Omaveloxolon (Skyclarys™)

Biogen GmbH

Anhang 4-K zu Modul 4A und 4B

Behandlung der Friedreich-Ataxie (FA) bei Erwachsenen und Jugendlichen ab 16 Jahren

Stand: 01.07.2025

Inhaltsverzeichnis

Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Patients With Concomitant Medications	105 (99.1%)*	42 (97.7%)*	147 (98.7%)*
3-OXOANDROSTEN (4) DERIVATIVES	2 (1.9%)	0	2 (1.3%)
TESTOSTERONE	1 (0.9%)	0	1 (0.7%)
TESTOSTERONE UNDECANOATE	1 (0.9%)	0	1 (0.7%)
ACE INHIBITORS, PLAIN	7 (6.6%)	0	7 (4.7%)
LISINOPRIL	5 (4.7%)	0	5 (3.4%)
RAMIPRIL	2 (1.9%)	0	2 (1.3%)
ACETIC ACID DERIVATIVES AND RELATED SUBSTANCES	4 (3.8%)	6 (14.0%)	10 (6.7%)
DICLOFENAC	2 (1.9%)	2 (4.7%)	4 (2.7%)
KETOROLAC	0	3 (7.0%)	3 (2.0%)
KETOROLAC TROMETHAMINE	2 (1.9%)	1 (2.3%)	3 (2.0%)
ADAMANTANE DERIVATIVES	3 (2.8%)	0	3 (2.0%)
AMANTADINE	3 (2.8%)	0	3 (2.0%)
ADRENERGIC AND DOPAMINERGIC AGENTS	2 (1.9%)	3 (7.0%)	5 (3.4%)
EPHEDRINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
PHENYLEPHRINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
NOREPINEPHRINE BITARTRATE	0	1 (2.3%)	1 (0.7%)
EPHEDRINE SULFATE	1 (0.9%)	0	1 (0.7%)
EPINEPHRINE	1 (0.9%)	0	1 (0.7%)

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ADRENERGICS AND OTHER DRUGS FOR OBSTRUCTIVE AIRWAY	2 (1.9%)	0	2 (1.3%)
BUDESONIDE W/FORMOTEROL FUMARATE	2 (1.9%)	0	2 (1.3%)
ALDOSTERONE ANTAGONISTS	1 (0.9%)	1 (2.3%)	2 (1.3%)
SPIRONOLACTONE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ALL OTHER THERAPEUTIC PRODUCTS	5 (4.7%)	1 (2.3%)	6 (4.0%)
CREATINE	4 (3.8%)	0	4 (2.7%)
CREATINE MONOHYDRATE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ALLERGEN EXTRACTS	1 (0.9%)	0	1 (0.7%)
ALLERGENS NOS	1 (0.9%)	0	1 (0.7%)
ALPHA AND BETA BLOCKING AGENTS	0	1 (2.3%)	1 (0.7%)
LABETALOL	0	1 (2.3%)	1 (0.7%)
ALPHA-ADRENORECEPTOR ANTAGONISTS	4 (3.8%)	0	4 (2.7%)
TAMSULOSIN HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)
ALFUZOSIN	1 (0.9%)	0	1 (0.7%)
PRAZOSIN	1 (0.9%)	0	1 (0.7%)
AMIDES	6 (5.7%)	4 (9.3%)	10 (6.7%)
LIDOCAINE	3 (2.8%)	2 (4.7%)	5 (3.4%)
MARCAINE WITH EPINEPHRINE /00879801/	1 (0.9%)	2 (4.7%)	3 (2.0%)
DELTAZINE WITH EPINEPHRINE	0	2 (4.7%)	2 (1.3%)
XYLOCAINE-EPINEPHRINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ROPIVACAINE	2 (1.9%)	0	2 (1.3%)
BUPIVACAINE	0	1 (2.3%)	1 (0.7%)

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AMIDES, continued...			
ARTICAINE	1 (0.9%)	0	1 (0.7%)
ARTICAINE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
AMINO ACIDS	2 (1.9%)	0	2 (1.3%)
TRANEXAMIC ACID	2 (1.9%)	0	2 (1.3%)
AMINO ACIDS AND DERIVATIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
LEVOGLUTAMIDE	0	1 (2.3%)	1 (0.7%)
TAURINE	1 (0.9%)	0	1 (0.7%)
AMINO ACIDS/CARBOHYDRATES/MINERALS/VITAMINS, COMBI	0	1 (2.3%)	1 (0.7%)
AMINO ACIDS/CARBOHYDRATES/MINERALS/VITAMINS,	0	1 (2.3%)	1 (0.7%)
AMINOALKYL ETHERS	9 (8.5%)	2 (4.7%)	11 (7.4%)
DIPHENHYDRAMINE HYDROCHLORIDE	7 (6.6%)	2 (4.7%)	9 (6.0%)
DIMENHYDRINATE	1 (0.9%)	0	1 (0.7%)
DIPHENHYDRAMINE	1 (0.9%)	0	1 (0.7%)
ANESTHETICS FOR TOPICAL USE	1 (0.9%)	4 (9.3%)	5 (3.4%)
LIDOCAINE	0	3 (7.0%)	3 (2.0%)
LIDOCAINE HYDROCHLORIDE	0	2 (4.7%)	2 (1.3%)
BENZOCAINE	1 (0.9%)	0	1 (0.7%)

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ANESTHETICS, GENERAL		2 (1.9%)	1 (2.3%)	3 (2.0%)
ANESTHETICS, GENERAL		2 (1.9%)	1 (2.3%)	3 (2.0%)
ANESTHETICS, LOCAL		1 (0.9%)	0	1 (0.7%)
ANAESTHETICS, LOCAL		1 (0.9%)	0	1 (0.7%)
ANGIOTENSIN II ANTAGONISTS, PLAIN		1 (0.9%)	2 (4.7%)	3 (2.0%)
LOSARTAN		1 (0.9%)	1 (2.3%)	2 (1.3%)
CANDESARTAN CILEXETIL		0	1 (2.3%)	1 (0.7%)
ANILIDES		51 (48.1%)	25 (58.1%)	76 (51.0%)
PARACETAMOL		34 (32.1%)	25 (58.1%)	59 (39.6%)
MEDINITE		8 (7.5%)	2 (4.7%)	10 (6.7%)
VICODIN		6 (5.7%)	2 (4.7%)	8 (5.4%)
VICKS FORMULA 44M	/01056501/	4 (3.8%)	0	4 (2.7%)
BENADRYL COLD AND FLU		3 (2.8%)	0	3 (2.0%)
THOMAPYRIN N		3 (2.8%)	0	3 (2.0%)
MIDOL	/00095101/	0	2 (4.7%)	2 (1.3%)
MIDOL	/01685001/	1 (0.9%)	1 (2.3%)	2 (1.3%)
CODRAL COLD & FLU		0	1 (2.3%)	1 (0.7%)
SOLPADEINE	/00154101/	0	1 (2.3%)	1 (0.7%)
AXOTAL	/00727001/	1 (0.9%)	0	1 (0.7%)
CO-TYLENOL	/00446801/	1 (0.9%)	0	1 (0.7%)
COTYLENOL		1 (0.9%)	0	1 (0.7%)
DOZOL		1 (0.9%)	0	1 (0.7%)
LENOLTEC WITH CODEINE NO 1		1 (0.9%)	0	1 (0.7%)
PANADEINE CO		1 (0.9%)	0	1 (0.7%)

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ANTACIDS WITH SODIUM BICARBONATE	1 (0.9%)	0	1 (0.7%)
X-EVESS	1 (0.9%)	0	1 (0.7%)
ANTIALLERGIC AGENTS, EXCL. CORTICOSTEROIDS	1 (0.9%)	0	1 (0.7%)
AZELASTINE	1 (0.9%)	0	1 (0.7%)
ANTIBIOTICS	8 (7.5%)	1 (2.3%)	9 (6.0%)
CLINDAMYCIN	4 (3.8%)	0	4 (2.7%)
TETRACYCLINE	0	1 (2.3%)	1 (0.7%)
ANTIBIOTICS	1 (0.9%)	0	1 (0.7%)
NYSTATIN	1 (0.9%)	0	1 (0.7%)
TOBRAMYCIN	1 (0.9%)	0	1 (0.7%)
VANCOMYCIN HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
ANTIDIARRHEAL MICROORGANISMS	6 (5.7%)	2 (4.7%)	8 (5.4%)
BIFIDOBACTERIUM LACTIS	4 (3.8%)	1 (2.3%)	5 (3.4%)
PHILLIPS COLON HEALTH	1 (0.9%)	1 (2.3%)	2 (1.3%)
BIFIDOBACTERIUM INFANTIS	1 (0.9%)	0	1 (0.7%)
CULTURELLE	1 (0.9%)	0	1 (0.7%)
ANTIDOTES	3 (2.8%)	2 (4.7%)	5 (3.4%)
SUGAMMADEX	2 (1.9%)	1 (2.3%)	3 (2.0%)
METHYLTHIONINIUM CHLORIDE	0	1 (2.3%)	1 (0.7%)
SUGAMMADEX SODIUM	1 (0.9%)	0	1 (0.7%)

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ANTIFUNGALS FOR SYSTEMIC USE	0	2 (4.7%)	2 (1.3%)
TERBINAFINE	0	1 (2.3%)	1 (0.7%)
TERBINAFINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
ANTIINFECTIVES	0	1 (2.3%)	1 (0.7%)
CHLORAMPHENICOL	0	1 (2.3%)	1 (0.7%)
ANTIINFECTIVES AND ANTISEPTICS FOR LOCAL ORAL TREA	1 (0.9%)	1 (2.3%)	2 (1.3%)
CHLORHEXIDINE GLUCONATE	0	1 (2.3%)	1 (0.7%)
METRONIDAZOLE	1 (0.9%)	0	1 (0.7%)
ANTIINFECTIVES FOR TREATMENT OF ACNE	0	2 (4.7%)	2 (1.3%)
CLINDAMYCIN	0	2 (4.7%)	2 (1.3%)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	2 (1.9%)	0	2 (1.3%)
CURCUMA LONGA RHIZOME	2 (1.9%)	0	2 (1.3%)
ANTIINFLAMMATORY PREPARATIONS, NON-STEROIDS FOR TO	1 (0.9%)	1 (2.3%)	2 (1.3%)
METHYLSULFONYLMETHANE	0	1 (2.3%)	1 (0.7%)
NIMESULIDE	1 (0.9%)	0	1 (0.7%)
ANTIMIGRAINE PREPARATIONS	1 (0.9%)	0	1 (0.7%)
ANTIMIGRAINE PREPARATIONS	1 (0.9%)	0	1 (0.7%)

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ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS	1 (0.9%)	1 (2.3%)	2 (1.3%)
COLLAGEN	1 (0.9%)	1 (2.3%)	2 (1.3%)
ANTIPROPULSIVES	3 (2.8%)	0	3 (2.0%)
LOPERAMIDE HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)
LOMOTIL	1 (0.9%)	0	1 (0.7%)
LOPERAMIDE	1 (0.9%)	0	1 (0.7%)
ANTIVERTIGO PREPARATIONS	1 (0.9%)	1 (2.3%)	2 (1.3%)
DIMENHYDRINATE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ANTIVIRALS	1 (0.9%)	0	1 (0.7%)
IMIQUIMOD	1 (0.9%)	0	1 (0.7%)
ANTIVIRALS FOR SYSTEMIC USE	2 (1.9%)	1 (2.3%)	3 (2.0%)
ANTIVIRALS FOR SYSTEMIC USE	2 (1.9%)	0	2 (1.3%)
ANTIVIRALS	0	1 (2.3%)	1 (0.7%)
ASCORBIC ACID (VITAMIN C), PLAIN	9 (8.5%)	5 (11.6%)	14 (9.4%)
ASCORBIC ACID	9 (8.5%)	5 (11.6%)	14 (9.4%)
AZASPIRODECANEDIONE DERIVATIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
BUSPIRONE	0	1 (2.3%)	1 (0.7%)
BUSPIRONE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)

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BARBITURATES, PLAIN	1 (0.9%)	0	1 (0.7%)
THIOPENTAL	1 (0.9%)	0	1 (0.7%)
BELLADONNA ALKALOIDS, SEMISYNTHETIC, QUATERNARY AM	0	1 (2.3%)	1 (0.7%)
HYOSCINE BUTYLBROMIDE	0	1 (2.3%)	1 (0.7%)
BELLADONNA ALKALOIDS, TERTIARY AMINES	1 (0.9%)	0	1 (0.7%)
HYOSCYAMINE	1 (0.9%)	0	1 (0.7%)
BENZODIAZEPINE DERIVATIVES	7 (6.6%)	8 (18.6%)	15 (10.1%)
LORAZEPAM	2 (1.9%)	3 (7.0%)	5 (3.4%)
MIDAZOLAM	2 (1.9%)	2 (4.7%)	4 (2.7%)
MIDAZOLAM HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)
CLONAZEPAM	0	1 (2.3%)	1 (0.7%)
DIAZEPAM	0	1 (2.3%)	1 (0.7%)
TRIAZOLAM	0	1 (2.3%)	1 (0.7%)
ALPRAZOLAM	1 (0.9%)	0	1 (0.7%)
BETA BLOCKING AGENTS, NON-SELECTIVE	2 (1.9%)	0	2 (1.3%)
PROPRANOLOL	1 (0.9%)	0	1 (0.7%)
SOTALOL	1 (0.9%)	0	1 (0.7%)

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BETA BLOCKING AGENTS, SELECTIVE	12 (11.3%)	7 (16.3%)	19 (12.8%)
METOPROLOL	7 (6.6%)	4 (9.3%)	11 (7.4%)
ATENOLOL	3 (2.8%)	1 (2.3%)	4 (2.7%)
METOPROLOL TARTRATE	2 (1.9%)	1 (2.3%)	3 (2.0%)
METOPROLOL SUCCINATE	2 (1.9%)	0	2 (1.3%)
BISOPROLOL FUMARATE	0	1 (2.3%)	1 (0.7%)
BISOPROLOL	1 (0.9%)	0	1 (0.7%)
BETA-LACTAMASE INHIBITORS	1 (0.9%)	0	1 (0.7%)
CLAVULANIC ACID	1 (0.9%)	0	1 (0.7%)
BETA-LACTAMASE RESISTANT PENICILLINS	0	1 (2.3%)	1 (0.7%)
FLUCLOXACILLIN	0	1 (2.3%)	1 (0.7%)
BETA-LACTAMASE SENSITIVE PENICILLINS	1 (0.9%)	0	1 (0.7%)
PHENOXYMETHYLPENICILLIN	1 (0.9%)	0	1 (0.7%)
BIGUANIDES	0	1 (2.3%)	1 (0.7%)
METFORMIN	0	1 (2.3%)	1 (0.7%)
BIGUANIDES AND AMIDINES	1 (0.9%)	0	1 (0.7%)
POLIHEXANIDE	1 (0.9%)	0	1 (0.7%)

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BILE ACID SEQUESTRANTS	1 (0.9%)	0	1 (0.7%)
COLESTIPOL	1 (0.9%)	0	1 (0.7%)
BISMUTH PREPARATIONS	5 (4.7%)	2 (4.7%)	7 (4.7%)
BISMUTH SUBSALICYLATE	5 (4.7%)	2 (4.7%)	7 (4.7%)
BISPHOSPHONATES	1 (0.9%)	0	1 (0.7%)
ALENDRONATE SODIUM	1 (0.9%)	0	1 (0.7%)
BULK PRODUCERS	2 (1.9%)	3 (7.0%)	5 (3.4%)
PLANTAGO OVATA	1 (0.9%)	2 (4.7%)	3 (2.0%)
POLYCARBOPHIL CALCIUM	1 (0.9%)	1 (2.3%)	2 (1.3%)
CALCIUM	4 (3.8%)	0	4 (2.7%)
CALCIUM GLUCONATE	2 (1.9%)	0	2 (1.3%)
CALCIUM	1 (0.9%)	0	1 (0.7%)
CALCIUM FLUORIDE	1 (0.9%)	0	1 (0.7%)
CALCIUM, COMBINATIONS WITH OTHER DRUGS	1 (0.9%)	1 (2.3%)	2 (1.3%)
CALCIUM W/MAGNESIUM	1 (0.9%)	1 (2.3%)	2 (1.3%)
CAPSAICIN AND SIMILAR AGENTS	1 (0.9%)	0	1 (0.7%)
CAPSAICIN	1 (0.9%)	0	1 (0.7%)

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CARBAMIC ACID ESTERS		3 (2.8%)	1 (2.3%)	4 (2.7%)
METHOCARBAMOL		2 (1.9%)	1 (2.3%)	3 (2.0%)
TANDRILAX		1 (0.9%)	0	1 (0.7%)
CARBOXAMIDE DERIVATIVES		1 (0.9%)	0	1 (0.7%)
OXCARBAZEPINE		1 (0.9%)	0	1 (0.7%)
CENTRALLY ACTING SYMPATHOMIMETICS		7 (6.6%)	3 (7.0%)	10 (6.7%)
METHYLPHENIDATE HYDROCHLORIDE		4 (3.8%)	0	4 (2.7%)
LISDEXAMFETAMINE MESILATE		1 (0.9%)	2 (4.7%)	3 (2.0%)
ARMODAFINIL		2 (1.9%)	1 (2.3%)	3 (2.0%)
OBETROL	/01345401/	2 (1.9%)	1 (2.3%)	3 (2.0%)
METHYLPHENIDATE		1 (0.9%)	1 (2.3%)	2 (1.3%)
DEXAMFETAMINE SULFATE		2 (1.9%)	0	2 (1.3%)
ATOMOXETINE		1 (0.9%)	0	1 (0.7%)
DEXAMFETAMINE		1 (0.9%)	0	1 (0.7%)
CHOLINE ESTERS		1 (0.9%)	0	1 (0.7%)
BETHANECHOL		1 (0.9%)	0	1 (0.7%)
COMBINATIONS AND COMPLEXES OF ALUMINIUM, CALCIUM A		9 (8.5%)	1 (2.3%)	10 (6.7%)
TUMS	/00193601/	7 (6.6%)	1 (2.3%)	8 (5.4%)
HYDROTALCITE		1 (0.9%)	0	1 (0.7%)
MAGALDRATE		1 (0.9%)	0	1 (0.7%)

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COMBINATIONS OF PENICILLINS, INCL. BETA-LACTAMASE	8 (7.5%)	4 (9.3%)	12 (8.1%)
AUGMENTIN /00756801/	3 (2.8%)	4 (9.3%)	7 (4.7%)
SPEKTRAMOX	4 (3.8%)	0	4 (2.7%)
AMOXI-CLAVULANICO	0	1 (2.3%)	1 (0.7%)
AMOXICILLIN W/CLAVULANATE POTASSIUM	1 (0.9%)	0	1 (0.7%)
COMBINATIONS OF SULFONAMIDES AND TRIMETHOPRIM, INC	1 (0.9%)	1 (2.3%)	2 (1.3%)
BACTRIM	1 (0.9%)	1 (2.3%)	2 (1.3%)
COMBINATIONS OF VITAMINS	1 (0.9%)	1 (2.3%)	2 (1.3%)
VITAMIN K+D	1 (0.9%)	1 (2.3%)	2 (1.3%)
CONTACT LAXATIVES	2 (1.9%)	3 (7.0%)	5 (3.4%)
SENNA ALEXANDRINA	2 (1.9%)	1 (2.3%)	3 (2.0%)
SENNA ALEXANDRINA FRUIT	0	1 (2.3%)	1 (0.7%)
SENNOSIDE A+B	0	1 (2.3%)	1 (0.7%)
CORTICOSTEROIDS	1 (0.9%)	4 (9.3%)	5 (3.4%)
FLUTICASONE PROPIONATE	1 (0.9%)	2 (4.7%)	3 (2.0%)
TRIAMCINOLONE ACETONIDE	0	2 (4.7%)	2 (1.3%)
HYDROCORTISONE	0	1 (2.3%)	1 (0.7%)

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Concomitant medications are coded using the World Health Organization (WHO) drug dictionary (Enhanced version, September 2011, B2 format) for Anatomical Therapeutic Chemical (ATC) classification and preferred drug name.

Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION	2 (1.9%)	1 (2.3%)	3 (2.0%)
MAXITROL	1 (0.9%)	1 (2.3%)	2 (1.3%)
OTOMIZE	1 (0.9%)	0	1 (0.7%)
CORTICOSTEROIDS FOR SYSTEMIC USE	1 (0.9%)	0	1 (0.7%)
CORTICOSTEROIDS FOR SYSTEMIC USE	1 (0.9%)	0	1 (0.7%)
CORTICOSTEROIDS, MODERATELY POTENT (GROUP II)	1 (0.9%)	2 (4.7%)	3 (2.0%)
TRIAMCINOLONE	1 (0.9%)	1 (2.3%)	2 (1.3%)
DESONIDE	0	1 (2.3%)	1 (0.7%)
CORTICOSTEROIDS, PLAIN	0	1 (2.3%)	1 (0.7%)
HYDROCORTISONE	0	1 (2.3%)	1 (0.7%)
CORTICOSTEROIDS, POTENT (GROUP III)	2 (1.9%)	2 (4.7%)	4 (2.7%)
BETAMETHASONE VALERATE	0	1 (2.3%)	1 (0.7%)
FLUOCINONIDE	0	1 (2.3%)	1 (0.7%)
MOMETASONE	0	1 (2.3%)	1 (0.7%)
BETAMETHASONE DIPROPIONATE	1 (0.9%)	0	1 (0.7%)
METHYLPREDNISOLONE ACEPONATE	1 (0.9%)	0	1 (0.7%)
CORTICOSTEROIDS, POTENT, COMBINATIONS WITH ANTISEP	0	1 (2.3%)	1 (0.7%)
BETNOVATE-C	0	1 (2.3%)	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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CORTICOSTEROIDS, VERY POTENT (GROUP IV)	0	1 (2.3%)	1 (0.7%)
CLOBETASOL PROPIONATE	0	1 (2.3%)	1 (0.7%)
CORTICOSTEROIDS, WEAK (GROUP I)	0	1 (2.3%)	1 (0.7%)
CORTISONE	0	1 (2.3%)	1 (0.7%)
COUGH AND COLD PREPARATIONS	1 (0.9%)	0	1 (0.7%)
EUCABAL /05482701/	1 (0.9%)	0	1 (0.7%)
COXIBS	2 (1.9%)	1 (2.3%)	3 (2.0%)
CELECOXIB	2 (1.9%)	1 (2.3%)	3 (2.0%)
DIAZEPINES, OXAZEPINES, THIAZEPINES AND OXEPINES	1 (0.9%)	0	1 (0.7%)
QUETIAPINE	1 (0.9%)	0	1 (0.7%)
DIHYDROPYRIDINE DERIVATIVES	1 (0.9%)	0	1 (0.7%)
AMLODIPINE	1 (0.9%)	0	1 (0.7%)
DIPHENYLMETHANE DERIVATIVES	1 (0.9%)	2 (4.7%)	3 (2.0%)
HYDROXYZINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
HYDROXYZINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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DOPA AND DOPA DERIVATIVES	1 (0.9%)	0	1 (0.7%)
SINEMET	1 (0.9%)	0	1 (0.7%)
DOPAMINE AGONISTS	2 (1.9%)	0	2 (1.3%)
ROPINIROLE	2 (1.9%)	0	2 (1.3%)
PRAMIPEXOLE DIHYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
DRUGS FOR FUNCTIONAL BOWEL DISORDERS	1 (0.9%)	0	1 (0.7%)
ANTISPASMODICS/ ANTICHOLINERGICS	1 (0.9%)	0	1 (0.7%)
DRUGS USED IN ERECTILE DYSFUNCTION	0	1 (2.3%)	1 (0.7%)
SILDENAFIL	0	1 (2.3%)	1 (0.7%)
DRUGS USED IN NICOTINE DEPENDENCE	1 (0.9%)	0	1 (0.7%)
NICOTINE	1 (0.9%)	0	1 (0.7%)
ELECTROLYTE SOLUTIONS	5 (4.7%)	4 (9.3%)	9 (6.0%)
SODIUM CHLORIDE	5 (4.7%)	3 (7.0%)	8 (5.4%)
POTASSIUM CHLORIDE	0	1 (2.3%)	1 (0.7%)
ELECTROLYTE /00909901/	1 (0.9%)	0	1 (0.7%)
ELECTROLYTE SOLUTIONS	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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EMERGENCY CONTRACEPTIVES	0	1 (2.3%)	1 (0.7%)
LEVONORGESTREL	0	1 (2.3%)	1 (0.7%)
EMOLLIENTS AND PROTECTIVES	0	2 (4.7%)	2 (1.3%)
DIMETICONE	0	1 (2.3%)	1 (0.7%)
EMOLLIENTS AND PROTECTIVES	0	1 (2.3%)	1 (0.7%)
ENZYME INHIBITORS	1 (0.9%)	0	1 (0.7%)
ANASTROZOLE	1 (0.9%)	0	1 (0.7%)
EXPECTORANTS	6 (5.7%)	2 (4.7%)	8 (5.4%)
GUAIFENESIN	6 (5.7%)	2 (4.7%)	8 (5.4%)
FIRST-GENERATION CEPHALOSPORINS	7 (6.6%)	7 (16.3%)	14 (9.4%)
CEFALEXIN	4 (3.8%)	5 (11.6%)	9 (6.0%)
CEFAZOLIN SODIUM	2 (1.9%)	1 (2.3%)	3 (2.0%)
CEFAZOLIN	2 (1.9%)	0	2 (1.3%)
CEFRADINE	0	1 (2.3%)	1 (0.7%)
FLUOROQUINOLONES	1 (0.9%)	1 (2.3%)	2 (1.3%)
MOXIFLOXACIN HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
CIPROFLOXACIN HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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FOLIC ACID AND DERIVATIVES	1 (0.9%)	2 (4.7%)	3 (2.0%)
FOLIC ACID	1 (0.9%)	1 (2.3%)	2 (1.3%)
JUICE PLUS	0	1 (2.3%)	1 (0.7%)
GLUCOCORTICOIDS	18 (17.0%)	7 (16.3%)	25 (16.8%)
DEXAMETHASONE	5 (4.7%)	3 (7.0%)	8 (5.4%)
PREDNISONE	5 (4.7%)	3 (7.0%)	8 (5.4%)
METHYLPREDNISOLONE	4 (3.8%)	2 (4.7%)	6 (4.0%)
FLUTICASONE PROPIONATE	0	1 (2.3%)	1 (0.7%)
BECLOMETASONE DIPROPIONATE	1 (0.9%)	0	1 (0.7%)
CORTISONE	1 (0.9%)	0	1 (0.7%)
CORTISONE ACETATE	1 (0.9%)	0	1 (0.7%)
GLUCOCORTICOSTEROIDS	1 (0.9%)	0	1 (0.7%)
METHYLPREDNISOLONE ACETATE	1 (0.9%)	0	1 (0.7%)
PREGNENOLONE	1 (0.9%)	0	1 (0.7%)
TRIAMCINOLONE ACETONIDE	1 (0.9%)	0	1 (0.7%)
H2-RECEPTOR ANTAGONISTS	3 (2.8%)	7 (16.3%)	10 (6.7%)
FAMOTIDINE	2 (1.9%)	7 (16.3%)	9 (6.0%)
RANITIDINE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
HEPARIN GROUP	8 (7.5%)	3 (7.0%)	11 (7.4%)
ENOXAPARIN SODIUM	3 (2.8%)	2 (4.7%)	5 (3.4%)
ENOXAPARIN	4 (3.8%)	1 (2.3%)	5 (3.4%)
HEPARIN	2 (1.9%)	0	2 (1.3%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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HERBAL ANTIINFLAMMATORY AND ANTIRHEUMATIC REMEDIES	1 (0.9%)	0	1 (0.7%)
ARNICA MONTANA	1 (0.9%)	0	1 (0.7%)
HERBAL ANTISEPTICS AND DISINFECTANTS	0	1 (2.3%)	1 (0.7%)
MELALEUCA ALTERNIFOLIA OIL	0	1 (2.3%)	1 (0.7%)
HERBAL ANTIVARICOSE REMEDIES	1 (0.9%)	0	1 (0.7%)
VITIS VINIFERA SEED EXTRACT	1 (0.9%)	0	1 (0.7%)
HERBAL EMOLLIENTS AND PROTECTIVES CONTAINING MUCIL	0	1 (2.3%)	1 (0.7%)
ALOE VERA	0	1 (2.3%)	1 (0.7%)
HERBAL EXPECTORANTS AND EMOLLIENTS	1 (0.9%)	0	1 (0.7%)
HEDERA HELIX EXTRACT	1 (0.9%)	0	1 (0.7%)
HERBAL REMEDIES FOR TREATMENT OF PREMENSTRUAL SYND	1 (0.9%)	0	1 (0.7%)
ANGELICA SINENSIS ROOT	1 (0.9%)	0	1 (0.7%)
HERBAL URINARY ANTISEPTICS AND ANTIINFECTIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
VACCINIUM MACROCARPON	0	1 (2.3%)	1 (0.7%)
VACCINIUM SPP. FRUIT	1 (0.9%)	0	1 (0.7%)

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HMG COA REDUCTASE INHIBITORS	7 (6.6%)	1 (2.3%)	8 (5.4%)
PRAVASTATIN	5 (4.7%)	0	5 (3.4%)
ATORVASTATIN CALCIUM	0	1 (2.3%)	1 (0.7%)
ATORVASTATIN	1 (0.9%)	0	1 (0.7%)
ROSUVASTATIN	1 (0.9%)	0	1 (0.7%)
ROSUVASTATIN CALCIUM	1 (0.9%)	0	1 (0.7%)
HMG COA REDUCTASE INHIBITORS IN COMBINATION WITH O	1 (0.9%)	0	1 (0.7%)
INEGY	1 (0.9%)	0	1 (0.7%)
HYDRAZINOPHTHALAZINE DERIVATIVES	1 (0.9%)	0	1 (0.7%)
HYDRALAZINE	1 (0.9%)	0	1 (0.7%)
HYPNOTICS AND SEDATIVES	2 (1.9%)	1 (2.3%)	3 (2.0%)
PROMETHAZINE	0	1 (2.3%)	1 (0.7%)
HYOSCINE	1 (0.9%)	0	1 (0.7%)
HYOSCINE HYDROBROMIDE	1 (0.9%)	0	1 (0.7%)
I.V. SOLUTIONS	2 (1.9%)	0	2 (1.3%)
I.V. SOLUTIONS	2 (1.9%)	0	2 (1.3%)
IMIDAZOLE AND TRIAZOLE DERIVATIVES	4 (3.8%)	1 (2.3%)	5 (3.4%)
LOTRISONE	2 (1.9%)	0	2 (1.3%)
MICONAZOLE NITRATE	0	1 (2.3%)	1 (0.7%)
CLOTRIMAZOLE	1 (0.9%)	0	1 (0.7%)
KETOCONAZOLE	1 (0.9%)	0	1 (0.7%)

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IMIDAZOLE DERIVATIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
METRONIDAZOLE	1 (0.9%)	1 (2.3%)	2 (1.3%)
INFLUENZA VACCINES	15 (14.2%)	15 (34.9%)	30 (20.1%)
INFLUENZA VACCINE	15 (14.2%)	15 (34.9%)	30 (20.1%)
INSULINS AND ANALOGUES FOR INJECTION, FAST-ACTING	1 (0.9%)	1 (2.3%)	2 (1.3%)
INSULIN ASPART	1 (0.9%)	1 (2.3%)	2 (1.3%)
INSULIN HUMAN	0	1 (2.3%)	1 (0.7%)
INSULINS AND ANALOGUES FOR INJECTION, LONG-ACTING	0	1 (2.3%)	1 (0.7%)
INSULIN DEGLUDEC	0	1 (2.3%)	1 (0.7%)
INTERFERONS	1 (0.9%)	2 (4.7%)	3 (2.0%)
INTERFERON GAMMA-1B	1 (0.9%)	2 (4.7%)	3 (2.0%)
INTRAUTERINE CONTRACEPTIVES	9 (8.5%)	1 (2.3%)	10 (6.7%)
LEVONORGESTREL	6 (5.7%)	1 (2.3%)	7 (4.7%)
INTRAUTERINE CONTRACEPTIVE DEVICE	3 (2.8%)	0	3 (2.0%)
INTRAUTERINE CONTRACEPTIVES	1 (0.9%)	0	1 (0.7%)
INTRAVAGINAL CONTRACEPTIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
NUVARING	1 (0.9%)	1 (2.3%)	2 (1.3%)

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IODINE PRODUCTS	1 (0.9%)	0	1 (0.7%)
POVIDONE-IODINE	1 (0.9%)	0	1 (0.7%)
IRON BIVALENT, ORAL PREPARATIONS	3 (2.8%)	3 (7.0%)	6 (4.0%)
FERROUS SULFATE	1 (0.9%)	3 (7.0%)	4 (2.7%)
FERROUS FUMARATE	0	1 (2.3%)	1 (0.7%)
FERROUS GLUCONATE	1 (0.9%)	0	1 (0.7%)
IRON	1 (0.9%)	0	1 (0.7%)
IRON IN OTHER COMBINATIONS	1 (0.9%)	0	1 (0.7%)
VITAMIN B COMPLEX WITH IRON	1 (0.9%)	0	1 (0.7%)
IRON PREPARATIONS	3 (2.8%)	1 (2.3%)	4 (2.7%)
IRON	3 (2.8%)	1 (2.3%)	4 (2.7%)
IRON TRIVALENT, PARENTERAL PREPARATIONS	1 (0.9%)	1 (2.3%)	2 (1.3%)
FERRIC CARBOXYMALTOSE	1 (0.9%)	1 (2.3%)	2 (1.3%)
LAXATIVES	1 (0.9%)	0	1 (0.7%)
LOWER BOWEL STIMULANT	1 (0.9%)	0	1 (0.7%)
LEUKOTRIENE RECEPTOR ANTAGONISTS	1 (0.9%)	1 (2.3%)	2 (1.3%)
MONTELUKAST	1 (0.9%)	1 (2.3%)	2 (1.3%)

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LOCAL ANESTHETICS	0	1 (2.3%)	1 (0.7%)
BUPIVACAINE	0	1 (2.3%)	1 (0.7%)
MACROLIDES	4 (3.8%)	4 (9.3%)	8 (5.4%)
AZITHROMYCIN	4 (3.8%)	4 (9.3%)	8 (5.4%)
CLARITHROMYCIN	1 (0.9%)	0	1 (0.7%)
MAGNESIUM	14 (13.2%)	4 (9.3%)	18 (12.1%)
MAGNESIUM	11 (10.4%)	4 (9.3%)	15 (10.1%)
MAGNESIUM CHLORIDE ANHYDROUS	1 (0.9%)	0	1 (0.7%)
MAGNESIUM CITRATE	1 (0.9%)	0	1 (0.7%)
MAGNESIUM GLYCINATE	1 (0.9%)	0	1 (0.7%)
MAGNESIUM OXIDE	1 (0.9%)	0	1 (0.7%)
MAGNESIUM SULFATE	1 (0.9%)	0	1 (0.7%)
MELATONIN RECEPTOR AGONISTS	15 (14.2%)	7 (16.3%)	22 (14.8%)
MELATONIN	15 (14.2%)	7 (16.3%)	22 (14.8%)
MONOCLONAL ANTIBODIES	1 (0.9%)	1 (2.3%)	2 (1.3%)
MONOCLONAL ANTIBODIES	1 (0.9%)	1 (2.3%)	2 (1.3%)
MULTIVITAMINS WITH MINERALS	4 (3.8%)	1 (2.3%)	5 (3.4%)
MULTIVITAMINS WITH MINERALS /90003801/	4 (3.8%)	1 (2.3%)	5 (3.4%)

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MULTIVITAMINS, PLAIN		1 (0.9%)	0	1 (0.7%)
PRENATAL	/02014401/	1 (0.9%)	0	1 (0.7%)
NATURAL OPIUM ALKALOIDS		12 (11.3%)	6 (14.0%)	18 (12.1%)
MORPHINE		2 (1.9%)	2 (4.7%)	4 (2.7%)
OXYCODONE		3 (2.8%)	1 (2.3%)	4 (2.7%)
HYDROMORPHONE		2 (1.9%)	1 (2.3%)	3 (2.0%)
HYDROMORPHONE HYDROCHLORIDE		2 (1.9%)	1 (2.3%)	3 (2.0%)
TYLOX	/00446701/	1 (0.9%)	1 (2.3%)	2 (1.3%)
OXYCODONE HYDROCHLORIDE		0	1 (2.3%)	1 (0.7%)
CODEINE		1 (0.9%)	0	1 (0.7%)
CODEINE SULFATE		1 (0.9%)	0	1 (0.7%)
HYDROCODONE		1 (0.9%)	0	1 (0.7%)
MORPHINE SULFATE		1 (0.9%)	0	1 (0.7%)
PERCOCET-5		1 (0.9%)	0	1 (0.7%)
NEURAMINIDASE INHIBITORS		2 (1.9%)	1 (2.3%)	3 (2.0%)
OSELTAMIVIR PHOSPHATE		1 (0.9%)	1 (2.3%)	2 (1.3%)
OSELTAMIVIR		1 (0.9%)	0	1 (0.7%)
NITROFURAN DERIVATIVES		3 (2.8%)	3 (7.0%)	6 (4.0%)
NITROFURANTOIN		2 (1.9%)	3 (7.0%)	5 (3.4%)
NITROFURANTOIN MONOHYDRATE		1 (0.9%)	0	1 (0.7%)

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Concomitant Medications
Safety Population

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NON-SELECTIVE MONOAMINE REUPTAKE INHIBITORS	1 (0.9%)	3 (7.0%)	4 (2.7%)
AMITRIPTYLINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
IMIPRAMINE	0	1 (2.3%)	1 (0.7%)
NUCLEOSIDES AND NUCLEOTIDES EXCL. REVERSE TRANSCRI	1 (0.9%)	0	1 (0.7%)
VALACICLOVIR HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
OPIOID ANESTHETICS	4 (3.8%)	1 (2.3%)	5 (3.4%)
FENTANYL	4 (3.8%)	0	4 (2.7%)
REMIFENTANIL	1 (0.9%)	1 (2.3%)	2 (1.3%)
ALFENTANIL	1 (0.9%)	0	1 (0.7%)
OPIUM ALKALOIDS AND DERIVATIVES	1 (0.9%)	2 (4.7%)	3 (2.0%)
COLDREX NIGHT RELIEF	0	1 (2.3%)	1 (0.7%)
DIMETANE DX	0	1 (2.3%)	1 (0.7%)
DEXTROMETHORPHAN	1 (0.9%)	0	1 (0.7%)
DEXTROMETHORPHAN HYDROBROMIDE	1 (0.9%)	0	1 (0.7%)
OPIUM DERIVATIVES AND EXPECTORANTS	5 (4.7%)	2 (4.7%)	7 (4.7%)
TUSSIN DM	3 (2.8%)	1 (2.3%)	4 (2.7%)
TUSSEX COUGH	0	1 (2.3%)	1 (0.7%)
CHERACOL /00693301/	1 (0.9%)	0	1 (0.7%)
CODEINE PHOS.W/GUAIFENESIN/PHENIRAMINE MAL.	1 (0.9%)	0	1 (0.7%)
ROBITUSSIN /00288801/	1 (0.9%)	0	1 (0.7%)

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Concomitant medications are coded using the World Health Organization (WHO) drug dictionary (Enhanced version, September 2011, B2 format) for Anatomical Therapeutic Chemical (ATC) classification and preferred drug name.

Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
ORGANIC NITRATES	2 (1.9%)	0	2 (1.3%)
GLYCERYL TRINITRATE	2 (1.9%)	0	2 (1.3%)
ISOSORBIDE MONONITRATE	1 (0.9%)	0	1 (0.7%)
OSMOTICALLY ACTING LAXATIVES	3 (2.8%)	2 (4.7%)	5 (3.4%)
MACROGOL	0	2 (4.7%)	2 (1.3%)
MAGNESIUM CARBONATE	1 (0.9%)	0	1 (0.7%)
MAGNESIUM CITRATE	1 (0.9%)	0	1 (0.7%)
MAGNESIUM HYDROXIDE	1 (0.9%)	0	1 (0.7%)
OTHER AGENTS FOR LOCAL ORAL TREATMENT	1 (0.9%)	0	1 (0.7%)
HYALURONIC ACID	1 (0.9%)	0	1 (0.7%)
OTHER AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL	1 (0.9%)	0	1 (0.7%)
PREPARATION H /00611001/	1 (0.9%)	0	1 (0.7%)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	2 (1.9%)	1 (2.3%)	3 (2.0%)
PROBIOTICS	1 (0.9%)	1 (2.3%)	2 (1.3%)
RESVERATROL	1 (0.9%)	0	1 (0.7%)
OTHER AMINOGLYCOSIDES	1 (0.9%)	0	1 (0.7%)
GENTAMICIN SULFATE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER ANALGESICS AND ANTIPYRETICS	13 (12.3%)	10 (23.3%)	23 (15.4%)
GABAPENTIN	11 (10.4%)	10 (23.3%)	21 (14.1%)
DEXTROMETHORPHAN HBR W/DOXYLAM. SUCC/PARACET.	1 (0.9%)	0	1 (0.7%)
PREGABALIN	1 (0.9%)	0	1 (0.7%)
OTHER ANTI-ACNE PREPARATIONS FOR TOPICAL USE	3 (2.8%)	1 (2.3%)	4 (2.7%)
BENZOYL PEROXIDE W/CLINDAMYCIN	1 (0.9%)	1 (2.3%)	2 (1.3%)
AZELAIC ACID	2 (1.9%)	0	2 (1.3%)
OTHER ANTIBIOTICS FOR TOPICAL USE	8 (7.5%)	1 (2.3%)	9 (6.0%)
NEOTRACIN /00038301/	2 (1.9%)	1 (2.3%)	3 (2.0%)
MUPIROCIN	2 (1.9%)	0	2 (1.3%)
FUSIDIC ACID	1 (0.9%)	0	1 (0.7%)
GENTAMICIN SULFATE	1 (0.9%)	0	1 (0.7%)
NEOSPORIN /00130801/	1 (0.9%)	0	1 (0.7%)
POLYSPORIN STERILE OPHTHALMIC	1 (0.9%)	0	1 (0.7%)
OTHER ANTIDEPRESSANTS	17 (16.0%)	8 (18.6%)	25 (16.8%)
BUPROPION HYDROCHLORIDE	9 (8.5%)	3 (7.0%)	12 (8.1%)
DULOXETINE	4 (3.8%)	0	4 (2.7%)
TRAZODONE	0	2 (4.7%)	2 (1.3%)
BUPROPION	1 (0.9%)	1 (2.3%)	2 (1.3%)
DULOXETINE HYDROCHLORIDE	1 (0.9%)	1 (2.3%)	2 (1.3%)
MIRTAZAPINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
VENLAFAXINE	2 (1.9%)	0	2 (1.3%)
VENLAFAXINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
TRAZODONE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
TRYPTOPHAN, L-	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER ANTIEMETICS	1 (0.9%)	1 (2.3%)	2 (1.3%)
PROCHLORPERAZINE	0	1 (2.3%)	1 (0.7%)
PROCHLORPERAZINE EDISYLATE	1 (0.9%)	0	1 (0.7%)
OTHER ANTIEPILEPTICS	3 (2.8%)	1 (2.3%)	4 (2.7%)
LAMOTRIGINE	3 (2.8%)	1 (2.3%)	4 (2.7%)
LEVETIRACETAM	1 (0.9%)	0	1 (0.7%)
OTHER ANTIFUNGALS FOR TOPICAL USE	2 (1.9%)	1 (2.3%)	3 (2.0%)
AMOROLFINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
NAFTIFINE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
TOLNAFTATE	1 (0.9%)	0	1 (0.7%)
OTHER ANTIHISTAMINES FOR SYSTEMIC USE	11 (10.4%)	5 (11.6%)	16 (10.7%)
LORATADINE	10 (9.4%)	5 (11.6%)	15 (10.1%)
AZELASTINE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
FEXOFENADINE	1 (0.9%)	0	1 (0.7%)
OTHER ANTIINFLAMMATORY AND ANTIRHEUMATIC AGENTS, N	1 (0.9%)	0	1 (0.7%)
REPLENEX	1 (0.9%)	0	1 (0.7%)
OTHER ANTIINFLAMMATORY/ANTIRHEUMATIC AGENTS IN COM	0	2 (4.7%)	2 (1.3%)
ADVIL PM /05810501/	0	1 (2.3%)	1 (0.7%)
ADVIL PM /06117501/	0	1 (2.3%)	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER ANTIMIGRAINE PREPARATIONS	0	1 (2.3%)	1 (0.7%)
OTHER ANTIMIGRAINE PREPARATIONS	0	1 (2.3%)	1 (0.7%)
OTHER ANTIPSORIATICS FOR TOPICAL USE	1 (0.9%)	0	1 (0.7%)
DAIVOBET	1 (0.9%)	0	1 (0.7%)
OTHER ANTIPSYCHOTICS	2 (1.9%)	0	2 (1.3%)
ARIPIPRAZOLE	1 (0.9%)	0	1 (0.7%)
RISPERIDONE	1 (0.9%)	0	1 (0.7%)
OTHER ANTITHROMBOTIC AGENTS	0	1 (2.3%)	1 (0.7%)
RIVAROXABAN	0	1 (2.3%)	1 (0.7%)
OTHER ANTIVIRALS	7 (6.6%)	2 (4.7%)	9 (6.0%)
OTHER ANTIVIRALS	7 (6.6%)	2 (4.7%)	9 (6.0%)
OTHER BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	1 (0.9%)	1 (2.3%)	2 (1.3%)
SEMAGLUTIDE	1 (0.9%)	1 (2.3%)	2 (1.3%)
PRAMLINTIDE ACETATE	1 (0.9%)	0	1 (0.7%)
OTHER CARDIAC PREPARATIONS	21 (19.8%)	7 (16.3%)	28 (18.8%)
UBIDECARENONE	21 (19.8%)	7 (16.3%)	28 (18.8%)
IVABRADINE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER CENTRALLY ACTING AGENTS	17 (16.0%)	13 (30.2%)	30 (20.1%)
BACLOFEN	15 (14.2%)	9 (20.9%)	24 (16.1%)
CYCLOBENZAPRINE	2 (1.9%)	3 (7.0%)	5 (3.4%)
TIZANIDINE	3 (2.8%)	0	3 (2.0%)
CYCLOBENZAPRINE HYDROCHLORIDE	0	2 (4.7%)	2 (1.3%)
OTHER CHEMOTHERAPEUTICS	1 (0.9%)	0	1 (0.7%)
METRONIDAZOLE	1 (0.9%)	0	1 (0.7%)
OTHER CICATRIZANTS	0	2 (4.7%)	2 (1.3%)
OCRILATE	0	2 (4.7%)	2 (1.3%)
OTHER COLD COMBINATION PREPARATIONS	2 (1.9%)	2 (4.7%)	4 (2.7%)
CO-TYLENOL /00446801/	2 (1.9%)	0	2 (1.3%)
CODRAL DAYTIME/NIGHTIME	0	1 (2.3%)	1 (0.7%)
TYLENOL SINUS MEDICATION	0	1 (2.3%)	1 (0.7%)
OTHER COMBINATIONS OF NUTRIENTS	2 (1.9%)	0	2 (1.3%)
ACETYLCYSTEINE	2 (1.9%)	0	2 (1.3%)
OTHER COUGH SUPPRESSANTS	4 (3.8%)	1 (2.3%)	5 (3.4%)
BENZONATATE	4 (3.8%)	1 (2.3%)	5 (3.4%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER DERMATOLOGICAL PREPARATIONS	2 (1.9%)	0	2 (1.3%)
PHYTOMENADIONE	1 (0.9%)	0	1 (0.7%)
SARNA	1 (0.9%)	0	1 (0.7%)
OTHER DERMATOLOGICALS	1 (0.9%)	1 (2.3%)	2 (1.3%)
OENOTHERA BIENNIS OIL	0	1 (2.3%)	1 (0.7%)
FINASTERIDE	1 (0.9%)	0	1 (0.7%)
OTHER DRUGS FOR FUNCTIONAL BOWEL DISORDERS	2 (1.9%)	0	2 (1.3%)
SILICON DIOXIDE W/SIMETICONE	1 (0.9%)	0	1 (0.7%)
SIMETICONE	1 (0.9%)	0	1 (0.7%)
OTHER DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEA	2 (1.9%)	2 (4.7%)	4 (2.7%)
GAVISCON /00237601/	1 (0.9%)	2 (4.7%)	3 (2.0%)
POLAPREZINC	1 (0.9%)	0	1 (0.7%)
OTHER DRUGS USED IN DIABETES	0	1 (2.3%)	1 (0.7%)
DAPAGLIFLOZIN	0	1 (2.3%)	1 (0.7%)
OTHER EMOLLIENTS AND PROTECTIVES	1 (0.9%)	0	1 (0.7%)
EPADERM	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER GENERAL ANESTHETICS	4 (3.8%)	4 (9.3%)	8 (5.4%)
PROPOFOL	3 (2.8%)	2 (4.7%)	5 (3.4%)
NITROUS OXIDE	0	2 (4.7%)	2 (1.3%)
KETAMINE	2 (1.9%)	0	2 (1.3%)
OTHER HYPNOTICS AND SEDATIVES	3 (2.8%)	1 (2.3%)	4 (2.7%)
DIPHENHYDRAMINE HYDROCHLORIDE	2 (1.9%)	1 (2.3%)	3 (2.0%)
DIPHENHYDRAMINE	1 (0.9%)	0	1 (0.7%)
OTHER IMMUNOSUPPRESSANTS	1 (0.9%)	0	1 (0.7%)
AZATHIOPRINE	1 (0.9%)	0	1 (0.7%)
OTHER INTESTINAL ANTIINFECTIVES	1 (0.9%)	0	1 (0.7%)
BERUSANOL	1 (0.9%)	0	1 (0.7%)
OTHER LAXATIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
LINACLOTIDE	0	1 (2.3%)	1 (0.7%)
GLYCEROL	1 (0.9%)	0	1 (0.7%)
OTHER LIPID MODIFYING AGENTS	4 (3.8%)	2 (4.7%)	6 (4.0%)
FISH OIL	3 (2.8%)	1 (2.3%)	4 (2.7%)
EZETIMIBE	0	1 (2.3%)	1 (0.7%)
CHOLEST OFF NATURE MADE	1 (0.9%)	0	1 (0.7%)

