
| Abdominal pain | 0 | (0.0) | 1 | (2.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Diarrhoea | 0 | (0.0) | 3 | (6.0) | 0 | (0.0) | 3 | (9.1) | 0 | (0.0) | 2 | (4.5) | 3 | (3.5) | 3 | (3.6) | 2 | (2.4) |
| Dyspepsia | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) | 0 | (0.0) |
| Gastroesophageal reflux disease | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Nausea | 0 | (0.0) | 2 | (4.0) | 2 | (5.0) | 0 | (0.0) | 1 | (2.9) | 1 | (2.3) | 0 | (0.0) | 3 | (3.6) | 3 | (3.6) |
| Salivary hypersecretion | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (6.8) | 0 | (0.0) | 0 | (0.0) | 3 | (3.6) |
| Stomach discomfort | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Vomiting | 0 | (0.0) | 2 | (4.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (6.8) | 0 | (0.0) | 2 | (2.4) | 3 | (3.6) |

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|-------------------------------------------------------------|-----------|---------------|-----------|---------------|-----------|---------------|----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| General disorders and administration site conditions | 11 | (20.8) | 23 | (46.0) | 17 | (42.5) | 7 | (21.2) | 20 | (58.8) | 18 | (40.9) | 18 | (20.9) | 43 | (51.2) | 35 | (41.7) |
| Application site bleeding | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Application site dermatitis | 2 | (3.8) | 5 | (10.0) | 4 | (10.0) | 3 | (9.1) | 4 | (11.8) | 3 | (6.8) | 5 | (5.8) | 9 | (10.7) | 7 | (8.3) |
| Application site desquamation | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Application site discharge | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |

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|---------------------------------|---------|-------|----------|--------|-----------|--------|---------|-------|----------|--------|-----------|--------|---------|-------|----------|--------|-----------|--------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Application site discolouration | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Application site erythema | 2 | (3.8) | 5 | (10.0) | 5 | (12.5) | 1 | (3.0) | 7 | (20.6) | 10 | (22.7) | 3 | (3.5) | 12 | (14.3) | 15 | (17.9) |
| Application site induration | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Application site irritation | 3 | (5.7) | 6 | (12.0) | 5 | (12.5) | 0 | (0.0) | 3 | (8.8) | 4 | (9.1) | 3 | (3.5) | 9 | (10.7) | 9 | (10.7) |
| Application site pain | 0 | (0.0) | 0 | (0.0) | 2 | (5.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) |
| Application site perspiration | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (4.5) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) |
| Application site pruritus | 4 | (7.5) | 12 | (24.0) | 10 | (25.0) | 2 | (6.1) | 10 | (29.4) | 12 | (27.3) | 6 | (7.0) | 22 | (26.2) | 22 | (26.2) |
| Application site reaction | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 1 | (1.2) |

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|----------------------------|---------|-------|----------|-------|-----------|--------|---------|-------|----------|-------|-----------|-------|---------|-------|----------|-------|-----------|-------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Application site swelling | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 2 | (2.4) |
| Application site urticaria | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 2 | (5.9) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 1 | (1.2) |
| Application site vesicles | 0 | (0.0) | 1 | (2.0) | 3 | (7.5) | 1 | (3.0) | 3 | (8.8) | 3 | (6.8) | 1 | (1.2) | 4 | (4.8) | 6 | (7.1) |
| Application site warmth | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Asthenia | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Chest discomfort | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Chills | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 1 | (2.9) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) | 0 | (0.0) |
| Fatigue | 1 | (1.9) | 1 | (2.0) | 4 | (10.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 1 | (1.2) | 2 | (2.4) | 4 | (4.8) |
| Feeling abnormal | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Malaise | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Oedema | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 0 | (0.0) |