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Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
OTHER MINERAL PRODUCTS	2 (1.9%)	1 (2.3%)	3 (2.0%)
OTHER MINERAL PRODUCTS	2 (1.9%)	0	2 (1.3%)
HERBAL NOS W/MINERALS NOS	0	1 (2.3%)	1 (0.7%)
OTHER MINERAL SUPPLEMENTS	2 (1.9%)	1 (2.3%)	3 (2.0%)
OTHER MINERAL SUPPLEMENTS	1 (0.9%)	1 (2.3%)	2 (1.3%)
MAGNESIUM W/ZINC	1 (0.9%)	0	1 (0.7%)
OTHER MUSCLE RELAXANTS, PERIPHERALLY ACTING AGENTS	2 (1.9%)	2 (4.7%)	4 (2.7%)
BOTULINUM TOXIN TYPE A	2 (1.9%)	2 (4.7%)	4 (2.7%)
OTHER NASAL PREPARATIONS	2 (1.9%)	1 (2.3%)	3 (2.0%)
SODIUM CHLORIDE	2 (1.9%)	0	2 (1.3%)
MUPIROCIN	0	1 (2.3%)	1 (0.7%)
OTHER OPHTHALMOLOGICALS	2 (1.9%)	1 (2.3%)	3 (2.0%)
CARMELLOSE	1 (0.9%)	1 (2.3%)	2 (1.3%)
CICLOSPORIN	1 (0.9%)	0	1 (0.7%)
OTHER OPIOIDS	7 (6.6%)	4 (9.3%)	11 (7.4%)
TRAMADOL	6 (5.7%)	4 (9.3%)	10 (6.7%)
TRAMADOL HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)

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Concomitant Medications
Safety Population

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OTHER PLAIN VITAMIN PREPARATIONS	11 (10.4%)	5 (11.6%)	16 (10.7%)
TOCOPHEROL	8 (7.5%)	3 (7.0%)	11 (7.4%)
NICOTINAMIDE	4 (3.8%)	0	4 (2.7%)
TOCOPHERYL ACETATE	2 (1.9%)	1 (2.3%)	3 (2.0%)
PYRIDOXINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)
RIBOFLAVIN	1 (0.9%)	0	1 (0.7%)
OTHER PSYCHOSTIMULANTS AND NOOTROPICS	11 (10.4%)	2 (4.7%)	13 (8.7%)
IDEBENONE	8 (7.5%)	2 (4.7%)	10 (6.7%)
DRONABINOL	2 (1.9%)	0	2 (1.3%)
ACETYLCARNITINE	1 (0.9%)	0	1 (0.7%)
CITICOLINE	1 (0.9%)	0	1 (0.7%)
CITRULLINE	1 (0.9%)	0	1 (0.7%)
OTHER QUATERNARY AMMONIUM COMPOUNDS	3 (2.8%)	2 (4.7%)	5 (3.4%)
ROCURONIUM	2 (1.9%)	2 (4.7%)	4 (2.7%)
ROCURONIUM BROMIDE	1 (0.9%)	0	1 (0.7%)
OTHER RESPIRATORY SYSTEM PRODUCTS	1 (0.9%)	0	1 (0.7%)
OTHER RESPIRATORY SYSTEM PRODUCTS	1 (0.9%)	0	1 (0.7%)
OTHER SYSTEMIC DRUGS FOR OBSTRUCTIVE AIRWAY DISEAS	0	1 (2.3%)	1 (0.7%)
OMALIZUMAB	0	1 (2.3%)	1 (0.7%)

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Concomitant Medications
Safety Population

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OTHER THERAPEUTIC PRODUCTS	1 (0.9%)	2 (4.7%)	3 (2.0%)
HOMEOPATHIC PREPARATION	0	1 (2.3%)	1 (0.7%)
QUERCETIN	0	1 (2.3%)	1 (0.7%)
TRAUMEEL /06048201/	1 (0.9%)	0	1 (0.7%)
OTHER UROLOGICALS, INCL. ANTISPASMODICS	1 (0.9%)	0	1 (0.7%)
OTHER UROLOGICALS, INCL ANTISPASMODICS	1 (0.9%)	0	1 (0.7%)
OXAZOL, THIAZINE, AND TRIAZINE DERIVATIVES	2 (1.9%)	0	2 (1.3%)
METAXALONE	2 (1.9%)	0	2 (1.3%)
OXICAMS	3 (2.8%)	3 (7.0%)	6 (4.0%)
MELOXICAM	3 (2.8%)	3 (7.0%)	6 (4.0%)
PAPILLOMAVIRUS VACCINES	1 (0.9%)	0	1 (0.7%)
HUMAN PAPILLOMA VACCINE	1 (0.9%)	0	1 (0.7%)
PENICILLINS WITH EXTENDED SPECTRUM	8 (7.5%)	9 (20.9%)	17 (11.4%)
AMOXICILLIN	8 (7.5%)	9 (20.9%)	17 (11.4%)
PERTUSSIS VACCINES	2 (1.9%)	0	2 (1.3%)
PERTUSSIS VACCINE	2 (1.9%)	0	2 (1.3%)

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Concomitant Medications
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PHENOTHIAZINES WITH PIPERAZINE STRUCTURE	0	1 (2.3%)	1 (0.7%)
PROCHLORPERAZINE EDISYLATE	0	1 (2.3%)	1 (0.7%)
PHENYLPIPERIDINE DERIVATIVES	3 (2.8%)	1 (2.3%)	4 (2.7%)
FENTANYL	2 (1.9%)	1 (2.3%)	3 (2.0%)
PETHIDINE	1 (0.9%)	0	1 (0.7%)
PIPERAZINE DERIVATIVES	12 (11.3%)	6 (14.0%)	18 (12.1%)
CETIRIZINE HYDROCHLORIDE	9 (8.5%)	1 (2.3%)	10 (6.7%)
CETIRIZINE	2 (1.9%)	5 (11.6%)	7 (4.7%)
CYCLIZINE	1 (0.9%)	0	1 (0.7%)
PLATELET AGGREGATION INHIBITORS EXCL. HEPARIN	1 (0.9%)	3 (7.0%)	4 (2.7%)
ACETYLSALICYLIC ACID	1 (0.9%)	2 (4.7%)	3 (2.0%)
APIXABAN	0	1 (2.3%)	1 (0.7%)
PREPARATIONS CONTAINING SULFUR	1 (0.9%)	0	1 (0.7%)
SULFACETAMIDE W/SULFUR	1 (0.9%)	0	1 (0.7%)
PREPARATIONS WITH NO EFFECT ON URIC ACID METABOLIS	0	1 (2.3%)	1 (0.7%)
COLCHICINE	0	1 (2.3%)	1 (0.7%)

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Concomitant medications are coded using the World Health Organization (WHO) drug dictionary (Enhanced version, September 2011, B2 format) for Anatomical Therapeutic Chemical (ATC) classification and preferred drug name.

Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
PROGESTOGENS	8 (7.5%)	6 (14.0%)	14 (9.4%)
MEDROXYPROGESTERONE ACETATE	4 (3.8%)	2 (4.7%)	6 (4.0%)
NORETHISTERONE	1 (0.9%)	3 (7.0%)	4 (2.7%)
ETONOGESTREL	2 (1.9%)	2 (4.7%)	4 (2.7%)
MEDROXYPROGESTERONE	1 (0.9%)	1 (2.3%)	2 (1.3%)
DESOGESTREL	0	1 (2.3%)	1 (0.7%)
PROGESTOGENS AND ESTROGENS IN COMBINATION	0	2 (4.7%)	2 (1.3%)
MARVELON	0	2 (4.7%)	2 (1.3%)
PROGESTOGENS AND ESTROGENS, FIXED COMBINATIONS	13 (12.3%)	9 (20.9%)	22 (14.8%)
EUGYNON /00022701/	5 (4.7%)	3 (7.0%)	8 (5.4%)
AIDA /06358701/	3 (2.8%)	1 (2.3%)	4 (2.7%)
ANOVLAR	1 (0.9%)	2 (4.7%)	3 (2.0%)
DROSPIRENONE W/ETHINYLESTRADIOL	1 (0.9%)	2 (4.7%)	3 (2.0%)
CILEST	2 (1.9%)	1 (2.3%)	3 (2.0%)
NORLESTRIN FE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ETHINYL ESTRADIOL W/NORGESTREL	0	1 (2.3%)	1 (0.7%)
NORMENSAL	0	1 (2.3%)	1 (0.7%)
DROSPIRENONE W/ETHINYLESTRADIOL BETADEX	1 (0.9%)	0	1 (0.7%)
PROLACTINE INHIBITORS	1 (0.9%)	0	1 (0.7%)
CABERGOLINE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
PROPIONIC ACID DERIVATIVES	63 (59.4%)	28 (65.1%)	91 (61.1%)
IBUPROFEN	55 (51.9%)	25 (58.1%)	80 (53.7%)
NAPROXEN	7 (6.6%)	3 (7.0%)	10 (6.7%)
NAPROXEN SODIUM	3 (2.8%)	4 (9.3%)	7 (4.7%)
KETOPROFEN LYSINE	2 (1.9%)	0	2 (1.3%)
FAMOTIDINE W/IBUPROFEN	1 (0.9%)	0	1 (0.7%)
IBUPROFEN LYSINATE	1 (0.9%)	0	1 (0.7%)
KETOPROFEN	1 (0.9%)	0	1 (0.7%)
PROPULSIVES	1 (0.9%)	2 (4.7%)	3 (2.0%)
METOCLOPRAMIDE	1 (0.9%)	2 (4.7%)	3 (2.0%)
PROTEASE INHIBITORS	1 (0.9%)	0	1 (0.7%)
RITONAVIR	1 (0.9%)	0	1 (0.7%)
PROTON PUMP INHIBITORS	17 (16.0%)	8 (18.6%)	25 (16.8%)
OMEPRAZOLE	8 (7.5%)	6 (14.0%)	14 (9.4%)
ESOMEPRAZOLE	3 (2.8%)	2 (4.7%)	5 (3.4%)
PANTOPRAZOLE	2 (1.9%)	1 (2.3%)	3 (2.0%)
LANSOPRAZOLE	1 (0.9%)	0	1 (0.7%)
OMEPRAZOLE MAGNESIUM	1 (0.9%)	0	1 (0.7%)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	1 (0.9%)	0	1 (0.7%)
RABEPRAZOLE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
PSYCHOLEPTICS	1 (0.9%)	0	1 (0.7%)
DYSTO LOGES S	1 (0.9%)	0	1 (0.7%)
PYRAZOLONES	1 (0.9%)	0	1 (0.7%)
METAMIZOLE SODIUM	1 (0.9%)	0	1 (0.7%)
RETINOIDS FOR TOPICAL USE IN ACNE	2 (1.9%)	1 (2.3%)	3 (2.0%)
ADAPALENE	1 (0.9%)	1 (2.3%)	2 (1.3%)
TRETINOIN	1 (0.9%)	0	1 (0.7%)
RETINOIDS FOR TREATMENT OF ACNE	2 (1.9%)	1 (2.3%)	3 (2.0%)
ISOTRETINOIN	2 (1.9%)	1 (2.3%)	3 (2.0%)
SALICYLIC ACID AND DERIVATIVES	7 (6.6%)	2 (4.7%)	9 (6.0%)
ACETYLSALICYLIC ACID	7 (6.6%)	0	7 (4.7%)
BEECHAM'S HOT LEMON COLD REMEDY	0	1 (2.3%)	1 (0.7%)
VINCENTS /00110301/	0	1 (2.3%)	1 (0.7%)
SALICYLIC ACID PREPARATIONS	0	1 (2.3%)	1 (0.7%)
SALACTOL	0	1 (2.3%)	1 (0.7%)
SALT SOLUTIONS	1 (0.9%)	0	1 (0.7%)
SODIUM CHLORIDE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
SECOND-GENERATION CEPHALOSPORINS	2 (1.9%)	2 (4.7%)	4 (2.7%)
CEFUROXIME AXETIL	2 (1.9%)	2 (4.7%)	4 (2.7%)
SELECTIVE BETA-2-ADRENORECEPTOR AGONISTS	8 (7.5%)	4 (9.3%)	12 (8.1%)
SALBUTAMOL	5 (4.7%)	4 (9.3%)	9 (6.0%)
SALBUTAMOL SULFATE	1 (0.9%)	1 (2.3%)	2 (1.3%)
LEVOSALBUTAMOL	1 (0.9%)	0	1 (0.7%)
LEVOSALBUTAMOL HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
SELECTIVE SEROTONIN (5HT1) AGONISTS	2 (1.9%)	1 (2.3%)	3 (2.0%)
RIZATRIPTAN	1 (0.9%)	1 (2.3%)	2 (1.3%)
SUMATRIPTAN	1 (0.9%)	1 (2.3%)	2 (1.3%)
ELETRIPTAN	1 (0.9%)	0	1 (0.7%)
SELECTIVE SEROTONIN (5HT1) AGONISTS	1 (0.9%)	0	1 (0.7%)
SELECTIVE SEROTONIN REUPTAKE INHIBITORS	24 (22.6%)	14 (32.6%)	38 (25.5%)
ESCITALOPRAM OXALATE	7 (6.6%)	2 (4.7%)	9 (6.0%)
SERTRALINE HYDROCHLORIDE	4 (3.8%)	4 (9.3%)	8 (5.4%)
FLUOXETINE	1 (0.9%)	5 (11.6%)	6 (4.0%)
SERTRALINE	6 (5.7%)	0	6 (4.0%)
ESCITALOPRAM	5 (4.7%)	0	5 (3.4%)
FLUOXETINE HYDROCHLORIDE	1 (0.9%)	2 (4.7%)	3 (2.0%)
CITALOPRAM HYDROBROMIDE	0	2 (4.7%)	2 (1.3%)
CITALOPRAM	2 (1.9%)	0	2 (1.3%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term		Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
SELENIUM		3 (2.8%)	0	3 (2.0%)
SELENIUM		3 (2.8%)	0	3 (2.0%)
SEROTONIN (5HT3) ANTAGONISTS		11 (10.4%)	5 (11.6%)	16 (10.7%)
ONDANSETRON		9 (8.5%)	5 (11.6%)	14 (9.4%)
ONDANSETRON HYDROCHLORIDE		3 (2.8%)	0	3 (2.0%)
SOFT PARAFFIN AND FAT PRODUCTS		1 (0.9%)	1 (2.3%)	2 (1.3%)
HYDROMOL	/00906601/	0	1 (2.3%)	1 (0.7%)
DIPROBASE	/01132701/	1 (0.9%)	0	1 (0.7%)
SOFTENERS, EMOLLIENTS		4 (3.8%)	4 (9.3%)	8 (5.4%)
DOCUSATE SODIUM		4 (3.8%)	4 (9.3%)	8 (5.4%)
PARAFFIN, LIQUID		1 (0.9%)	0	1 (0.7%)
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE		2 (1.9%)	2 (4.7%)	4 (2.7%)
FLEBOBAG RING LACT		2 (1.9%)	2 (4.7%)	4 (2.7%)
SPECIFIC IMMUNOGLOBULINS		1 (0.9%)	0	1 (0.7%)
IMMUNOGLOBULIN G HUMAN		1 (0.9%)	0	1 (0.7%)
SUBSTITUTED ALKYLAMINES		1 (0.9%)	0	1 (0.7%)
CHLORPHENAMINE MALEATE		1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

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SULFONAMIDES, PLAIN	1 (0.9%)	1 (2.3%)	2 (1.3%)
FUROSEMIDE	0	1 (2.3%)	1 (0.7%)
TORASEMIDE	1 (0.9%)	0	1 (0.7%)
SULFUR-CONTAINING IMIDAZOLE DERIVATIVES	0	1 (2.3%)	1 (0.7%)
THIAMAZOLE	0	1 (2.3%)	1 (0.7%)
SYMPATHOMIMETICS	6 (5.7%)	4 (9.3%)	10 (6.7%)
PSEUDOEPHEDRINE HYDROCHLORIDE	5 (4.7%)	2 (4.7%)	7 (4.7%)
PSEUDOEPHEDRINE	0	2 (4.7%)	2 (1.3%)
CONTAC /00014501/	0	1 (2.3%)	1 (0.7%)
PHENYLEPHRINE	0	1 (2.3%)	1 (0.7%)
ADVIL ALLERGY SINUS	1 (0.9%)	0	1 (0.7%)
PHENYLEPHRINE HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
SYMPATHOMIMETICS, PLAIN	3 (2.8%)	0	3 (2.0%)
OXYMETAZOLINE HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)
OXYMETAZOLINE	1 (0.9%)	0	1 (0.7%)
SYNTHETIC ANTICHOLINERGICS, ESTERS WITH TERTIARY A	1 (0.9%)	2 (4.7%)	3 (2.0%)
DICYCLOVERINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
DICYCLOVERINE HYDROCHLORIDE	0	1 (2.3%)	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
SYNTHETIC ANTICHOLINERGICS, QUATERNARY AMMONIUM CO	1 (0.9%)	0	1 (0.7%)
GLYCOPYRRONIUM BROMIDE	1 (0.9%)	0	1 (0.7%)
TETANUS VACCINES	2 (1.9%)	2 (4.7%)	4 (2.7%)
TETANUS VACCINE	1 (0.9%)	2 (4.7%)	3 (2.0%)
DITEMER	1 (0.9%)	0	1 (0.7%)
TETRACYCLINES	7 (6.6%)	3 (7.0%)	10 (6.7%)
DOXYCYCLINE	6 (5.7%)	3 (7.0%)	9 (6.0%)
DOXYCYCLINE HYCLATE	1 (0.9%)	0	1 (0.7%)
THIAZIDES, PLAIN	1 (0.9%)	0	1 (0.7%)
HYDROCHLOROTHIAZIDE	1 (0.9%)	0	1 (0.7%)
THIRD-GENERATION CEPHALOSPORINS	3 (2.8%)	1 (2.3%)	4 (2.7%)
CEFDINIR	2 (1.9%)	0	2 (1.3%)
CEFPODOXIME	0	1 (2.3%)	1 (0.7%)
CEFTRIAXONE	0	1 (2.3%)	1 (0.7%)
CEFOTAXIME SODIUM	1 (0.9%)	0	1 (0.7%)
CEFTRIAXONE SODIUM	1 (0.9%)	0	1 (0.7%)
THYROID HORMONES	2 (1.9%)	0	2 (1.3%)
LEVOTHYROXINE	2 (1.9%)	0	2 (1.3%)
LIOTHYRONINE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
TONICS	1 (0.9%)	0	1 (0.7%)
CURCUMIN	1 (0.9%)	0	1 (0.7%)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	1 (0.9%)	0	1 (0.7%)
TRAUMEEL /05818201/	1 (0.9%)	0	1 (0.7%)
TRIAZOLE DERIVATIVES	1 (0.9%)	0	1 (0.7%)
FLUCONAZOLE	1 (0.9%)	0	1 (0.7%)
TRIMETHOPRIM AND DERIVATIVES	1 (0.9%)	0	1 (0.7%)
TRIMETHOPRIM	1 (0.9%)	0	1 (0.7%)
TUMOR NECROSIS FACTOR ALPHA (TNF-) INHIBITORS	1 (0.9%)	0	1 (0.7%)
INFLIXIMAB	1 (0.9%)	0	1 (0.7%)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	10 (9.4%)	4 (9.3%)	14 (9.4%)
CANNABIS SATIVA OIL	4 (3.8%)	1 (2.3%)	5 (3.4%)
CANNABIS SATIVA	5 (4.7%)	0	5 (3.4%)
UNSPECIFIED HERBAL	0	3 (7.0%)	3 (2.0%)
SHEN NENG GANMAOLING	0	1 (2.3%)	1 (0.7%)
CANNABIS SATIVA EXTRACT	1 (0.9%)	0	1 (0.7%)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
URINARY ANTISPASMODICS	16 (15.1%)	5 (11.6%)	21 (14.1%)
OXYBUTYNIN	8 (7.5%)	2 (4.7%)	10 (6.7%)
URINARY ANTISPASMODICS	5 (4.7%)	3 (7.0%)	8 (5.4%)
TOLTERODINE	6 (5.7%)	1 (2.3%)	7 (4.7%)
TOLTERODINE L-TARTRATE	0	2 (4.7%)	2 (1.3%)
SOLIFENACIN SUCCINATE	0	1 (2.3%)	1 (0.7%)
OXYBUTYNIN HYDROCHLORIDE	1 (0.9%)	0	1 (0.7%)
SOLIFENACIN	1 (0.9%)	0	1 (0.7%)
VARIOUS ALIMENTARY TRACT AND METABOLISM PRODUCTS	2 (1.9%)	0	2 (1.3%)
THIOCTIC ACID	2 (1.9%)	0	2 (1.3%)
VIRAL VACCINES	60 (56.6%)	34 (79.1%)	94 (63.1%)
VIRAL VACCINES	60 (56.6%)	34 (79.1%)	94 (63.1%)
VITAMIN A, PLAIN	1 (0.9%)	0	1 (0.7%)
RETINOL	1 (0.9%)	0	1 (0.7%)
VITAMIN B-COMPLEX WITH VITAMIN C	2 (1.9%)	0	2 (1.3%)
VITAMIN B COMPLEX WITH VITAMIN C /06664601/	2 (1.9%)	0	2 (1.3%)
VITAMIN B-COMPLEX, OTHER COMBINATIONS	4 (3.8%)	0	4 (2.7%)
SUPER B COMPLEX /01995301/	4 (3.8%)	0	4 (2.7%)

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Table 14.1.5.1
Concomitant Medications
Safety Population

Medication Class Dictionary-Derived Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
VITAMIN B-COMPLEX, PLAIN	3 (2.8%)	2 (4.7%)	5 (3.4%)
VITAMIN B COMPLEX	3 (2.8%)	2 (4.7%)	5 (3.4%)
VITAMIN B1, PLAIN	4 (3.8%)	0	4 (2.7%)
THIAMINE	2 (1.9%)	0	2 (1.3%)
THIAMINE HYDROCHLORIDE	2 (1.9%)	0	2 (1.3%)
VITAMIN B12 (CYANOCOBALAMIN AND ANALOGUES)	12 (11.3%)	3 (7.0%)	15 (10.1%)
CYANOCOBALAMIN	12 (11.3%)	3 (7.0%)	15 (10.1%)
VITAMIN D AND ANALOGUES	30 (28.3%)	14 (32.6%)	44 (29.5%)
ERGOCALCIFEROL	21 (19.8%)	11 (25.6%)	32 (21.5%)
COLECALCIFEROL	10 (9.4%)	3 (7.0%)	13 (8.7%)
VITAMINS WITH MINERALS	14 (13.2%)	9 (20.9%)	23 (15.4%)
MULTIVITAMINS W/MINERALS	14 (13.2%)	8 (18.6%)	22 (14.8%)
EMERGEN C	0	1 (2.3%)	1 (0.7%)
VITAMINS, OTHER COMBINATIONS	1 (0.9%)	0	1 (0.7%)
AIRBORNE	1 (0.9%)	0	1 (0.7%)
WATERSOLUBLE, NEPHROTROPIC, LOW OSMOLAR X-RAY CONT	1 (0.9%)	0	1 (0.7%)
IOPAMIDOL	1 (0.9%)	0	1 (0.7%)

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Concomitant Medications
Safety Population

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XANTHINE DERIVATIVES	1 (0.9%)	1 (2.3%)	2 (1.3%)
CAFFEINE	1 (0.9%)	1 (2.3%)	2 (1.3%)
ZINC	5 (4.7%)	3 (7.0%)	8 (5.4%)
ZINC	5 (4.7%)	3 (7.0%)	8 (5.4%)
ZINC PRODUCTS	2 (1.9%)	0	2 (1.3%)
SUDOCREM	1 (0.9%)	0	1 (0.7%)
ZINC OXIDE	1 (0.9%)	0	1 (0.7%)

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Table 14.1.6.1
Duration of Study Treatment and Exposure to Study Drug
Safety Population

Parameter (units) Statistic/Category	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Cumulative Dose Dispensed (mg)			
n	106	43	149
Mean (SD)	209547.2 (82563.53)	231802.3 (63148.08)	215969.8 (77911.55)
Median	243000.0	243000.0	243000.0
Min, Max	4500, 297000	4500, 297000	4500, 297000
Number of Doses Received			
n	106	43	149
Mean (SD)	1223.3 (514.86)	1376.2 (408.53)	1267.4 (490.16)
Median	1452.0	1487.7	1464.3
Min, Max	12, 1763	18, 1768	12, 1768
Duration of Treatment (Days)			
n	106	43	149
Mean (SD)	1160.6 (470.76)	1290.7 (352.38)	1198.1 (442.68)
Median	1350.5	1357.0	1353.0
Min, Max	21, 1570	18, 1606	18, 1606
Study Drug Compliance (%)			
n	106	43	149
Mean (SD)	83.776 (16.1822)	87.243 (11.1551)	84.776 (14.9526)
Median	88.869	91.831	89.527
Min, Max	16.67, 100.00	51.11, 99.17	16.67, 100.00
Total Number of Doses Dispensed			
n	106	43	149
Mean (SD)	1397.0 (550.42)	1545.3 (420.99)	1439.8 (519.41)
Median	1620.0	1620.0	1620.0
Min, Max	30, 1980	30, 1980	30, 1980
Total Number of Doses Returned			
n	106	43	149
Mean (SD)	173.7 (116.79)	169.2 (138.19)	172.4 (122.89)
Median	149.3	115.3	139.0
Min, Max	0, 769	12, 665	0, 769

Table 14.1.6.3
Study Drug Exposure by Duration
Safety Population

Parameter (units) Statistic/Category	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Exposure to Study Drug (Weeks)			
<=24 Weeks	106 (100%)	43 (100%)	149 (100%)
>24 Weeks	96 (90.6%)	41 (95.3%)	137 (91.9%)
<=48 Weeks	106 (100%)	43 (100%)	149 (100%)
>48 Weeks	94 (88.7%)	40 (93.0%)	134 (89.9%)
<=72 Weeks	106 (100%)	43 (100%)	149 (100%)
>72 Weeks	89 (84.0%)	40 (93.0%)	129 (86.6%)
<=96 Weeks	106 (100%)	43 (100%)	149 (100%)
>96 Weeks	86 (81.1%)	40 (93.0%)	126 (84.6%)
<=120 Weeks	106 (100%)	43 (100%)	149 (100%)
>120 Weeks	84 (79.2%)	39 (90.7%)	123 (82.6%)
<=144 Weeks	106 (100%)	43 (100%)	149 (100%)
>144 Weeks	83 (78.3%)	39 (90.7%)	122 (81.9%)
<=168 Weeks	106 (100%)	43 (100%)	149 (100%)
>168 Weeks	77 (72.6%)	35 (81.4%)	112 (75.2%)
<=192 Weeks	106 (100%)	43 (100%)	149 (100%)
>192 Weeks	59 (55.7%)	29 (67.4%)	88 (59.1%)
<=216 Weeks	106 (100%)	43 (100%)	149 (100%)
>216 Weeks	18 (17.0%)	7 (16.3%)	25 (16.8%)

Table 14.3.1.1.1
Overall Summary of Treatment-emergent Adverse Events
Safety Population

	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and percent of subjects with at least one adverse event	103 (97.2%)	42 (97.7%)	145 (97.3%)
Number and percent of subjects with a related adverse event	58 (54.7%)	18 (41.9%)	76 (51.0%)
Number and percent of subjects with a severe adverse event	15 (14.2%)	4 (9.3%)	19 (12.8%)
Number and percent of subjects with a serious adverse event	10 (9.4%)	7 (16.3%)	17 (11.4%)
Number and percent of subjects with a related serious adverse event	0	1 (2.3%)	1 (0.7%)
Number and percent of subjects with an adverse event leading to permanent treatment discontinuation	9 (8.5%)	1 (2.3%)	10 (6.7%)
Number of adverse events	963	434	1397
Number of related adverse events	123	35	158
Number of severe adverse events	25	10	35
Number of serious adverse events	15	10	25
Number of related serious adverse events	0	1	1
Number of adverse events leading to treatment discontinuation	12	2	14

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.1.6
Overall Summary of Adverse Events Occurred >30 Days Past the Last Dose
Safety Population

	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and percent of subjects with at least one adverse event	0	0	0
Number and percent of subjects with a related adverse event	0	0	0
Number and percent of subjects with a severe adverse event	0	0	0
Number and percent of subjects with a serious adverse event	0	0	0
Number and percent of subjects with a related serious adverse event	0	0	0
Number and percent of subjects with an adverse event leading to permanent treatment discontinuation	0	0	0
Number of adverse events	0	0	0
Number of related adverse events	0	0	0
Number of severe adverse events	0	0	0
Number of serious adverse events	0	0	0
Number of related serious adverse events	0	0	0
Number of adverse events leading to treatment discontinuation	0	0	0

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.2.1
Treatment-emergent Adverse Events Related to Study Treatment by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	123:58 (54.7%)	35:18 (41.9%)	158:76 (51.0%)
Blood and lymphatic system disorders	0	1:1 (2.3%)	1:1 (0.7%)
Anaemia	0	1:1 (2.3%)	1:1 (0.7%)
Cardiac disorders	2:2 (1.9%)	0	2:2 (1.3%)
Angina pectoris	1:1 (0.9%)	0	1:1 (0.7%)
Atrial fibrillation	1:1 (0.9%)	0	1:1 (0.7%)
Congenital, familial and genetic disorders	1:1 (0.9%)	0	1:1 (0.7%)
Friedreich's ataxia	1:1 (0.9%)	0	1:1 (0.7%)
Eye disorders	1:1 (0.9%)	0	1:1 (0.7%)
Diplopia	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorders	34:24 (22.6%)	13:10 (23.3%)	47:34 (22.8%)
Nausea	13:12 (11.3%)	5:5 (11.6%)	18:17 (11.4%)
Abdominal pain	5:4 (3.8%)	5:5 (11.6%)	10:9 (6.0%)
Diarrhoea	7:5 (4.7%)	2:2 (4.7%)	9:7 (4.7%)
Gastrooesophageal reflux disease	3:2 (1.9%)	0	3:2 (1.3%)
Constipation	2:2 (1.9%)	0	2:2 (1.3%)
Frequent bowel movements	0	1:1 (2.3%)	1:1 (0.7%)
Breath odour	1:1 (0.9%)	0	1:1 (0.7%)
Defaecation urgency	1:1 (0.9%)	0	1:1 (0.7%)
Dyspepsia	1:1 (0.9%)	0	1:1 (0.7%)
Vomiting	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.2.1
Treatment-emergent Adverse Events Related to Study Treatment by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
General disorders and administration site conditions	9:8 (7.5%)	3:3 (7.0%)	12:11 (7.4%)
Fatigue	5:5 (4.7%)	3:3 (7.0%)	8:8 (5.4%)
Asthenia	3:2 (1.9%)	0	3:2 (1.3%)
Gait disturbance	1:1 (0.9%)	0	1:1 (0.7%)
Investigations	45:28 (26.4%)	8:4 (9.3%)	53:32 (21.5%)
Alanine aminotransferase increased	26:24 (22.6%)	4:2 (4.7%)	30:26 (17.4%)
Aspartate aminotransferase increased	13:10 (9.4%)	1:1 (2.3%)	14:11 (7.4%)
Brain natriuretic peptide increased	3:3 (2.8%)	0	3:3 (2.0%)
Gamma-glutamyltransferase increased	2:2 (1.9%)	0	2:2 (1.3%)
Blood cholesterol increased	0	1:1 (2.3%)	1:1 (0.7%)
Blood glucose increased	0	1:1 (2.3%)	1:1 (0.7%)
Weight decreased	0	1:1 (2.3%)	1:1 (0.7%)
Blood creatine phosphokinase increased	1:1 (0.9%)	0	1:1 (0.7%)
Metabolism and nutrition disorders	4:4 (3.8%)	2:2 (4.7%)	6:6 (4.0%)
Abnormal loss of weight	0	1:1 (2.3%)	1:1 (0.7%)
Folate deficiency	0	1:1 (2.3%)	1:1 (0.7%)
Decreased appetite	1:1 (0.9%)	0	1:1 (0.7%)
Dehydration	1:1 (0.9%)	0	1:1 (0.7%)
Dyslipidaemia	1:1 (0.9%)	0	1:1 (0.7%)
Increased appetite	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal and connective tissue disorders	7:5 (4.7%)	2:1 (2.3%)	9:6 (4.0%)
Myalgia	4:3 (2.8%)	2:1 (2.3%)	6:4 (2.7%)
Muscle spasms	2:2 (1.9%)	0	2:2 (1.3%)
Arthralgia	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.2.1
Treatment-emergent Adverse Events Related to Study Treatment by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Nervous system disorders	13:10 (9.4%)	1:1 (2.3%)	14:11 (7.4%)
Headache	8:8 (7.5%)	1:1 (2.3%)	9:9 (6.0%)
Migraine	2:1 (0.9%)	0	2:1 (0.7%)
Ataxia	1:1 (0.9%)	0	1:1 (0.7%)
Dizziness	1:1 (0.9%)	0	1:1 (0.7%)
Speech disorder	1:1 (0.9%)	0	1:1 (0.7%)
Psychiatric disorders	1:1 (0.9%)	0	1:1 (0.7%)
Insomnia	1:1 (0.9%)	0	1:1 (0.7%)
Reproductive system and breast disorders	2:2 (1.9%)	0	2:2 (1.3%)
Menorrhagia	1:1 (0.9%)	0	1:1 (0.7%)
Menstruation irregular	1:1 (0.9%)	0	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	0	1:1 (2.3%)	1:1 (0.7%)
Pulmonary embolism	0	1:1 (2.3%)	1:1 (0.7%)
Skin and subcutaneous tissue disorders	4:4 (3.8%)	3:2 (4.7%)	7:6 (4.0%)
Alopecia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Acne	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus generalised	0	1:1 (2.3%)	1:1 (0.7%)
Dermatitis psoriasiform	1:1 (0.9%)	0	1:1 (0.7%)
Night sweats	1:1 (0.9%)	0	1:1 (0.7%)
Rash macular	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.2.1
Treatment-emergent Adverse Events Related to Study Treatment by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Vascular disorders	0	1:1 (2.3%)	1:1 (0.7%)
Deep vein thrombosis	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.2.4
Serious Related Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	0	1:1 (2.3%)	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	0	1:1 (2.3%)	1:1 (0.7%)
Pulmonary embolism	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Subjects	Mild	30 (28.3%)	6 (14.0%)	36 (24.2%)
	Moderate	58 (54.7%)	32 (74.4%)	90 (60.4%)
	Severe	15 (14.2%)	4 (9.3%)	19 (12.8%)
Blood and lymphatic system disorders	Mild	1 (0.9%)	3 (7.0%)	4 (2.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Anaemia	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Iron deficiency anaemia	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Lymphadenopathy	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Cardiac disorders	Mild	5 (4.7%)	2 (4.7%)	7 (4.7%)
	Moderate	5 (4.7%)	1 (2.3%)	6 (4.0%)
	Severe	1 (0.9%)	1 (2.3%)	2 (1.3%)
Angina pectoris	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Atrial fibrillation	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Cardiac failure congestive	Mild	0	0	0
	Moderate	0	0	0
	Severe	0	1 (2.3%)	1 (0.7%)
Cardiomyopathy	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Myocarditis	Mild	0	0	0
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Cardiac disorders, continued...				
Palpitations	Mild	2 (1.9%)	2 (4.7%)	4 (2.7%)
	Moderate	0	0	0
	Severe	0	0	0
Sinus tachycardia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	1 (2.3%)	1 (0.7%)
Tachycardia	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Ventricular hypertrophy	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Congenital, familial and genetic disorders	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Friedreich's ataxia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Congenital, familial and genetic disorders, continued...				
Hereditary haemochromatosis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Ear and labyrinth disorders	Mild	4 (3.8%)	2 (4.7%)	6 (4.0%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Deafness	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Ear haemorrhage	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Ear pain	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Hearing impaired	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Ear and labyrinth disorders, continued...				
Hypoacusis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tinnitus	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Endocrine disorders	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Basedow's disease	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Eye disorders	Mild	3 (2.8%)	3 (7.0%)	6 (4.0%)
	Moderate	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Eye disorders, continued...				
Altered visual depth perception	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Blepharitis	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Blepharospasm	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Diplopia	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Dry eye	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Gastrointestinal disorders	Mild	44 (41.5%)	15 (34.9%)	59 (39.6%)
	Moderate	14 (13.2%)	10 (23.3%)	24 (16.1%)
	Severe	2 (1.9%)	2 (4.7%)	4 (2.7%)

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...				
Abdominal discomfort	Mild	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Abdominal distension	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Abdominal pain	Mild	7 (6.6%)	4 (9.3%)	11 (7.4%)
	Moderate	2 (1.9%)	3 (7.0%)	5 (3.4%)
	Severe	0	0	0
Abdominal pain lower	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	1 (2.3%)	1 (0.7%)
Abdominal pain upper	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Anal fissure	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...				
Aphthous stomatitis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Barrett's oesophagus	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Bowel movement irregularity	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Breath odour	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Cheilitis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Constipation	Mild	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Moderate	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Severe	0	1 (2.3%)	1 (0.7%)

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Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...				
Defaecation urgency	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Dental discomfort	Mild	0	0	0
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Diarrhoea	Mild	15 (14.2%)	3 (7.0%)	18 (12.1%)
	Moderate	2 (1.9%)	2 (4.7%)	4 (2.7%)
	Severe	0	0	0
Dry mouth	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Dyspepsia	Mild	6 (5.7%)	1 (2.3%)	7 (4.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dysphagia	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0

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Gastrointestinal disorders, continued...				
Faecal incontinence	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Faecaloma	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Faeces hard	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Faeces pale	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Frequent bowel movements	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Gastrointestinal disorder	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Gastrointestinal disorders, continued...				
Gastrooesophageal reflux disease	Mild	7 (6.6%)	4 (9.3%)	11 (7.4%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Gingival bleeding	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Haematochezia	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Haemorrhoids	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Melaena	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Nausea	Mild	16 (15.1%)	7 (16.3%)	23 (15.4%)
	Moderate	6 (5.7%)	0	6 (4.0%)
	Severe	1 (0.9%)	0	1 (0.7%)

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Gastrointestinal disorders, continued...				
Rectal polyp	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Stomatitis	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Tongue coated	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tooth disorder	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Tooth impacted	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Toothache	Mild	1 (0.9%)	3 (7.0%)	4 (2.7%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0

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Gastrointestinal disorders, continued...				
Traumatic tooth displacement	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Vomiting	Mild	4 (3.8%)	4 (9.3%)	8 (5.4%)
	Moderate	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Severe	0	0	0
General disorders and administration site conditions	Mild	30 (28.3%)	11 (25.6%)	41 (27.5%)
	Moderate	7 (6.6%)	1 (2.3%)	8 (5.4%)
	Severe	1 (0.9%)	2 (4.7%)	3 (2.0%)
Adverse drug reaction	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Asthenia	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	2 (4.7%)	2 (1.3%)
Chest discomfort	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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General disorders and administration site conditions, continued...				
Chest pain	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Cyst	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Facial pain	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Fatigue	Mild	10 (9.4%)	5 (11.6%)	15 (10.1%)
	Moderate	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Severe	0	0	0
Feeling abnormal	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Feeling hot	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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General disorders and administration site conditions, continued...				
Gait disturbance	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Inflammation	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Influenza like illness	Mild	3 (2.8%)	2 (4.7%)	5 (3.4%)
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Irritability	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Malaise	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Non-cardiac chest pain	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0

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General disorders and administration site conditions, continued...							
Oedema peripheral	Mild	4	(3.8%)	1	(2.3%)	5	(3.4%)
	Moderate	0		0		0	
	Severe	0		0		0	
Pain	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	1	(0.9%)	0		1	(0.7%)
	Severe	0		0		0	
Pyrexia	Mild	9	(8.5%)	2	(4.7%)	11	(7.4%)
	Moderate	0		0		0	
	Severe	0		0		0	
Hepatobiliary disorders	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		1	(2.3%)	1	(0.7%)
	Severe	0		0		0	
Cholelithiasis	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		1	(2.3%)	1	(0.7%)
	Severe	0		0		0	