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| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Oedema peripheral | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Pain | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Injury, poisoning and procedural complications | 0 | (0.0) | 2 | (4.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 1 | (1.2) |
| Excoriation | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Fall | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Skin laceration | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Wound | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Investigations | 2 | (3.8) | 2 | (4.0) | 1 | (2.5) | 2 | (6.1) | 0 | (0.0) | 0 | (0.0) | 4 | (4.7) | 2 | (2.4) | 1 | (1.2) |
| Blood creatine phosphokinase increased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |

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| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Body temperature increased | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Electrocardiogram st segment depression | 1 | (1.9) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) | 0 | (0.0) |
| Electrocardiogram t wave inversion | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Heart rate increased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Heart rate irregular | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Metabolism and nutrition disorders | 3 | (5.7) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (3.5) | 0 | (0.0) | 1 | (1.2) |
| Decreased appetite | 1 | (1.9) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 1 | (1.2) |
| Food craving | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |

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| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Increased appetite | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Musculoskeletal and connective tissue disorders | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 1 | (2.3) | 1 | (1.2) | 0 | (0.0) | 1 | (1.2) |
| Myalgia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Shoulder pain | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Nervous system disorders | 3 | (5.7) | 8 | (16.0) | 7 | (17.5) | 2 | (6.1) | 4 | (11.8) | 8 | (18.2) | 5 | (5.8) | 12 | (14.3) | 15 | (17.9) |
| Balance disorder | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Burning sensation | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (4.5) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) |
| Complex partial seizures | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |

Participants With Drug-Related Adverse Events
Weeks 0 to 12
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| | f | | | | | | m | | | | | | Total | | | | | |
|----------------------------|---------|-------|----------|-------|-----------|-------|---------|-------|----------|-------|-----------|-------|---------|-------|----------|-------|-----------|-------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Coordination abnormal | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Dizziness | 1 | (1.9) | 3 | (6.0) | 2 | (5.0) | 1 | (3.0) | 3 | (8.8) | 4 | (9.1) | 2 | (2.3) | 6 | (7.1) | 6 | (7.1) |
| Headache | 2 | (3.8) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 2 | (2.3) | 1 | (1.2) | 1 | (1.2) |
| Hypersomnia | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Lethargy | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Paraesthesia oral | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Parosmia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Somnolence | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Stupor | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Syncope | 0 | (0.0) | 4 | (8.0) | 2 | (5.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 4 | (4.8) | 3 | (3.6) |
| Syncope vasovagal | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Transient ischaemic attack | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |

| | | | | | | | | | | | | | | | | | | |
|------------------------------|----------|--------------|----------|---------------|----------|--------------|----------|--------------|----------|--------------|----------|--------------|----------|--------------|----------|---------------|----------|--------------|
| Psychiatric disorders | 1 | (1.9) | 6 | (12.0) | 1 | (2.5) | 1 | (3.0) | 3 | (8.8) | 4 | (9.1) | 2 | (2.3) | 9 | (10.7) | 5 | (6.0) |
|------------------------------|----------|--------------|----------|---------------|----------|--------------|----------|--------------|----------|--------------|----------|--------------|----------|--------------|----------|---------------|----------|--------------|

Participants With Drug-Related Adverse Events
Weeks 0 to 12
All Participants as Treated

| | f | | | | | | m | | | | | | Total | | | | | |
|------------------------------------|----------|--------------|----------|--------------|-----------|--------------|----------|--------------|----------|--------------|-----------|--------------|----------|--------------|----------|--------------|-----------|--------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Agitation | 0 | (0.0) | 2 | (4.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 0 | (0.0) |
| Anxiety | 0 | (0.0) | 3 | (6.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (3.6) | 0 | (0.0) |
| Confusional state | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 1 | (3.0) | 1 | (2.9) | 0 | (0.0) | 1 | (1.2) | 2 | (2.4) | 0 | (0.0) |
| Delirium | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Depressed mood | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Hallucination, visual | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Insomnia | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (4.5) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) |
| Irritability | 1 | (1.9) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) | 0 | (0.0) |
| Libido decreased | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Listless | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Restlessness | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Renal and urinary disorders | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |