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Immune system disorders	Mild	3 (2.8%)	1 (2.3%)	4 (2.7%)
	Moderate	0	0	0
	Severe	0	0	0
Hypersensitivity	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Seasonal allergy	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Infections and infestations	Mild	52 (49.1%)	23 (53.5%)	75 (50.3%)
	Moderate	13 (12.3%)	13 (30.2%)	26 (17.4%)
	Severe	5 (4.7%)	0	5 (3.4%)
Body tinea	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Infections and infestations, continued...				
Bronchitis	Mild	5 (4.7%)	1 (2.3%)	6 (4.0%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Chlamydial infection	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Corona virus infection	Mild	38 (35.8%)	13 (30.2%)	51 (34.2%)
	Moderate	7 (6.6%)	9 (20.9%)	16 (10.7%)
	Severe	4 (3.8%)	0	4 (2.7%)
Ear infection	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Escherichia infection	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Eye infection	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0

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Infections and infestations, continued...				
Fungal infection	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Furuncle	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Gastroenteritis	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Gastroenteritis norovirus	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Gastroenteritis viral	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Gastrointestinal infection	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Infections and infestations, continued...				
Hordeolum	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Influenza	Mild	6 (5.7%)	4 (9.3%)	10 (6.7%)
	Moderate	4 (3.8%)	0	4 (2.7%)
	Severe	1 (0.9%)	0	1 (0.7%)
Laryngitis	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Localised infection	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Lower respiratory tract infection	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Nasopharyngitis	Mild	4 (3.8%)	6 (14.0%)	10 (6.7%)
	Moderate	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Severe	0	0	0

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Infections and infestations, continued...				
Onychomycosis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Otitis externa	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Otitis media	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Paronychia	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Pharyngitis	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Pilonidal cyst	Mild	0	0	0
	Moderate	0	2 (4.7%)	2 (1.3%)
	Severe	0	0	0

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Infections and infestations, continued...				
Pneumonia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Postoperative wound infection	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Purulence	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Rash pustular	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Respiratory tract infection	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Rhinitis	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0

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Infections and infestations, continued...				
Sepsis	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Sinusitis	Mild	4 (3.8%)	2 (4.7%)	6 (4.0%)
	Moderate	0	0	0
	Severe	0	0	0
Staphylococcal infection	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tinea cruris	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tinea versicolour	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tonsillitis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Infections and infestations, continued...				
Tooth abscess	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Upper respiratory tract infection	Mild	17 (16.0%)	10 (23.3%)	27 (18.1%)
	Moderate	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Severe	0	0	0
Urinary tract infection	Mild	5 (4.7%)	4 (9.3%)	9 (6.0%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Viral infection	Mild	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Viral rhinitis	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Viral upper respiratory tract infection	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Infections and infestations, continued...				
Vulvovaginal mycotic infection	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Wound infection	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Injury, poisoning and procedural complications	Mild	43 (40.6%)	12 (27.9%)	55 (36.9%)
	Moderate	25 (23.6%)	14 (32.6%)	39 (26.2%)
	Severe	3 (2.8%)	0	3 (2.0%)
Anaemia postoperative	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Ankle fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Arthropod bite	Mild	0	0	0
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0

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Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Avulsion fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Back injury	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Chillblains	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Clavicle fracture	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Concussion	Mild	3 (2.8%)	1 (2.3%)	4 (2.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Contusion	Mild	17 (16.0%)	4 (9.3%)	21 (14.1%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0

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Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Excoriation	Mild	17 (16.0%)	4 (9.3%)	21 (14.1%)
	Moderate	0	0	0
	Severe	0	0	0
Eye injury	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Facial bones fracture	Mild	0	0	0
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Fibula fracture	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	1 (0.9%)	0	1 (0.7%)
Foot fracture	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	3 (2.8%)	0	3 (2.0%)
	Severe	0	0	0
Hand fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Severe	0	0	0

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Head injury	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Hip fracture	Mild	0	0	0
	Moderate	0	0	0
	Severe	2 (1.9%)	0	2 (1.3%)
Humerus fracture	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Injury	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Joint dislocation	Mild	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Joint injury	Mild	4 (3.8%)	3 (7.0%)	7 (4.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Laceration	Mild	10 (9.4%)	4 (9.3%)	14 (9.4%)
	Moderate	3 (2.8%)	2 (4.7%)	5 (3.4%)
	Severe	0	0	0
Ligament rupture	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Ligament sprain	Mild	14 (13.2%)	2 (4.7%)	16 (10.7%)
	Moderate	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Severe	0	0	0
Limb injury	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Lower limb fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Mouth injury	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Muscle strain	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Periorbital haematoma	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Post-traumatic neck syndrome	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Procedural pain	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Rib fracture	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Soft tissue injury	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

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Injury, poisoning and procedural complications, continued...				
Spinal column injury	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Stress fracture	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Sunburn	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Tendon rupture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Thermal burn	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Tibia fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

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Injury, poisoning and procedural complications, continued...				
Tooth fracture	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	3 (2.8%)	0	3 (2.0%)
	Severe	0	0	0
Tooth injury	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Traumatic haematoma	Mild	3 (2.8%)	0	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Upper limb fracture	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Vaccination complication	Mild	10 (9.4%)	7 (16.3%)	17 (11.4%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Wound	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...				
Wrist fracture	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Investigations	Mild	27 (25.5%)	9 (20.9%)	36 (24.2%)
	Moderate	12 (11.3%)	3 (7.0%)	15 (10.1%)
	Severe	1 (0.9%)	0	1 (0.7%)
Alanine aminotransferase increased	Mild	18 (17.0%)	2 (4.7%)	20 (13.4%)
	Moderate	5 (4.7%)	2 (4.7%)	7 (4.7%)
	Severe	1 (0.9%)	0	1 (0.7%)
Aspartate aminotransferase increased	Mild	9 (8.5%)	0	9 (6.0%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Blood alkaline phosphatase increased	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Blood cholesterol increased	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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Investigations, continued...				
Blood creatine phosphokinase increased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Blood folate decreased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Blood glucose increased	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Blood triglycerides increased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Blood urea increased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Brain natriuretic peptide increased	Mild	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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Investigations, continued...				
Ceruloplasmin increased	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Electrocardiogram T wave inversion	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Gamma-glutamyltransferase increased	Mild	3 (2.8%)	0	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Glomerular filtration rate decreased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Glucose tolerance test abnormal	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Heart rate increased	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Safety Population

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Investigations, continued...				
N-terminal prohormone brain natriuretic peptide increased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Serum ferritin decreased	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Serum ferritin increased	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Troponin increased	Mild	0	0	0
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Vitamin D decreased	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Weight decreased	Mild	3 (2.8%)	4 (9.3%)	7 (4.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Safety Population

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Investigations, continued...				
Weight increased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
White blood cell count decreased	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Metabolism and nutrition disorders	Mild	10 (9.4%)	6 (14.0%)	16 (10.7%)
	Moderate	5 (4.7%)	0	5 (3.4%)
	Severe	0	0	0
Abnormal loss of weight	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Decreased appetite	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Dehydration	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0

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Safety Population

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Metabolism and nutrition disorders, continued...				
Diabetes mellitus	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dyslipidaemia	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Folate deficiency	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Hypercholesterolaemia	Mild	3 (2.8%)	0	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Increased appetite	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Iron deficiency	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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Metabolism and nutrition disorders, continued...				
Type 2 diabetes mellitus	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Vitamin B12 deficiency	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Vitamin D deficiency	Mild	3 (2.8%)	2 (4.7%)	5 (3.4%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Musculoskeletal and connective tissue disorders	Mild	25 (23.6%)	14 (32.6%)	39 (26.2%)
	Moderate	21 (19.8%)	5 (11.6%)	26 (17.4%)
	Severe	2 (1.9%)	2 (4.7%)	4 (2.7%)
Arthralgia	Mild	12 (11.3%)	4 (9.3%)	16 (10.7%)
	Moderate	8 (7.5%)	2 (4.7%)	10 (6.7%)
	Severe	0	0	0
Arthritis	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Safety Population

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Musculoskeletal and connective tissue disorders, continued...				
Back pain	Mild	3 (2.8%)	4 (9.3%)	7 (4.7%)
	Moderate	5 (4.7%)	1 (2.3%)	6 (4.0%)
	Severe	1 (0.9%)	2 (4.7%)	3 (2.0%)
Bursitis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Flank pain	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Intervertebral disc protrusion	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Limb discomfort	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Muscle atrophy	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Safety Population

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Musculoskeletal and connective tissue disorders, continued...							
Muscle spasms	Mild	9	(8.5%)	2	(4.7%)	11	(7.4%)
	Moderate	7	(6.6%)	1	(2.3%)	8	(5.4%)
	Severe	0		0		0	
Muscle tightness	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	1	(0.9%)	0		1	(0.7%)
Muscular weakness	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Musculoskeletal chest pain	Mild	0		2	(4.7%)	2	(1.3%)
	Moderate	0		1	(2.3%)	1	(0.7%)
	Severe	0		0		0	
Musculoskeletal pain	Mild	4	(3.8%)	2	(4.7%)	6	(4.0%)
	Moderate	2	(1.9%)	0		2	(1.3%)
	Severe	0		0		0	
Musculoskeletal stiffness	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	

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Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Musculoskeletal and connective tissue disorders, continued...				
Myalgia	Mild	4 (3.8%)	2 (4.7%)	6 (4.0%)
	Moderate	0	0	0
	Severe	0	0	0
Neck pain	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Osteoporosis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Pain in extremity	Mild	5 (4.7%)	3 (7.0%)	8 (5.4%)
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Pain in jaw	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Rotator cuff syndrome	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Musculoskeletal and connective tissue disorders, continued...				
Scoliosis	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Sensation of heaviness	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Spinal disorder	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Synovial cyst	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Mild	1 (0.9%)	4 (9.3%)	5 (3.4%)
	Moderate	3 (2.8%)	0	3 (2.0%)
	Severe	0	0	0
Benign neoplasm of eyelid	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Neoplasms benign, malignant and unspecified (incl cysts and polyps), continued...				
Haemangioma of skin	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Morton's neuroma	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Pituitary tumour benign	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Skin papilloma	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Uterine leiomyoma	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Nervous system disorders	Mild	20 (18.9%)	12 (27.9%)	32 (21.5%)
	Moderate	13 (12.3%)	5 (11.6%)	18 (12.1%)
	Severe	2 (1.9%)	1 (2.3%)	3 (2.0%)

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Nervous system disorders, continued...				
Ataxia	Mild	0	0	0
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Balance disorder	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Convulsion	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Disturbance in attention	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dizziness	Mild	5 (4.7%)	3 (7.0%)	8 (5.4%)
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Dysgeusia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Safety Population

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Nervous system disorders, continued...				
Epilepsy	Mild	0	0	0
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Headache	Mild	14 (13.2%)	5 (11.6%)	19 (12.8%)
	Moderate	6 (5.7%)	1 (2.3%)	7 (4.7%)
	Severe	0	0	0
Hyperaesthesia	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Hypoaesthesia	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Loss of consciousness	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Migraine	Mild	0	0	0
	Moderate	4 (3.8%)	0	4 (2.7%)
	Severe	0	0	0

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Nervous system disorders, continued...				
Migraine with aura	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Muscle spasticity	Mild	1 (0.9%)	2 (4.7%)	3 (2.0%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Neuralgia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Neuropathy peripheral	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	2 (4.7%)	2 (1.3%)
	Severe	0	0	0
Paraesthesia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Post-traumatic headache	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Nervous system disorders, continued...							
Presyncope	Mild	0		0		0	
	Moderate	1	(0.9%)	1	(2.3%)	2	(1.3%)
	Severe	0		0		0	
Restless legs syndrome	Mild	1	(0.9%)	2	(4.7%)	3	(2.0%)
	Moderate	0		0		0	
	Severe	0		0		0	
Somnolence	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Speech disorder	Mild	0		0		0	
	Moderate	2	(1.9%)	0		2	(1.3%)
	Severe	0		0		0	
Syncope	Mild	0		0		0	
	Moderate	0		0		0	
	Severe	0		1	(2.3%)	1	(0.7%)
Tremor	Mild	0		0		0	
	Moderate	0		1	(2.3%)	1	(0.7%)
	Severe	0		0		0	

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Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Psychiatric disorders	Mild	11 (10.4%)	7 (16.3%)	18 (12.1%)
	Moderate	5 (4.7%)	3 (7.0%)	8 (5.4%)
	Severe	3 (2.8%)	0	3 (2.0%)
Abnormal dreams	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Anxiety	Mild	4 (3.8%)	0	4 (2.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Attention deficit/hyperactivity disorder	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Bipolar disorder	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Confusional state	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Psychiatric disorders, continued...				
Delirium	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Depression	Mild	5 (4.7%)	5 (11.6%)	10 (6.7%)
	Moderate	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Severe	2 (1.9%)	0	2 (1.3%)
Initial insomnia	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Insomnia	Mild	4 (3.8%)	1 (2.3%)	5 (3.4%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Insomnia related to another mental condition	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Libido decreased	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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Psychiatric disorders, continued...				
Major depression	Mild	0	0	0
	Moderate	0	0	0
	Severe	1 (0.9%)	0	1 (0.7%)
Mood swings	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Suicidal behaviour	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Suicidal ideation	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Suicide attempt	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	1 (0.9%)	0	1 (0.7%)
Renal and urinary disorders	Mild	8 (7.5%)	4 (9.3%)	12 (8.1%)
	Moderate	6 (5.7%)	1 (2.3%)	7 (4.7%)
	Severe	1 (0.9%)	0	1 (0.7%)

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Safety Population

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Renal and urinary disorders, continued...				
Glycosuria	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Haematuria	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Incontinence	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Micturition urgency	Mild	3 (2.8%)	3 (7.0%)	6 (4.0%)
	Moderate	3 (2.8%)	0	3 (2.0%)
	Severe	0	0	0
Nephrolithiasis	Mild	0	0	0
	Moderate	4 (3.8%)	0	4 (2.7%)
	Severe	1 (0.9%)	0	1 (0.7%)
Nocturia	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Renal and urinary disorders, continued...				
Pollakiuria	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Renal colic	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Renal cyst	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Urinary incontinence	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Urinary retention	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Urine odour abnormal	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Safety Population

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Reproductive system and breast disorders	Mild	9 (8.5%)	6 (14.0%)	15 (10.1%)
	Moderate	4 (3.8%)	2 (4.7%)	6 (4.0%)
	Severe	0	0	0
Amenorrhoea	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Breast tenderness	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dysmenorrhoea	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Erectile dysfunction	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Mammary duct ectasia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

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Reproductive system and breast disorders, continued...				
Menorrhagia	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Menstruation irregular	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0
Metrorrhagia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Ovarian cyst	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Pelvic pain	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Polycystic ovaries	Mild	0	0	0
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0

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Reproductive system and breast disorders, continued...				
Polymenorrhoea	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Prostatitis	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Vaginal laceration	Mild	0	0	0
	Moderate	2 (1.9%)	0	2 (1.3%)
	Severe	0	0	0
Vulvovaginal burning sensation	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Vulvovaginal pruritus	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Respiratory, thoracic and mediastinal disorders	Mild	22 (20.8%)	7 (16.3%)	29 (19.5%)
	Moderate	2 (1.9%)	3 (7.0%)	5 (3.4%)
	Severe	0	1 (2.3%)	1 (0.7%)

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Respiratory, thoracic and mediastinal disorders, continued...							
Asthma	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Choking	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Cough	Mild	10	(9.4%)	3	(7.0%)	13	(8.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Dysphonia	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Dyspnoea	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		1	(2.3%)	1	(0.7%)
	Severe	0		1	(2.3%)	1	(0.7%)
Epistaxis	Mild	5	(4.7%)	1	(2.3%)	6	(4.0%)
	Moderate	1	(0.9%)	0		1	(0.7%)
	Severe	0		0		0	

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)		Omaveloxolone - Omaveloxolone (N=43)		Overall Omaveloxolone (N=149)	
Respiratory, thoracic and mediastinal disorders, continued...							
Nasal congestion	Mild	3	(2.8%)	0		3	(2.0%)
	Moderate	0		0		0	
	Severe	0		0		0	
Nasal disorder	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Nasal obstruction	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Nasal septum deviation	Mild	0		0		0	
	Moderate	1	(0.9%)	0		1	(0.7%)
	Severe	0		0		0	
Nasal turbinate hypertrophy	Mild	0		0		0	
	Moderate	1	(0.9%)	0		1	(0.7%)
	Severe	0		0		0	
Oropharyngeal pain	Mild	3	(2.8%)	0		3	(2.0%)
	Moderate	0		0		0	
	Severe	0		0		0	

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Respiratory, thoracic and mediastinal disorders, continued...				
Pulmonary congestion	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Pulmonary embolism	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Respiratory failure	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Rhinitis allergic	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Rhinorrhoea	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Sinus congestion	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Respiratory, thoracic and mediastinal disorders, continued...				
Sleep apnoea syndrome	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Upper-airway cough syndrome	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Wheezing	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Skin and subcutaneous tissue disorders	Mild	22 (20.8%)	9 (20.9%)	31 (20.8%)
	Moderate	5 (4.7%)	4 (9.3%)	9 (6.0%)
	Severe	0	0	0
Acne	Mild	0	2 (4.7%)	2 (1.3%)
	Moderate	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Severe	0	0	0
Alopecia	Mild	2 (1.9%)	1 (2.3%)	3 (2.0%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...				
Blister	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dandruff	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dermal cyst	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dermatitis contact	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Dermatitis psoriasiform	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Dry skin	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)		Omaveloxolone - Omaveloxolone (N=43)		Overall Omaveloxolone (N=149)	
Skin and subcutaneous tissue disorders, continued...							
Ecchymosis	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Eczema	Mild	3	(2.8%)	3	(7.0%)	6	(4.0%)
	Moderate	0		0		0	
	Severe	0		0		0	
Erythema	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Heat rash	Mild	0		1	(2.3%)	1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	
Hyperhidrosis	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	2	(1.9%)	0		2	(1.3%)
	Severe	0		0		0	
Ingrowing nail	Mild	1	(0.9%)	0		1	(0.7%)
	Moderate	0		0		0	
	Severe	0		0		0	

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...				
Milia	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Nail discolouration	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Night sweats	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Petechiae	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Pruritus	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Pruritus generalised	Mild	0	1 (2.3%)	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...				
Psoriasis	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Rash macular	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Rash maculo-papular	Mild	1 (0.9%)	1 (2.3%)	2 (1.3%)
	Moderate	0	0	0
	Severe	0	0	0
Rosacea	Mild	0	0	0
	Moderate	0	1 (2.3%)	1 (0.7%)
	Severe	0	0	0
Skin disorder	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Skin swelling	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...				
Skin ulcer	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Swelling face	Mild	1 (0.9%)	0	1 (0.7%)
	Moderate	0	0	0
	Severe	0	0	0
Urticaria	Mild	2 (1.9%)	0	2 (1.3%)
	Moderate	1 (0.9%)	0	1 (0.7%)
	Severe	0	0	0
Vascular disorders	Mild	6 (5.7%)	1 (2.3%)	7 (4.7%)
	Moderate	0	2 (4.7%)	2 (1.3%)
	Severe	0	0	0
Deep vein thrombosis	Mild	0	0	0
	Moderate	0	2 (4.7%)	2 (1.3%)
	Severe	0	0	0
Haematoma	Mild	3 (2.8%)	1 (2.3%)	4 (2.7%)
	Moderate	0	0	0
	Severe	0	0	0

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.3.1
Treatment-emergent Adverse Events by System Organ Class and Preferred Term by Worst Severity
Safety Population

System Organ Class Preferred Term	Severity	Placebo - Omaveloxolone (N=106)		Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)	
Vascular disorders, continued...						
Hypertension	Mild	2	(1.9%)	0	2	(1.3%)
	Moderate	0		0	0	
	Severe	0		0	0	
Hypotension	Mild	1	(0.9%)	0	1	(0.7%)
	Moderate	0		0	0	
	Severe	0		0	0	

The number of patients who experienced at least one adverse event at that maximum severity is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are also presented alphabetically.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.4.1
Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	15:10 (9.4%)	10:7 (16.3%)	25:17 (11.4%)
Cardiac disorders	1:1 (0.9%)	2:1 (2.3%)	3:2 (1.3%)
Cardiac failure congestive	0	1:1 (2.3%)	1:1 (0.7%)
Sinus tachycardia	0	1:1 (2.3%)	1:1 (0.7%)
Myocarditis	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorders	0	2:2 (4.7%)	2:2 (1.3%)
Constipation	0	1:1 (2.3%)	1:1 (0.7%)
Diarrhoea	0	1:1 (2.3%)	1:1 (0.7%)
Infections and infestations	3:2 (1.9%)	2:2 (4.7%)	5:4 (2.7%)
Pilonidal cyst	0	1:1 (2.3%)	1:1 (0.7%)
Upper respiratory tract infection	0	1:1 (2.3%)	1:1 (0.7%)
Gastroenteritis norovirus	1:1 (0.9%)	0	1:1 (0.7%)
Sepsis	1:1 (0.9%)	0	1:1 (0.7%)
Viral upper respiratory tract infection	1:1 (0.9%)	0	1:1 (0.7%)
Injury, poisoning and procedural complications	4:4 (3.8%)	0	4:4 (2.7%)
Hip fracture	2:2 (1.9%)	0	2:2 (1.3%)
Ankle fracture	1:1 (0.9%)	0	1:1 (0.7%)
Facial bones fracture	1:1 (0.9%)	0	1:1 (0.7%)
Investigations	1:1 (0.9%)	0	1:1 (0.7%)
Troponin increased	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.
Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.4.1
Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Musculoskeletal and connective tissue disorders	0	1:1 (2.3%)	1:1 (0.7%)
Back pain	0	1:1 (2.3%)	1:1 (0.7%)
Nervous system disorders	1:1 (0.9%)	0	1:1 (0.7%)
Epilepsy	1:1 (0.9%)	0	1:1 (0.7%)
Psychiatric disorders	5:2 (1.9%)	0	5:2 (1.3%)
Suicide attempt	2:2 (1.9%)	0	2:2 (1.3%)
Major depression	2:1 (0.9%)	0	2:1 (0.7%)
Depression	1:1 (0.9%)	0	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	0	3:3 (7.0%)	3:3 (2.0%)
Dyspnoea	0	1:1 (2.3%)	1:1 (0.7%)
Pulmonary embolism	0	1:1 (2.3%)	1:1 (0.7%)
Respiratory failure	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.
Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.5.1

Treatment-emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term

Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	12:9 (8.5%)	2:1 (2.3%)	14:10 (6.7%)
Gastrointestinal disorders	2:1 (0.9%)	2:1 (2.3%)	4:2 (1.3%)
Abdominal pain	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Frequent bowel movements	0	1:1 (2.3%)	1:1 (0.7%)
Diarrhoea	1:1 (0.9%)	0	1:1 (0.7%)
General disorders and administration site conditions	2:2 (1.9%)	0	2:2 (1.3%)
Fatigue	2:2 (1.9%)	0	2:2 (1.3%)
Investigations	5:4 (3.8%)	0	5:4 (2.7%)
Alanine aminotransferase increased	4:4 (3.8%)	0	4:4 (2.7%)
Aspartate aminotransferase increased	1:1 (0.9%)	0	1:1 (0.7%)
Psychiatric disorders	1:1 (0.9%)	0	1:1 (0.7%)
Bipolar disorder	1:1 (0.9%)	0	1:1 (0.7%)
Reproductive system and breast disorders	1:1 (0.9%)	0	1:1 (0.7%)
Menstruation irregular	1:1 (0.9%)	0	1:1 (0.7%)
Skin and subcutaneous tissue disorders	1:1 (0.9%)	0	1:1 (0.7%)
Alopecia	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	963:103 (97.2%)	434:42 (97.7%)	1397:145 (97.3%)
Blood and lymphatic system disorders	2:2 (1.9%)	5:3 (7.0%)	7:5 (3.4%)
Iron deficiency anaemia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Anaemia	0	3:2 (4.7%)	3:2 (1.3%)
Lymphadenopathy	0	1:1 (2.3%)	1:1 (0.7%)
Cardiac disorders	14:11 (10.4%)	5:4 (9.3%)	19:15 (10.1%)
Palpitations	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Sinus tachycardia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Angina pectoris	3:3 (2.8%)	0	3:3 (2.0%)
Cardiomyopathy	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Myocarditis	2:1 (0.9%)	0	2:1 (0.7%)
Tachycardia	2:1 (0.9%)	0	2:1 (0.7%)
Cardiac failure congestive	0	1:1 (2.3%)	1:1 (0.7%)
Atrial fibrillation	1:1 (0.9%)	0	1:1 (0.7%)
Ventricular hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)
Congenital, familial and genetic disorders	2:2 (1.9%)	0	2:2 (1.3%)
Friedreich's ataxia	1:1 (0.9%)	0	1:1 (0.7%)
Hereditary haemochromatosis	1:1 (0.9%)	0	1:1 (0.7%)
Ear and labyrinth disorders	6:5 (4.7%)	2:2 (4.7%)	8:7 (4.7%)
Deafness	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Ear haemorrhage	1:1 (0.9%)	0	1:1 (0.7%)
Ear pain	1:1 (0.9%)	0	1:1 (0.7%)
Hearing impaired	1:1 (0.9%)	0	1:1 (0.7%)
Hypoacusis	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Ear and labyrinth disorders, continued...			
Tinnitus	1:1 (0.9%)	0	1:1 (0.7%)
Endocrine disorders	0	1:1 (2.3%)	1:1 (0.7%)
Basedow's disease	0	1:1 (2.3%)	1:1 (0.7%)
Eye disorders	5:4 (3.8%)	5:5 (11.6%)	10:9 (6.0%)
Diplopia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Blepharitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Blepharospasm	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dry eye	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Altered visual depth perception	0	1:1 (2.3%)	1:1 (0.7%)
Gastrointestinal disorders	120:60 (56.6%)	61:27 (62.8%)	181:87 (58.4%)
Nausea	29:23 (21.7%)	7:7 (16.3%)	36:30 (20.1%)
Diarrhoea	21:17 (16.0%)	6:5 (11.6%)	27:22 (14.8%)
Abdominal pain	12:9 (8.5%)	8:7 (16.3%)	20:16 (10.7%)
Vomiting	8:8 (7.5%)	6:5 (11.6%)	14:13 (8.7%)
Gastrooesophageal reflux disease	8:7 (6.6%)	5:5 (11.6%)	13:12 (8.1%)
Constipation	5:5 (4.7%)	5:4 (9.3%)	10:9 (6.0%)
Dyspepsia	6:6 (5.7%)	1:1 (2.3%)	7:7 (4.7%)
Toothache	2:2 (1.9%)	4:4 (9.3%)	6:6 (4.0%)
Haemorrhoids	3:2 (1.9%)	2:2 (4.7%)	5:4 (2.7%)
Abdominal discomfort	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Abdominal pain upper	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Stomatitis	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Dysphagia	0	2:2 (4.7%)	2:2 (1.3%)
Tooth disorder	0	2:2 (4.7%)	2:2 (1.3%)
Abdominal pain lower	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Breath odour	2:2 (1.9%)	0	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...			
Defaecation urgency	2:2 (1.9%)	0	2:2 (1.3%)
Dry mouth	2:2 (1.9%)	0	2:2 (1.3%)
Cheilitis	2:1 (0.9%)	0	2:1 (0.7%)
Anal fissure	0	1:1 (2.3%)	1:1 (0.7%)
Barrett's oesophagus	0	1:1 (2.3%)	1:1 (0.7%)
Bowel movement irregularity	0	1:1 (2.3%)	1:1 (0.7%)
Faecal incontinence	0	1:1 (2.3%)	1:1 (0.7%)
Faecaloma	0	1:1 (2.3%)	1:1 (0.7%)
Frequent bowel movements	0	1:1 (2.3%)	1:1 (0.7%)
Rectal polyp	0	1:1 (2.3%)	1:1 (0.7%)
Tooth impacted	0	1:1 (2.3%)	1:1 (0.7%)
Abdominal distension	1:1 (0.9%)	0	1:1 (0.7%)
Aphthous stomatitis	1:1 (0.9%)	0	1:1 (0.7%)
Dental discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Faeces hard	1:1 (0.9%)	0	1:1 (0.7%)
Faeces pale	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Gingival bleeding	1:1 (0.9%)	0	1:1 (0.7%)
Haematochezia	1:1 (0.9%)	0	1:1 (0.7%)
Melaena	1:1 (0.9%)	0	1:1 (0.7%)
Tongue coated	1:1 (0.9%)	0	1:1 (0.7%)
Traumatic tooth displacement	1:1 (0.9%)	0	1:1 (0.7%)
General disorders and administration site conditions	50:38 (35.8%)	19:14 (32.6%)	69:52 (34.9%)
Fatigue	14:14 (13.2%)	7:6 (14.0%)	21:20 (13.4%)
Pyrexia	10:9 (8.5%)	2:2 (4.7%)	12:11 (7.4%)
Influenza like illness	5:4 (3.8%)	2:2 (4.7%)	7:6 (4.0%)
Asthenia	4:3 (2.8%)	2:2 (4.7%)	6:5 (3.4%)
Oedema peripheral	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
General disorders and administration site conditions, continued...			
Non-cardiac chest pain	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Cyst	3:2 (1.9%)	0	3:2 (1.3%)
Pain	2:2 (1.9%)	0	2:2 (1.3%)
Adverse drug reaction	0	1:1 (2.3%)	1:1 (0.7%)
Chest pain	0	1:1 (2.3%)	1:1 (0.7%)
Feeling abnormal	0	1:1 (2.3%)	1:1 (0.7%)
Irritability	0	1:1 (2.3%)	1:1 (0.7%)
Chest discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Facial pain	1:1 (0.9%)	0	1:1 (0.7%)
Feeling hot	1:1 (0.9%)	0	1:1 (0.7%)
Gait disturbance	1:1 (0.9%)	0	1:1 (0.7%)
Inflammation	1:1 (0.9%)	0	1:1 (0.7%)
Malaise	1:1 (0.9%)	0	1:1 (0.7%)
Hepatobiliary disorders	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Cholelithiasis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Immune system disorders	3:3 (2.8%)	2:1 (2.3%)	5:4 (2.7%)
Seasonal allergy	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Hypersensitivity	1:1 (0.9%)	0	1:1 (0.7%)
Infections and infestations	163:70 (66.0%)	92:36 (83.7%)	255:106 (71.1%)
Corona virus infection	56:49 (46.2%)	25:22 (51.2%)	81:71 (47.7%)
Upper respiratory tract infection	26:18 (17.0%)	19:12 (27.9%)	45:30 (20.1%)
Influenza	14:11 (10.4%)	4:4 (9.3%)	18:15 (10.1%)
Nasopharyngitis	8:6 (5.7%)	9:7 (16.3%)	17:13 (8.7%)
Urinary tract infection	6:6 (5.7%)	6:5 (11.6%)	12:11 (7.4%)
Bronchitis	6:6 (5.7%)	1:1 (2.3%)	7:7 (4.7%)
Sinusitis	7:4 (3.8%)	2:2 (4.7%)	9:6 (4.0%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Infections and infestations, continued...			
Viral infection	2:1 (0.9%)	2:2 (4.7%)	4:3 (2.0%)
Gastroenteritis viral	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Rhinitis	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Pilonidal cyst	0	5:2 (4.7%)	5:2 (1.3%)
Tonsillitis	3:2 (1.9%)	0	3:2 (1.3%)
Paronychia	0	2:2 (4.7%)	2:2 (1.3%)
Chlamydial infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Ear infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Gastroenteritis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Pneumonia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Viral rhinitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Eye infection	2:2 (1.9%)	0	2:2 (1.3%)
Gastroenteritis norovirus	2:2 (1.9%)	0	2:2 (1.3%)
Lower respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Otitis externa	4:1 (0.9%)	0	4:1 (0.7%)
Rash pustular	2:1 (0.9%)	0	2:1 (0.7%)
Tinea versicolour	2:1 (0.9%)	0	2:1 (0.7%)
Body tinea	0	1:1 (2.3%)	1:1 (0.7%)
Escherichia infection	0	1:1 (2.3%)	1:1 (0.7%)
Fungal infection	0	1:1 (2.3%)	1:1 (0.7%)
Laryngitis	0	1:1 (2.3%)	1:1 (0.7%)
Localised infection	0	1:1 (2.3%)	1:1 (0.7%)
Pharyngitis	0	1:1 (2.3%)	1:1 (0.7%)
Postoperative wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Purulence	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal mycotic infection	0	1:1 (2.3%)	1:1 (0.7%)
Wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Furuncle	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Infections and infestations, continued...			
Gastrointestinal infection	1:1 (0.9%)	0	1:1 (0.7%)
Hordeolum	1:1 (0.9%)	0	1:1 (0.7%)
Onychomycosis	1:1 (0.9%)	0	1:1 (0.7%)
Otitis media	1:1 (0.9%)	0	1:1 (0.7%)
Sepsis	1:1 (0.9%)	0	1:1 (0.7%)
Staphylococcal infection	1:1 (0.9%)	0	1:1 (0.7%)
Tinea cruris	1:1 (0.9%)	0	1:1 (0.7%)
Tooth abscess	1:1 (0.9%)	0	1:1 (0.7%)
Viral upper respiratory tract infection	1:1 (0.9%)	0	1:1 (0.7%)
Injury, poisoning and procedural complications	171:71 (67.0%)	74:26 (60.5%)	245:97 (65.1%)
Contusion	26:18 (17.0%)	10:5 (11.6%)	36:23 (15.4%)
Excoriation	27:17 (16.0%)	7:4 (9.3%)	34:21 (14.1%)
Ligament sprain	22:18 (17.0%)	7:3 (7.0%)	29:21 (14.1%)
Laceration	16:13 (12.3%)	8:6 (14.0%)	24:19 (12.8%)
Vaccination complication	18:11 (10.4%)	10:7 (16.3%)	28:18 (12.1%)
Joint injury	4:4 (3.8%)	4:4 (9.3%)	8:8 (5.4%)
Foot fracture	5:5 (4.7%)	1:1 (2.3%)	6:6 (4.0%)
Joint dislocation	2:2 (1.9%)	3:3 (7.0%)	5:5 (3.4%)
Concussion	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)
Tooth fracture	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)
Hand fracture	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Muscle strain	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Periorbital haematoma	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Ankle fracture	4:3 (2.8%)	0	4:3 (2.0%)
Limb injury	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Procedural pain	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Wound	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Traumatic haematoma	3:3 (2.8%)	0	3:3 (2.0%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...			
Ligament rupture	0	2:2 (4.7%)	2:2 (1.3%)
Eye injury	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Facial bones fracture	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Head injury	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Arthropod bite	2:2 (1.9%)	0	2:2 (1.3%)
Avulsion fracture	2:2 (1.9%)	0	2:2 (1.3%)
Fibula fracture	2:2 (1.9%)	0	2:2 (1.3%)
Hip fracture	2:2 (1.9%)	0	2:2 (1.3%)
Injury	2:2 (1.9%)	0	2:2 (1.3%)
Clavicle fracture	0	1:1 (2.3%)	1:1 (0.7%)
Mouth injury	0	1:1 (2.3%)	1:1 (0.7%)
Post-traumatic neck syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Rib fracture	0	1:1 (2.3%)	1:1 (0.7%)
Spinal column injury	0	1:1 (2.3%)	1:1 (0.7%)
Sunburn	0	1:1 (2.3%)	1:1 (0.7%)
Upper limb fracture	0	1:1 (2.3%)	1:1 (0.7%)
Anaemia postoperative	1:1 (0.9%)	0	1:1 (0.7%)
Back injury	1:1 (0.9%)	0	1:1 (0.7%)
Chillblains	1:1 (0.9%)	0	1:1 (0.7%)
Humerus fracture	1:1 (0.9%)	0	1:1 (0.7%)
Lower limb fracture	1:1 (0.9%)	0	1:1 (0.7%)
Soft tissue injury	1:1 (0.9%)	0	1:1 (0.7%)
Stress fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tendon rupture	1:1 (0.9%)	0	1:1 (0.7%)
Thermal burn	1:1 (0.9%)	0	1:1 (0.7%)
Tibia fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tooth injury	1:1 (0.9%)	0	1:1 (0.7%)
Wrist fracture	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Investigations	72:40 (37.7%)	21:12 (27.9%)	93:52 (34.9%)
Alanine aminotransferase increased	27:24 (22.6%)	6:4 (9.3%)	33:28 (18.8%)
Aspartate aminotransferase increased	13:10 (9.4%)	1:1 (2.3%)	14:11 (7.4%)
Weight decreased	4:4 (3.8%)	4:4 (9.3%)	8:8 (5.4%)
Brain natriuretic peptide increased	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Vitamin D decreased	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Serum ferritin decreased	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Gamma-glutamyltransferase increased	3:3 (2.8%)	0	3:3 (2.0%)
Troponin increased	3:2 (1.9%)	0	3:2 (1.3%)
Blood glucose increased	0	2:2 (4.7%)	2:2 (1.3%)
Blood cholesterol increased	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Blood creatine phosphokinase increased	2:2 (1.9%)	0	2:2 (1.3%)
N-terminal prohormone brain natriuretic peptide increased	2:2 (1.9%)	0	2:2 (1.3%)
Blood alkaline phosphatase increased	0	1:1 (2.3%)	1:1 (0.7%)
Ceruloplasmin increased	0	1:1 (2.3%)	1:1 (0.7%)
Serum ferritin increased	0	1:1 (2.3%)	1:1 (0.7%)
White blood cell count decreased	0	1:1 (2.3%)	1:1 (0.7%)
Blood folate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Blood triglycerides increased	1:1 (0.9%)	0	1:1 (0.7%)
Blood urea increased	1:1 (0.9%)	0	1:1 (0.7%)
Electrocardiogram T wave inversion	1:1 (0.9%)	0	1:1 (0.7%)
Glomerular filtration rate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Glucose tolerance test abnormal	1:1 (0.9%)	0	1:1 (0.7%)
Heart rate increased	1:1 (0.9%)	0	1:1 (0.7%)
Weight increased	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Metabolism and nutrition disorders	19:15 (14.2%)	7:6 (14.0%)	26:21 (14.1%)
Vitamin D deficiency	4:4 (3.8%)	2:2 (4.7%)	6:6 (4.0%)
Decreased appetite	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Dehydration	3:3 (2.8%)	0	3:3 (2.0%)
Hypercholesterolaemia	3:3 (2.8%)	0	3:3 (2.0%)
Iron deficiency	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Vitamin B12 deficiency	2:2 (1.9%)	0	2:2 (1.3%)
Abnormal loss of weight	0	1:1 (2.3%)	1:1 (0.7%)
Folate deficiency	0	1:1 (2.3%)	1:1 (0.7%)
Type 2 diabetes mellitus	0	1:1 (2.3%)	1:1 (0.7%)
Diabetes mellitus	1:1 (0.9%)	0	1:1 (0.7%)
Dyslipidaemia	1:1 (0.9%)	0	1:1 (0.7%)
Increased appetite	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal and connective tissue disorders	101:48 (45.3%)	35:21 (48.8%)	136:69 (46.3%)
Arthralgia	24:20 (18.9%)	6:6 (14.0%)	30:26 (17.4%)
Muscle spasms	23:16 (15.1%)	3:3 (7.0%)	26:19 (12.8%)
Back pain	16:9 (8.5%)	9:7 (16.3%)	25:16 (10.7%)
Pain in extremity	7:7 (6.6%)	3:3 (7.0%)	10:10 (6.7%)
Musculoskeletal pain	7:6 (5.7%)	2:2 (4.7%)	9:8 (5.4%)
Myalgia	5:4 (3.8%)	3:2 (4.7%)	8:6 (4.0%)
Musculoskeletal chest pain	0	3:3 (7.0%)	3:3 (2.0%)
Pain in jaw	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Muscle tightness	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Neck pain	3:2 (1.9%)	0	3:2 (1.3%)
Bursitis	2:2 (1.9%)	0	2:2 (1.3%)
Limb discomfort	2:1 (0.9%)	0	2:1 (0.7%)
Muscular weakness	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Musculoskeletal and connective tissue disorders, continued...			
Rotator cuff syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Scoliosis	0	1:1 (2.3%)	1:1 (0.7%)
Sensation of heaviness	0	1:1 (2.3%)	1:1 (0.7%)
Arthritis	1:1 (0.9%)	0	1:1 (0.7%)
Flank pain	1:1 (0.9%)	0	1:1 (0.7%)
Intervertebral disc protrusion	1:1 (0.9%)	0	1:1 (0.7%)
Muscle atrophy	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal stiffness	1:1 (0.9%)	0	1:1 (0.7%)
Osteoporosis	1:1 (0.9%)	0	1:1 (0.7%)
Spinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Synovial cyst	1:1 (0.9%)	0	1:1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5:4 (3.8%)	4:4 (9.3%)	9:8 (5.4%)
Skin papilloma	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Benign neoplasm of eyelid	0	1:1 (2.3%)	1:1 (0.7%)
Haemangioma of skin	0	1:1 (2.3%)	1:1 (0.7%)
Uterine leiomyoma	0	1:1 (2.3%)	1:1 (0.7%)
Morton's neuroma	1:1 (0.9%)	0	1:1 (0.7%)
Pituitary tumour benign	1:1 (0.9%)	0	1:1 (0.7%)
Nervous system disorders	85:35 (33.0%)	24:18 (41.9%)	109:53 (35.6%)
Headache	50:20 (18.9%)	7:6 (14.0%)	57:26 (17.4%)
Dizziness	8:6 (5.7%)	3:3 (7.0%)	11:9 (6.0%)
Migraine	6:4 (3.8%)	0	6:4 (2.7%)
Muscle spasticity	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Neuropathy peripheral	0	3:3 (7.0%)	3:3 (2.0%)
Restless legs syndrome	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Loss of consciousness	3:2 (1.9%)	0	3:2 (1.3%)
Hypoaesthesia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Nervous system disorders, continued...			
Presyncope	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Ataxia	2:2 (1.9%)	0	2:2 (1.3%)
Dysgeusia	2:2 (1.9%)	0	2:2 (1.3%)
Speech disorder	2:2 (1.9%)	0	2:2 (1.3%)
Disturbance in attention	0	1:1 (2.3%)	1:1 (0.7%)
Hyperaesthesia	0	1:1 (2.3%)	1:1 (0.7%)
Syncope	0	1:1 (2.3%)	1:1 (0.7%)
Tremor	0	1:1 (2.3%)	1:1 (0.7%)
Balance disorder	1:1 (0.9%)	0	1:1 (0.7%)
Convulsion	1:1 (0.9%)	0	1:1 (0.7%)
Epilepsy	1:1 (0.9%)	0	1:1 (0.7%)
Migraine with aura	1:1 (0.9%)	0	1:1 (0.7%)
Neuralgia	1:1 (0.9%)	0	1:1 (0.7%)
Paraesthesia	1:1 (0.9%)	0	1:1 (0.7%)
Post-traumatic headache	1:1 (0.9%)	0	1:1 (0.7%)
Somnolence	1:1 (0.9%)	0	1:1 (0.7%)
Psychiatric disorders	30:19 (17.9%)	15:10 (23.3%)	45:29 (19.5%)
Depression	9:9 (8.5%)	6:6 (14.0%)	15:15 (10.1%)
Insomnia	6:5 (4.7%)	2:1 (2.3%)	8:6 (4.0%)
Anxiety	5:5 (4.7%)	0	5:5 (3.4%)
Attention deficit/hyperactivity disorder	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Initial insomnia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Suicide attempt	2:2 (1.9%)	0	2:2 (1.3%)
Major depression	2:1 (0.9%)	0	2:1 (0.7%)
Confusional state	0	1:1 (2.3%)	1:1 (0.7%)
Delirium	0	1:1 (2.3%)	1:1 (0.7%)
Mood swings	0	1:1 (2.3%)	1:1 (0.7%)
Suicidal behaviour	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Psychiatric disorders, continued...			
Suicidal ideation	0	1:1 (2.3%)	1:1 (0.7%)
Abnormal dreams	1:1 (0.9%)	0	1:1 (0.7%)
Bipolar disorder	1:1 (0.9%)	0	1:1 (0.7%)
Insomnia related to another mental condition	1:1 (0.9%)	0	1:1 (0.7%)
Libido decreased	1:1 (0.9%)	0	1:1 (0.7%)
Renal and urinary disorders	21:15 (14.2%)	8:5 (11.6%)	29:20 (13.4%)
Micturition urgency	6:6 (5.7%)	3:3 (7.0%)	9:9 (6.0%)
Nephrolithiasis	6:5 (4.7%)	0	6:5 (3.4%)
Urinary incontinence	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Incontinence	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Renal cyst	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Glycosuria	0	1:1 (2.3%)	1:1 (0.7%)
Nocturia	0	1:1 (2.3%)	1:1 (0.7%)
Haematuria	1:1 (0.9%)	0	1:1 (0.7%)
Pollakiuria	1:1 (0.9%)	0	1:1 (0.7%)
Renal colic	1:1 (0.9%)	0	1:1 (0.7%)
Urinary retention	1:1 (0.9%)	0	1:1 (0.7%)
Urine odour abnormal	1:1 (0.9%)	0	1:1 (0.7%)
Reproductive system and breast disorders	19:13 (12.3%)	10:8 (18.6%)	29:21 (14.1%)
Dysmenorrhoea	5:2 (1.9%)	2:1 (2.3%)	7:3 (2.0%)
Ovarian cyst	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Menstruation irregular	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Menorrhagia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Vaginal laceration	2:2 (1.9%)	0	2:2 (1.3%)
Breast tenderness	0	1:1 (2.3%)	1:1 (0.7%)
Erectile dysfunction	0	1:1 (2.3%)	1:1 (0.7%)
Polymenorrhoea	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Reproductive system and breast disorders, continued...			
Vulvovaginal burning sensation	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal pruritus	0	1:1 (2.3%)	1:1 (0.7%)
Amenorrhoea	1:1 (0.9%)	0	1:1 (0.7%)
Mammary duct ectasia	1:1 (0.9%)	0	1:1 (0.7%)
Metrorrhagia	1:1 (0.9%)	0	1:1 (0.7%)
Pelvic pain	1:1 (0.9%)	0	1:1 (0.7%)
Polycystic ovaries	1:1 (0.9%)	0	1:1 (0.7%)
Prostatitis	1:1 (0.9%)	0	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	37:24 (22.6%)	16:11 (25.6%)	53:35 (23.5%)
Cough	10:10 (9.4%)	4:3 (7.0%)	14:13 (8.7%)
Epistaxis	7:6 (5.7%)	1:1 (2.3%)	8:7 (4.7%)
Dyspnoea	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Nasal congestion	3:3 (2.8%)	0	3:3 (2.0%)
Oropharyngeal pain	3:3 (2.8%)	0	3:3 (2.0%)
Rhinorrhoea	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Sleep apnoea syndrome	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rhinitis allergic	2:2 (1.9%)	0	2:2 (1.3%)
Asthma	0	2:1 (2.3%)	2:1 (0.7%)
Wheezing	0	2:1 (2.3%)	2:1 (0.7%)
Nasal disorder	2:1 (0.9%)	0	2:1 (0.7%)
Choking	0	1:1 (2.3%)	1:1 (0.7%)
Pulmonary embolism	0	1:1 (2.3%)	1:1 (0.7%)
Respiratory failure	0	1:1 (2.3%)	1:1 (0.7%)
Dysphonia	1:1 (0.9%)	0	1:1 (0.7%)
Nasal obstruction	1:1 (0.9%)	0	1:1 (0.7%)
Nasal septum deviation	1:1 (0.9%)	0	1:1 (0.7%)
Nasal turbinate hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)
Pulmonary congestion	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Respiratory, thoracic and mediastinal disorders, continued...			
Sinus congestion	1:1 (0.9%)	0	1:1 (0.7%)
Upper-airway cough syndrome	1:1 (0.9%)	0	1:1 (0.7%)
Skin and subcutaneous tissue disorders	31:27 (25.5%)	24:13 (30.2%)	55:40 (26.8%)
Eczema	3:3 (2.8%)	5:3 (7.0%)	8:6 (4.0%)
Acne	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Alopecia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Night sweats	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Hyperhidrosis	3:3 (2.8%)	0	3:3 (2.0%)
Urticaria	3:3 (2.8%)	0	3:3 (2.0%)
Rash macular	4:2 (1.9%)	0	4:2 (1.3%)
Psoriasis	1:1 (0.9%)	2:1 (2.3%)	3:2 (1.3%)
Pruritus	0	2:2 (4.7%)	2:2 (1.3%)
Dermatitis contact	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rash maculo-papular	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dandruff	0	1:1 (2.3%)	1:1 (0.7%)
Dermal cyst	0	1:1 (2.3%)	1:1 (0.7%)
Erythema	0	1:1 (2.3%)	1:1 (0.7%)
Heat rash	0	1:1 (2.3%)	1:1 (0.7%)
Nail discolouration	0	1:1 (2.3%)	1:1 (0.7%)
Petechiae	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus generalised	0	1:1 (2.3%)	1:1 (0.7%)
Rosacea	0	1:1 (2.3%)	1:1 (0.7%)
Blister	1:1 (0.9%)	0	1:1 (0.7%)
Dermatitis psoriasiform	1:1 (0.9%)	0	1:1 (0.7%)
Dry skin	1:1 (0.9%)	0	1:1 (0.7%)
Ecchymosis	1:1 (0.9%)	0	1:1 (0.7%)
Ingrowing nail	1:1 (0.9%)	0	1:1 (0.7%)
Milia	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.1
Overall Summary of Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...			
Skin disorder	1:1 (0.9%)	0	1:1 (0.7%)
Skin swelling	1:1 (0.9%)	0	1:1 (0.7%)
Skin ulcer	1:1 (0.9%)	0	1:1 (0.7%)
Swelling face	1:1 (0.9%)	0	1:1 (0.7%)
Vascular disorders	6:6 (5.7%)	3:3 (7.0%)	9:9 (6.0%)
Haematoma	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Deep vein thrombosis	0	2:2 (4.7%)	2:2 (1.3%)
Hypertension	2:2 (1.9%)	0	2:2 (1.3%)
Hypotension	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	216:78 (73.6%)	62:28 (65.1%)	278:106 (71.1%)
Blood and lymphatic system disorders	0	2:2 (4.7%)	2:2 (1.3%)
Iron deficiency anaemia	0	1:1 (2.3%)	1:1 (0.7%)
Lymphadenopathy	0	1:1 (2.3%)	1:1 (0.7%)
Cardiac disorders	2:2 (1.9%)	0	2:2 (1.3%)
Angina pectoris	1:1 (0.9%)	0	1:1 (0.7%)
Tachycardia	1:1 (0.9%)	0	1:1 (0.7%)
Ear and labyrinth disorders	1:1 (0.9%)	0	1:1 (0.7%)
Ear pain	1:1 (0.9%)	0	1:1 (0.7%)
Eye disorders	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Blepharitis	0	1:1 (2.3%)	1:1 (0.7%)
Diplopia	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorders	39:30 (28.3%)	17:13 (30.2%)	56:43 (28.9%)
Nausea	14:13 (12.3%)	5:5 (11.6%)	19:18 (12.1%)
Diarrhoea	7:6 (5.7%)	3:3 (7.0%)	10:9 (6.0%)
Abdominal pain	4:4 (3.8%)	5:5 (11.6%)	9:9 (6.0%)
Vomiting	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Gastrooesophageal reflux disease	3:2 (1.9%)	0	3:2 (1.3%)
Barrett's oesophagus	0	1:1 (2.3%)	1:1 (0.7%)
Frequent bowel movements	0	1:1 (2.3%)	1:1 (0.7%)
Stomatitis	0	1:1 (2.3%)	1:1 (0.7%)
Abdominal discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Abdominal pain lower	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...			
Abdominal pain upper	1:1 (0.9%)	0	1:1 (0.7%)
Breath odour	1:1 (0.9%)	0	1:1 (0.7%)
Constipation	1:1 (0.9%)	0	1:1 (0.7%)
Defaecation urgency	1:1 (0.9%)	0	1:1 (0.7%)
Dental discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Dyspepsia	1:1 (0.9%)	0	1:1 (0.7%)
General disorders and administration site conditions	16:14 (13.2%)	4:4 (9.3%)	20:18 (12.1%)
Fatigue	7:7 (6.6%)	3:3 (7.0%)	10:10 (6.7%)
Pyrexia	3:3 (2.8%)	0	3:3 (2.0%)
Asthenia	2:2 (1.9%)	0	2:2 (1.3%)
Oedema peripheral	2:2 (1.9%)	0	2:2 (1.3%)
Non-cardiac chest pain	0	1:1 (2.3%)	1:1 (0.7%)
Feeling hot	1:1 (0.9%)	0	1:1 (0.7%)
Pain	1:1 (0.9%)	0	1:1 (0.7%)
Infections and infestations	20:18 (17.0%)	10:8 (18.6%)	30:26 (17.4%)
Nasopharyngitis	2:2 (1.9%)	5:5 (11.6%)	7:7 (4.7%)