Participants With Drug-Related Adverse Events
Weeks 0 to 12
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| | f | | | | | | m | | | | | | Total | | | | | |
|--------------------------------------------------------|-----------|---------------|-----------|---------------|-----------|---------------|----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|-----------|---------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Enuresis | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Micturition urgency | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Reproductive system and breast disorders | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Pelvic pain | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Respiratory, thoracic and mediastinal disorders | 2 | (3.8) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (2.3) | 0 | (0.0) | 0 | (0.0) |
| Dyspnoea | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Emphysema | 1 | (1.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Skin and subcutaneous tissue disorders | 12 | (22.6) | 21 | (42.0) | 13 | (32.5) | 5 | (15.2) | 18 | (52.9) | 26 | (59.1) | 17 | (19.8) | 39 | (46.4) | 39 | (46.4) |

Participants With Drug-Related Adverse Events
Weeks 0 to 12
All Participants as Treated

| | f | | | | | | m | | | | | | Total | | | | | |
|----------------------|---------|--------|----------|--------|-----------|--------|---------|-------|----------|--------|-----------|--------|---------|--------|----------|--------|-----------|--------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Blister | 0 | (0.0) | 2 | (4.0) | 0 | (0.0) | 0 | (0.0) | 3 | (8.8) | 1 | (2.3) | 0 | (0.0) | 5 | (6.0) | 1 | (1.2) |
| Cold sweat | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Dermatitis contact | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Erythema | 6 | (11.3) | 7 | (14.0) | 7 | (17.5) | 3 | (9.1) | 6 | (17.6) | 7 | (15.9) | 9 | (10.5) | 13 | (15.5) | 14 | (16.7) |
| Hyperhidrosis | 1 | (1.9) | 1 | (2.0) | 2 | (5.0) | 0 | (0.0) | 3 | (8.8) | 6 | (13.6) | 1 | (1.2) | 4 | (4.8) | 8 | (9.5) |
| Pruritus | 6 | (11.3) | 12 | (24.0) | 11 | (27.5) | 1 | (3.0) | 9 | (26.5) | 15 | (34.1) | 7 | (8.1) | 21 | (25.0) | 26 | (31.0) |
| Pruritus generalised | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Rash | 2 | (3.8) | 6 | (12.0) | 2 | (5.0) | 1 | (3.0) | 5 | (14.7) | 5 | (11.4) | 3 | (3.5) | 11 | (13.1) | 7 | (8.3) |
| Rash erythematous | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 2 | (2.4) | 0 | (0.0) |
| Rash maculo-papular | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Rash papular | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |
| Rash pruritic | 0 | (0.0) | 1 | (2.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 1 | (2.3) | 0 | (0.0) | 1 | (1.2) | 2 | (2.4) |
| Skin | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |

Participants With Drug-Related Adverse Events
Weeks 0 to 12
All Participants as Treated

| | f | | | | | | m | | | | | | Total | | | | | |
|---------------------------|----------|-------------------|----------|-------------------|-----------|-------------------|----------|-------------------|----------|-------------------|-----------|-------------------|----------|-------------------|----------|-------------------|-----------|-------------------|
| | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | | Placebo | | Low Dose | | High Dose | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Skin irritation | 2 | (3.8) | 5 | (10.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 4 | (9.1) | 2 | (2.3) | 6 | (7.1) | 5 | (6.0) |
| Skin ulcer | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Urticaria | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 1 | (2.9) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) |
| Vascular disorders | 0 | (0.0) | 2 | (4.0) | 1 | (2.5) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 2 | (2.4) | 1 | (1.2) |
| Hypertension | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) |
| Hypotension | 0 | (0.0) | 1 | (2.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 1 | (1.2) | 0 | (0.0) |
| Orthostatic hypotension | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (3.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) | 0 | (0.0) | 0 | (0.0) |
| Wound haemorrhage | 0 | (0.0) | 0 | (0.0) | 1 | (2.5) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1.2) |

Every participant is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Adverse event terms are from MedDRA Version 24.0.

Source: [CDISCPilot: adam-adsl; adae]