Upper respiratory tract infection	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Urinary tract infection	3:3 (2.8%)	0	3:3 (2.0%)
Ear infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Influenza	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Sinusitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Localised infection	0	1:1 (2.3%)	1:1 (0.7%)
Bronchitis	1:1 (0.9%)	0	1:1 (0.7%)
Furuncle	1:1 (0.9%)	0	1:1 (0.7%)
Gastroenteritis viral	1:1 (0.9%)	0	1:1 (0.7%)
Rhinitis	1:1 (0.9%)	0	1:1 (0.7%)
Sepsis	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Infections and infestations, continued...			
Tinea versicolour	1:1 (0.9%)	0	1:1 (0.7%)
Tooth abscess	1:1 (0.9%)	0	1:1 (0.7%)
Viral infection	1:1 (0.9%)	0	1:1 (0.7%)
Injury, poisoning and procedural complications	28:21 (19.8%)	6:4 (9.3%)	34:25 (16.8%)
Excoriation	10:7 (6.6%)	0	10:7 (4.7%)
Contusion	6:5 (4.7%)	0	6:5 (3.4%)
Ligament sprain	4:3 (2.8%)	1:1 (2.3%)	5:4 (2.7%)
Laceration	1:1 (0.9%)	2:1 (2.3%)	3:2 (1.3%)
Head injury	0	1:1 (2.3%)	1:1 (0.7%)
Mouth injury	0	1:1 (2.3%)	1:1 (0.7%)
Post-traumatic neck syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Back injury	1:1 (0.9%)	0	1:1 (0.7%)
Fibula fracture	1:1 (0.9%)	0	1:1 (0.7%)
Foot fracture	1:1 (0.9%)	0	1:1 (0.7%)
Joint injury	1:1 (0.9%)	0	1:1 (0.7%)
Muscle strain	1:1 (0.9%)	0	1:1 (0.7%)
Procedural pain	1:1 (0.9%)	0	1:1 (0.7%)
Wound	1:1 (0.9%)	0	1:1 (0.7%)
Investigations	39:24 (22.6%)	3:3 (7.0%)	42:27 (18.1%)
Alanine aminotransferase increased	23:22 (20.8%)	0	23:22 (14.8%)
Aspartate aminotransferase increased	11:10 (9.4%)	0	11:10 (6.7%)
Gamma-glutamyltransferase increased	2:2 (1.9%)	0	2:2 (1.3%)
Blood glucose increased	0	1:1 (2.3%)	1:1 (0.7%)
Serum ferritin increased	0	1:1 (2.3%)	1:1 (0.7%)
Weight decreased	0	1:1 (2.3%)	1:1 (0.7%)
Blood creatine phosphokinase increased	1:1 (0.9%)	0	1:1 (0.7%)
Electrocardiogram T wave inversion	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Investigations, continued...			
Glucose tolerance test abnormal	1:1 (0.9%)	0	1:1 (0.7%)
Metabolism and nutrition disorders	3:3 (2.8%)	0	3:3 (2.0%)
Decreased appetite	2:2 (1.9%)	0	2:2 (1.3%)
Increased appetite	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal and connective tissue disorders	19:14 (13.2%)	3:3 (7.0%)	22:17 (11.4%)
Myalgia	5:4 (3.8%)	1:1 (2.3%)	6:5 (3.4%)
Arthralgia	6:5 (4.7%)	0	6:5 (3.4%)
Muscle spasms	3:3 (2.8%)	0	3:3 (2.0%)
Pain in extremity	2:2 (1.9%)	0	2:2 (1.3%)
Back pain	0	1:1 (2.3%)	1:1 (0.7%)
Rotator cuff syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Flank pain	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal stiffness	1:1 (0.9%)	0	1:1 (0.7%)
Neck pain	1:1 (0.9%)	0	1:1 (0.7%)
Nervous system disorders	20:16 (15.1%)	3:3 (7.0%)	23:19 (12.8%)
Headache	15:12 (11.3%)	1:1 (2.3%)	16:13 (8.7%)
Dizziness	2:2 (1.9%)	0	2:2 (1.3%)
Presyncope	0	1:1 (2.3%)	1:1 (0.7%)
Restless legs syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Balance disorder	1:1 (0.9%)	0	1:1 (0.7%)
Migraine	1:1 (0.9%)	0	1:1 (0.7%)
Migraine with aura	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Psychiatric disorders	6:5 (4.7%)	2:2 (4.7%)	8:7 (4.7%)
Insomnia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Depression	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Abnormal dreams	1:1 (0.9%)	0	1:1 (0.7%)
Anxiety	1:1 (0.9%)	0	1:1 (0.7%)
Bipolar disorder	1:1 (0.9%)	0	1:1 (0.7%)
Renal and urinary disorders	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Urinary incontinence	0	1:1 (2.3%)	1:1 (0.7%)
Nephrolithiasis	1:1 (0.9%)	0	1:1 (0.7%)
Reproductive system and breast disorders	7:6 (5.7%)	2:2 (4.7%)	9:8 (5.4%)
Menstruation irregular	2:2 (1.9%)	0	2:2 (1.3%)
Dysmenorrhoea	2:1 (0.9%)	0	2:1 (0.7%)
Breast tenderness	0	1:1 (2.3%)	1:1 (0.7%)
Menorrhagia	0	1:1 (2.3%)	1:1 (0.7%)
Metrorrhagia	1:1 (0.9%)	0	1:1 (0.7%)
Prostatitis	1:1 (0.9%)	0	1:1 (0.7%)
Vaginal laceration	1:1 (0.9%)	0	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	6:3 (2.8%)	1:1 (2.3%)	7:4 (2.7%)
Nasal congestion	3:3 (2.8%)	0	3:3 (2.0%)
Asthma	0	1:1 (2.3%)	1:1 (0.7%)
Cough	1:1 (0.9%)	0	1:1 (0.7%)
Oropharyngeal pain	1:1 (0.9%)	0	1:1 (0.7%)
Upper-airway cough syndrome	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.6
Overall Summary of Treatment-emergent Adverse Events Onset before 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders	6:6 (5.7%)	7:4 (9.3%)	13:10 (6.7%)
Psoriasis	0	2:1 (2.3%)	2:1 (0.7%)
Alopecia	0	1:1 (2.3%)	1:1 (0.7%)
Eczema	0	1:1 (2.3%)	1:1 (0.7%)
Petechiae	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus	0	1:1 (2.3%)	1:1 (0.7%)
Rash maculo-papular	0	1:1 (2.3%)	1:1 (0.7%)
Dermatitis contact	1:1 (0.9%)	0	1:1 (0.7%)
Dermatitis psoriasiform	1:1 (0.9%)	0	1:1 (0.7%)
Ingrowing nail	1:1 (0.9%)	0	1:1 (0.7%)
Night sweats	1:1 (0.9%)	0	1:1 (0.7%)
Rash macular	1:1 (0.9%)	0	1:1 (0.7%)
Skin swelling	1:1 (0.9%)	0	1:1 (0.7%)
Vascular disorders	2:2 (1.9%)	0	2:2 (1.3%)
Haematoma	1:1 (0.9%)	0	1:1 (0.7%)
Hypotension	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	747:94 (88.7%)	372:41 (95.3%)	1119:135 (90.6%)
Blood and lymphatic system disorders	2:2 (1.9%)	3:2 (4.7%)	5:4 (2.7%)
Anaemia	0	3:2 (4.7%)	3:2 (1.3%)
Iron deficiency anaemia	2:2 (1.9%)	0	2:2 (1.3%)
Cardiac disorders	12:10 (9.4%)	5:4 (9.3%)	17:14 (9.4%)
Palpitations	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Sinus tachycardia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Cardiomyopathy	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Angina pectoris	2:2 (1.9%)	0	2:2 (1.3%)
Myocarditis	2:1 (0.9%)	0	2:1 (0.7%)
Cardiac failure congestive	0	1:1 (2.3%)	1:1 (0.7%)
Atrial fibrillation	1:1 (0.9%)	0	1:1 (0.7%)
Tachycardia	1:1 (0.9%)	0	1:1 (0.7%)
Ventricular hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)
Congenital, familial and genetic disorders	2:2 (1.9%)	0	2:2 (1.3%)
Friedreich's ataxia	1:1 (0.9%)	0	1:1 (0.7%)
Hereditary haemochromatosis	1:1 (0.9%)	0	1:1 (0.7%)
Ear and labyrinth disorders	5:4 (3.8%)	2:2 (4.7%)	7:6 (4.0%)
Deafness	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Ear haemorrhage	1:1 (0.9%)	0	1:1 (0.7%)
Hearing impaired	1:1 (0.9%)	0	1:1 (0.7%)
Hypoacusis	1:1 (0.9%)	0	1:1 (0.7%)
Tinnitus	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Endocrine disorders	0	1:1 (2.3%)	1:1 (0.7%)
Basedow's disease	0	1:1 (2.3%)	1:1 (0.7%)
Eye disorders	4:3 (2.8%)	4:4 (9.3%)	8:7 (4.7%)
Blepharospasm	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Diplopia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dry eye	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Altered visual depth perception	0	1:1 (2.3%)	1:1 (0.7%)
Blepharitis	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorders	81:45 (42.5%)	44:25 (58.1%)	125:70 (47.0%)
Diarrhoea	14:13 (12.3%)	3:2 (4.7%)	17:15 (10.1%)
Nausea	15:13 (12.3%)	2:2 (4.7%)	17:15 (10.1%)
Abdominal pain	8:7 (6.6%)	3:3 (7.0%)	11:10 (6.7%)
Gastrooesophageal reflux disease	5:5 (4.7%)	5:5 (11.6%)	10:10 (6.7%)
Vomiting	5:5 (4.7%)	5:4 (9.3%)	10:9 (6.0%)
Constipation	4:4 (3.8%)	5:4 (9.3%)	9:8 (5.4%)
Toothache	2:2 (1.9%)	4:4 (9.3%)	6:6 (4.0%)
Dyspepsia	5:5 (4.7%)	1:1 (2.3%)	6:6 (4.0%)
Haemorrhoids	3:2 (1.9%)	2:2 (4.7%)	5:4 (2.7%)
Abdominal discomfort	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Dysphagia	0	2:2 (4.7%)	2:2 (1.3%)
Tooth disorder	0	2:2 (4.7%)	2:2 (1.3%)
Abdominal pain upper	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dry mouth	2:2 (1.9%)	0	2:2 (1.3%)
Cheilitis	2:1 (0.9%)	0	2:1 (0.7%)
Stomatitis	2:1 (0.9%)	0	2:1 (0.7%)
Abdominal pain lower	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...			
Anal fissure	0	1:1 (2.3%)	1:1 (0.7%)
Bowel movement irregularity	0	1:1 (2.3%)	1:1 (0.7%)
Faecal incontinence	0	1:1 (2.3%)	1:1 (0.7%)
Faecaloma	0	1:1 (2.3%)	1:1 (0.7%)
Rectal polyp	0	1:1 (2.3%)	1:1 (0.7%)
Tooth impacted	0	1:1 (2.3%)	1:1 (0.7%)
Abdominal distension	1:1 (0.9%)	0	1:1 (0.7%)
Aphthous stomatitis	1:1 (0.9%)	0	1:1 (0.7%)
Breath odour	1:1 (0.9%)	0	1:1 (0.7%)
Defaecation urgency	1:1 (0.9%)	0	1:1 (0.7%)
Faeces hard	1:1 (0.9%)	0	1:1 (0.7%)
Faeces pale	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Gingival bleeding	1:1 (0.9%)	0	1:1 (0.7%)
Haematochezia	1:1 (0.9%)	0	1:1 (0.7%)
Melaena	1:1 (0.9%)	0	1:1 (0.7%)
Tongue coated	1:1 (0.9%)	0	1:1 (0.7%)
Traumatic tooth displacement	1:1 (0.9%)	0	1:1 (0.7%)
General disorders and administration site conditions	34:27 (25.5%)	15:13 (30.2%)	49:40 (26.8%)
Fatigue	7:7 (6.6%)	4:4 (9.3%)	11:11 (7.4%)
Pyrexia	7:7 (6.6%)	2:2 (4.7%)	9:9 (6.0%)
Influenza like illness	5:4 (3.8%)	2:2 (4.7%)	7:6 (4.0%)
Asthenia	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Oedema peripheral	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Cyst	3:2 (1.9%)	0	3:2 (1.3%)
Non-cardiac chest pain	2:2 (1.9%)	0	2:2 (1.3%)
Adverse drug reaction	0	1:1 (2.3%)	1:1 (0.7%)
Chest pain	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
General disorders and administration site conditions, continued...			
Feeling abnormal	0	1:1 (2.3%)	1:1 (0.7%)
Irritability	0	1:1 (2.3%)	1:1 (0.7%)
Chest discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Facial pain	1:1 (0.9%)	0	1:1 (0.7%)
Gait disturbance	1:1 (0.9%)	0	1:1 (0.7%)
Inflammation	1:1 (0.9%)	0	1:1 (0.7%)
Malaise	1:1 (0.9%)	0	1:1 (0.7%)
Pain	1:1 (0.9%)	0	1:1 (0.7%)
Hepatobiliary disorders	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Cholelithiasis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Immune system disorders	3:3 (2.8%)	2:1 (2.3%)	5:4 (2.7%)
Seasonal allergy	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Hypersensitivity	1:1 (0.9%)	0	1:1 (0.7%)
Infections and infestations	143:67 (63.2%)	82:34 (79.1%)	225:101 (67.8%)
Corona virus infection	56:49 (46.2%)	25:22 (51.2%)	81:71 (47.7%)
Upper respiratory tract infection	22:16 (15.1%)	18:12 (27.9%)	40:28 (18.8%)
Influenza	13:11 (10.4%)	3:3 (7.0%)	16:14 (9.4%)
Nasopharyngitis	6:4 (3.8%)	4:4 (9.3%)	10:8 (5.4%)
Urinary tract infection	3:3 (2.8%)	6:5 (11.6%)	9:8 (5.4%)
Bronchitis	5:5 (4.7%)	1:1 (2.3%)	6:6 (4.0%)
Sinusitis	6:4 (3.8%)	1:1 (2.3%)	7:5 (3.4%)
Viral infection	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Pilonidal cyst	0	5:2 (4.7%)	5:2 (1.3%)
Tonsillitis	3:2 (1.9%)	0	3:2 (1.3%)
Paronychia	0	2:2 (4.7%)	2:2 (1.3%)
Chlamydial infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Infections and infestations, continued...			
Gastroenteritis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Gastroenteritis viral	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Pneumonia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rhinitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Viral rhinitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Eye infection	2:2 (1.9%)	0	2:2 (1.3%)
Gastroenteritis norovirus	2:2 (1.9%)	0	2:2 (1.3%)
Lower respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Otitis externa	4:1 (0.9%)	0	4:1 (0.7%)
Rash pustular	2:1 (0.9%)	0	2:1 (0.7%)
Body tinea	0	1:1 (2.3%)	1:1 (0.7%)
Escherichia infection	0	1:1 (2.3%)	1:1 (0.7%)
Fungal infection	0	1:1 (2.3%)	1:1 (0.7%)
Laryngitis	0	1:1 (2.3%)	1:1 (0.7%)
Pharyngitis	0	1:1 (2.3%)	1:1 (0.7%)
Postoperative wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Purulence	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal mycotic infection	0	1:1 (2.3%)	1:1 (0.7%)
Wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Gastrointestinal infection	1:1 (0.9%)	0	1:1 (0.7%)
Hordeolum	1:1 (0.9%)	0	1:1 (0.7%)
Onychomycosis	1:1 (0.9%)	0	1:1 (0.7%)
Otitis media	1:1 (0.9%)	0	1:1 (0.7%)
Staphylococcal infection	1:1 (0.9%)	0	1:1 (0.7%)
Tinea cruris	1:1 (0.9%)	0	1:1 (0.7%)
Tinea versicolour	1:1 (0.9%)	0	1:1 (0.7%)
Viral upper respiratory tract infection	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications	143:63 (59.4%)	68:26 (60.5%)	211:89 (59.7%)
Contusion	20:15 (14.2%)	10:5 (11.6%)	30:20 (13.4%)
Vaccination complication	18:11 (10.4%)	10:7 (16.3%)	28:18 (12.1%)
Laceration	15:12 (11.3%)	6:6 (14.0%)	21:18 (12.1%)
Ligament sprain	18:15 (14.2%)	6:2 (4.7%)	24:17 (11.4%)
Excoriation	17:12 (11.3%)	7:4 (9.3%)	24:16 (10.7%)
Joint injury	3:3 (2.8%)	4:4 (9.3%)	7:7 (4.7%)
Joint dislocation	2:2 (1.9%)	3:3 (7.0%)	5:5 (3.4%)
Concussion	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)
Tooth fracture	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)
Foot fracture	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Hand fracture	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Periorbital haematoma	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Ankle fracture	4:3 (2.8%)	0	4:3 (2.0%)
Limb injury	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Muscle strain	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Traumatic haematoma	3:3 (2.8%)	0	3:3 (2.0%)
Ligament rupture	0	2:2 (4.7%)	2:2 (1.3%)
Eye injury	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Facial bones fracture	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Procedural pain	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Wound	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Arthropod bite	2:2 (1.9%)	0	2:2 (1.3%)
Avulsion fracture	2:2 (1.9%)	0	2:2 (1.3%)
Hip fracture	2:2 (1.9%)	0	2:2 (1.3%)
Injury	2:2 (1.9%)	0	2:2 (1.3%)
Clavicle fracture	0	1:1 (2.3%)	1:1 (0.7%)
Rib fracture	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Injury, poisoning and procedural complications, continued...			
Spinal column injury	0	1:1 (2.3%)	1:1 (0.7%)
Sunburn	0	1:1 (2.3%)	1:1 (0.7%)
Upper limb fracture	0	1:1 (2.3%)	1:1 (0.7%)
Anaemia postoperative	1:1 (0.9%)	0	1:1 (0.7%)
Chillblains	1:1 (0.9%)	0	1:1 (0.7%)
Fibula fracture	1:1 (0.9%)	0	1:1 (0.7%)
Head injury	1:1 (0.9%)	0	1:1 (0.7%)
Humerus fracture	1:1 (0.9%)	0	1:1 (0.7%)
Lower limb fracture	1:1 (0.9%)	0	1:1 (0.7%)
Soft tissue injury	1:1 (0.9%)	0	1:1 (0.7%)
Stress fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tendon rupture	1:1 (0.9%)	0	1:1 (0.7%)
Thermal burn	1:1 (0.9%)	0	1:1 (0.7%)
Tibia fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tooth injury	1:1 (0.9%)	0	1:1 (0.7%)
Wrist fracture	1:1 (0.9%)	0	1:1 (0.7%)
Investigations	33:21 (19.8%)	18:9 (20.9%)	51:30 (20.1%)
Alanine aminotransferase increased	4:4 (3.8%)	6:4 (9.3%)	10:8 (5.4%)
Weight decreased	4:4 (3.8%)	3:3 (7.0%)	7:7 (4.7%)
Brain natriuretic peptide increased	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Vitamin D decreased	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Serum ferritin decreased	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Aspartate aminotransferase increased	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Troponin increased	3:2 (1.9%)	0	3:2 (1.3%)
Blood cholesterol increased	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
N-terminal prohormone brain natriuretic peptide increased	2:2 (1.9%)	0	2:2 (1.3%)
Blood alkaline phosphatase increased	0	1:1 (2.3%)	1:1 (0.7%)
Blood glucose increased	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Investigations, continued...			
Ceruloplasmin increased	0	1:1 (2.3%)	1:1 (0.7%)
White blood cell count decreased	0	1:1 (2.3%)	1:1 (0.7%)
Blood creatine phosphokinase increased	1:1 (0.9%)	0	1:1 (0.7%)
Blood folate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Blood triglycerides increased	1:1 (0.9%)	0	1:1 (0.7%)
Blood urea increased	1:1 (0.9%)	0	1:1 (0.7%)
Gamma-glutamyltransferase increased	1:1 (0.9%)	0	1:1 (0.7%)
Glomerular filtration rate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Heart rate increased	1:1 (0.9%)	0	1:1 (0.7%)
Weight increased	1:1 (0.9%)	0	1:1 (0.7%)
Metabolism and nutrition disorders	16:12 (11.3%)	7:6 (14.0%)	23:18 (12.1%)
Vitamin D deficiency	4:4 (3.8%)	2:2 (4.7%)	6:6 (4.0%)
Dehydration	3:3 (2.8%)	0	3:3 (2.0%)
Hypercholesterolaemia	3:3 (2.8%)	0	3:3 (2.0%)
Iron deficiency	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Vitamin B12 deficiency	2:2 (1.9%)	0	2:2 (1.3%)
Abnormal loss of weight	0	1:1 (2.3%)	1:1 (0.7%)
Decreased appetite	0	1:1 (2.3%)	1:1 (0.7%)
Folate deficiency	0	1:1 (2.3%)	1:1 (0.7%)
Type 2 diabetes mellitus	0	1:1 (2.3%)	1:1 (0.7%)
Diabetes mellitus	1:1 (0.9%)	0	1:1 (0.7%)
Dyslipidaemia	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal and connective tissue disorders	82:40 (37.7%)	32:21 (48.8%)	114:61 (40.9%)
Arthralgia	18:16 (15.1%)	6:6 (14.0%)	24:22 (14.8%)
Back pain	16:9 (8.5%)	8:7 (16.3%)	24:16 (10.7%)
Muscle spasms	20:13 (12.3%)	3:3 (7.0%)	23:16 (10.7%)
Musculoskeletal pain	7:6 (5.7%)	2:2 (4.7%)	9:8 (5.4%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Musculoskeletal and connective tissue disorders, continued...			
Pain in extremity	5:5 (4.7%)	3:3 (7.0%)	8:8 (5.4%)
Musculoskeletal chest pain	0	3:3 (7.0%)	3:3 (2.0%)
Pain in jaw	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Muscle tightness	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Myalgia	0	2:2 (4.7%)	2:2 (1.3%)
Bursitis	2:2 (1.9%)	0	2:2 (1.3%)
Neck pain	2:2 (1.9%)	0	2:2 (1.3%)
Limb discomfort	2:1 (0.9%)	0	2:1 (0.7%)
Muscular weakness	0	1:1 (2.3%)	1:1 (0.7%)
Scoliosis	0	1:1 (2.3%)	1:1 (0.7%)
Sensation of heaviness	0	1:1 (2.3%)	1:1 (0.7%)
Arthritis	1:1 (0.9%)	0	1:1 (0.7%)
Intervertebral disc protrusion	1:1 (0.9%)	0	1:1 (0.7%)
Muscle atrophy	1:1 (0.9%)	0	1:1 (0.7%)
Osteoporosis	1:1 (0.9%)	0	1:1 (0.7%)
Spinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Synovial cyst	1:1 (0.9%)	0	1:1 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5:4 (3.8%)	4:4 (9.3%)	9:8 (5.4%)
Skin papilloma	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Benign neoplasm of eyelid	0	1:1 (2.3%)	1:1 (0.7%)
Haemangioma of skin	0	1:1 (2.3%)	1:1 (0.7%)
Uterine leiomyoma	0	1:1 (2.3%)	1:1 (0.7%)
Morton's neuroma	1:1 (0.9%)	0	1:1 (0.7%)
Pituitary tumour benign	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Nervous system disorders	65:27 (25.5%)	21:15 (34.9%)	86:42 (28.2%)
Headache	35:11 (10.4%)	6:5 (11.6%)	41:16 (10.7%)
Dizziness	6:5 (4.7%)	3:3 (7.0%)	9:8 (5.4%)
Migraine	5:4 (3.8%)	0	5:4 (2.7%)
Muscle spasticity	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Neuropathy peripheral	0	3:3 (7.0%)	3:3 (2.0%)
Loss of consciousness	3:2 (1.9%)	0	3:2 (1.3%)
Hypoaesthesia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Restless legs syndrome	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Ataxia	2:2 (1.9%)	0	2:2 (1.3%)
Dysgeusia	2:2 (1.9%)	0	2:2 (1.3%)
Speech disorder	2:2 (1.9%)	0	2:2 (1.3%)
Disturbance in attention	0	1:1 (2.3%)	1:1 (0.7%)
Hyperaesthesia	0	1:1 (2.3%)	1:1 (0.7%)
Syncope	0	1:1 (2.3%)	1:1 (0.7%)
Tremor	0	1:1 (2.3%)	1:1 (0.7%)
Convulsion	1:1 (0.9%)	0	1:1 (0.7%)
Epilepsy	1:1 (0.9%)	0	1:1 (0.7%)
Neuralgia	1:1 (0.9%)	0	1:1 (0.7%)
Paraesthesia	1:1 (0.9%)	0	1:1 (0.7%)
Post-traumatic headache	1:1 (0.9%)	0	1:1 (0.7%)
Presyncope	1:1 (0.9%)	0	1:1 (0.7%)
Somnolence	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Psychiatric disorders	24:17 (16.0%)	13:9 (20.9%)	37:26 (17.4%)
Depression	8:8 (7.5%)	5:5 (11.6%)	13:13 (8.7%)
Insomnia	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Anxiety	4:4 (3.8%)	0	4:4 (2.7%)
Attention deficit/hyperactivity disorder	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Initial insomnia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Suicide attempt	2:2 (1.9%)	0	2:2 (1.3%)
Major depression	2:1 (0.9%)	0	2:1 (0.7%)
Confusional state	0	1:1 (2.3%)	1:1 (0.7%)
Delirium	0	1:1 (2.3%)	1:1 (0.7%)
Mood swings	0	1:1 (2.3%)	1:1 (0.7%)
Suicidal behaviour	0	1:1 (2.3%)	1:1 (0.7%)
Suicidal ideation	0	1:1 (2.3%)	1:1 (0.7%)
Insomnia related to another mental condition	1:1 (0.9%)	0	1:1 (0.7%)
Libido decreased	1:1 (0.9%)	0	1:1 (0.7%)
Renal and urinary disorders	20:14 (13.2%)	7:4 (9.3%)	27:18 (12.1%)
Micturition urgency	6:6 (5.7%)	3:3 (7.0%)	9:9 (6.0%)
Nephrolithiasis	5:4 (3.8%)	0	5:4 (2.7%)
Incontinence	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Renal cyst	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Urinary incontinence	2:2 (1.9%)	0	2:2 (1.3%)
Glycosuria	0	1:1 (2.3%)	1:1 (0.7%)
Nocturia	0	1:1 (2.3%)	1:1 (0.7%)
Haematuria	1:1 (0.9%)	0	1:1 (0.7%)
Pollakiuria	1:1 (0.9%)	0	1:1 (0.7%)
Renal colic	1:1 (0.9%)	0	1:1 (0.7%)
Urinary retention	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Renal and urinary disorders, continued...			
Urine odour abnormal	1:1 (0.9%)	0	1:1 (0.7%)
Reproductive system and breast disorders	12:8 (7.5%)	8:6 (14.0%)	20:14 (9.4%)
Dysmenorrhoea	3:2 (1.9%)	2:1 (2.3%)	5:3 (2.0%)
Ovarian cyst	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Erectile dysfunction	0	1:1 (2.3%)	1:1 (0.7%)
Menstruation irregular	0	1:1 (2.3%)	1:1 (0.7%)
Polymenorrhoea	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal burning sensation	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal pruritus	0	1:1 (2.3%)	1:1 (0.7%)
Amenorrhoea	1:1 (0.9%)	0	1:1 (0.7%)
Mammary duct ectasia	1:1 (0.9%)	0	1:1 (0.7%)
Menorrhagia	1:1 (0.9%)	0	1:1 (0.7%)
Pelvic pain	1:1 (0.9%)	0	1:1 (0.7%)
Polycystic ovaries	1:1 (0.9%)	0	1:1 (0.7%)
Vaginal laceration	1:1 (0.9%)	0	1:1 (0.7%)
Respiratory, thoracic and mediastinal disorders	31:21 (19.8%)	15:11 (25.6%)	46:32 (21.5%)
Cough	9:9 (8.5%)	4:3 (7.0%)	13:12 (8.1%)
Epistaxis	7:6 (5.7%)	1:1 (2.3%)	8:7 (4.7%)
Dyspnoea	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Rhinorrhoea	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Sleep apnoea syndrome	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Oropharyngeal pain	2:2 (1.9%)	0	2:2 (1.3%)
Rhinitis allergic	2:2 (1.9%)	0	2:2 (1.3%)
Wheezing	0	2:1 (2.3%)	2:1 (0.7%)
Nasal disorder	2:1 (0.9%)	0	2:1 (0.7%)
Asthma	0	1:1 (2.3%)	1:1 (0.7%)
Choking	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Respiratory, thoracic and mediastinal disorders, continued...			
Pulmonary embolism	0	1:1 (2.3%)	1:1 (0.7%)
Respiratory failure	0	1:1 (2.3%)	1:1 (0.7%)
Dysphonia	1:1 (0.9%)	0	1:1 (0.7%)
Nasal obstruction	1:1 (0.9%)	0	1:1 (0.7%)
Nasal septum deviation	1:1 (0.9%)	0	1:1 (0.7%)
Nasal turbinate hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)
Pulmonary congestion	1:1 (0.9%)	0	1:1 (0.7%)
Sinus congestion	1:1 (0.9%)	0	1:1 (0.7%)
Skin and subcutaneous tissue disorders	25:22 (20.8%)	17:9 (20.9%)	42:31 (20.8%)
Eczema	3:3 (2.8%)	4:2 (4.7%)	7:5 (3.4%)
Acne	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Hyperhidrosis	3:3 (2.8%)	0	3:3 (2.0%)
Urticaria	3:3 (2.8%)	0	3:3 (2.0%)
Rash macular	3:2 (1.9%)	0	3:2 (1.3%)
Night sweats	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Alopecia	2:2 (1.9%)	0	2:2 (1.3%)
Dandruff	0	1:1 (2.3%)	1:1 (0.7%)
Dermal cyst	0	1:1 (2.3%)	1:1 (0.7%)
Dermatitis contact	0	1:1 (2.3%)	1:1 (0.7%)
Erythema	0	1:1 (2.3%)	1:1 (0.7%)
Heat rash	0	1:1 (2.3%)	1:1 (0.7%)
Nail discolouration	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus generalised	0	1:1 (2.3%)	1:1 (0.7%)
Rosacea	0	1:1 (2.3%)	1:1 (0.7%)
Blister	1:1 (0.9%)	0	1:1 (0.7%)
Dry skin	1:1 (0.9%)	0	1:1 (0.7%)
Ecchymosis	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.6.7
Overall Summary of Treatment-emergent Adverse Events Onset after 12 Weeks by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...			
Milia	1:1 (0.9%)	0	1:1 (0.7%)
Psoriasis	1:1 (0.9%)	0	1:1 (0.7%)
Rash maculo-papular	1:1 (0.9%)	0	1:1 (0.7%)
Skin disorder	1:1 (0.9%)	0	1:1 (0.7%)
Skin ulcer	1:1 (0.9%)	0	1:1 (0.7%)
Swelling face	1:1 (0.9%)	0	1:1 (0.7%)
Vascular disorders	4:4 (3.8%)	3:3 (7.0%)	7:7 (4.7%)
Haematoma	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Deep vein thrombosis	0	2:2 (4.7%)	2:2 (1.3%)
Hypertension	2:2 (1.9%)	0	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.

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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Number and Percent of Adverse Events	948:103 (97.2%)	424:42 (97.7%)	1372:145 (97.3%)
Blood and lymphatic system disorders	2:2 (1.9%)	5:3 (7.0%)	7:5 (3.4%)
Iron deficiency anaemia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Anaemia	0	3:2 (4.7%)	3:2 (1.3%)
Lymphadenopathy	0	1:1 (2.3%)	1:1 (0.7%)
Cardiac disorders	13:11 (10.4%)	3:3 (7.0%)	16:14 (9.4%)
Palpitations	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Angina pectoris	3:3 (2.8%)	0	3:3 (2.0%)
Cardiomyopathy	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Sinus tachycardia	2:2 (1.9%)	0	2:2 (1.3%)
Tachycardia	2:1 (0.9%)	0	2:1 (0.7%)
Atrial fibrillation	1:1 (0.9%)	0	1:1 (0.7%)
Myocarditis	1:1 (0.9%)	0	1:1 (0.7%)
Ventricular hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Congenital, familial and genetic disorders	2:2 (1.9%)	0	2:2 (1.3%)
Friedreich's ataxia	1:1 (0.9%)	0	1:1 (0.7%)
Hereditary haemochromatosis	1:1 (0.9%)	0	1:1 (0.7%)
Ear and labyrinth disorders	6:5 (4.7%)	2:2 (4.7%)	8:7 (4.7%)
Deafness	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Ear haemorrhage	1:1 (0.9%)	0	1:1 (0.7%)
Ear pain	1:1 (0.9%)	0	1:1 (0.7%)
Hearing impaired	1:1 (0.9%)	0	1:1 (0.7%)
Hypoacusis	1:1 (0.9%)	0	1:1 (0.7%)
Tinnitus	1:1 (0.9%)	0	1:1 (0.7%)
Endocrine disorders	0	1:1 (2.3%)	1:1 (0.7%)
Basedow's disease	0	1:1 (2.3%)	1:1 (0.7%)
Eye disorders	5:4 (3.8%)	5:5 (11.6%)	10:9 (6.0%)
Diplopia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Blepharitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Blepharospasm	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dry eye	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Eye disorders, continued...			
Altered visual depth perception	0	1:1 (2.3%)	1:1 (0.7%)
Gastrointestinal disorders	120:60 (56.6%)	59:27 (62.8%)	179:87 (58.4%)
Nausea	29:23 (21.7%)	7:7 (16.3%)	36:30 (20.1%)
Diarrhoea	21:17 (16.0%)	5:4 (9.3%)	26:21 (14.1%)
Abdominal pain	12:9 (8.5%)	8:7 (16.3%)	20:16 (10.7%)
Vomiting	8:8 (7.5%)	6:5 (11.6%)	14:13 (8.7%)
Gastrooesophageal reflux disease	8:7 (6.6%)	5:5 (11.6%)	13:12 (8.1%)
Constipation	5:5 (4.7%)	4:4 (9.3%)	9:9 (6.0%)
Dyspepsia	6:6 (5.7%)	1:1 (2.3%)	7:7 (4.7%)
Toothache	2:2 (1.9%)	4:4 (9.3%)	6:6 (4.0%)
Haemorrhoids	3:2 (1.9%)	2:2 (4.7%)	5:4 (2.7%)
Abdominal discomfort	2:2 (1.9%)	2:2 (4.7%)	4:4 (2.7%)
Abdominal pain upper	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Stomatitis	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Dysphagia	0	2:2 (4.7%)	2:2 (1.3%)
Tooth disorder	0	2:2 (4.7%)	2:2 (1.3%)
Abdominal pain lower	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Breath odour	2:2 (1.9%)	0	2:2 (1.3%)
Defaecation urgency	2:2 (1.9%)	0	2:2 (1.3%)
Dry mouth	2:2 (1.9%)	0	2:2 (1.3%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Gastrointestinal disorders, continued...			
Cheilitis	2:1 (0.9%)	0	2:1 (0.7%)
Anal fissure	0	1:1 (2.3%)	1:1 (0.7%)
Barrett's oesophagus	0	1:1 (2.3%)	1:1 (0.7%)
Bowel movement irregularity	0	1:1 (2.3%)	1:1 (0.7%)
Faecal incontinence	0	1:1 (2.3%)	1:1 (0.7%)
Faecaloma	0	1:1 (2.3%)	1:1 (0.7%)
Frequent bowel movements	0	1:1 (2.3%)	1:1 (0.7%)
Rectal polyp	0	1:1 (2.3%)	1:1 (0.7%)
Tooth impacted	0	1:1 (2.3%)	1:1 (0.7%)
Abdominal distension	1:1 (0.9%)	0	1:1 (0.7%)
Aphthous stomatitis	1:1 (0.9%)	0	1:1 (0.7%)
Dental discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Faeces hard	1:1 (0.9%)	0	1:1 (0.7%)
Faeces pale	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Gingival bleeding	1:1 (0.9%)	0	1:1 (0.7%)
Haematochezia	1:1 (0.9%)	0	1:1 (0.7%)
Melaena	1:1 (0.9%)	0	1:1 (0.7%)
Tongue coated	1:1 (0.9%)	0	1:1 (0.7%)
Traumatic tooth displacement	1:1 (0.9%)	0	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
General disorders and administration site conditions	50:38 (35.8%)	19:14 (32.6%)	69:52 (34.9%)
Fatigue	14:14 (13.2%)	7:6 (14.0%)	21:20 (13.4%)
Pyrexia	10:9 (8.5%)	2:2 (4.7%)	12:11 (7.4%)
Influenza like illness	5:4 (3.8%)	2:2 (4.7%)	7:6 (4.0%)
Asthenia	4:3 (2.8%)	2:2 (4.7%)	6:5 (3.4%)
Oedema peripheral	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)
Non-cardiac chest pain	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Cyst	3:2 (1.9%)	0	3:2 (1.3%)
Pain	2:2 (1.9%)	0	2:2 (1.3%)
Adverse drug reaction	0	1:1 (2.3%)	1:1 (0.7%)
Chest pain	0	1:1 (2.3%)	1:1 (0.7%)
Feeling abnormal	0	1:1 (2.3%)	1:1 (0.7%)
Irritability	0	1:1 (2.3%)	1:1 (0.7%)
Chest discomfort	1:1 (0.9%)	0	1:1 (0.7%)
Facial pain	1:1 (0.9%)	0	1:1 (0.7%)
Feeling hot	1:1 (0.9%)	0	1:1 (0.7%)
Gait disturbance	1:1 (0.9%)	0	1:1 (0.7%)
Inflammation	1:1 (0.9%)	0	1:1 (0.7%)
Malaise	1:1 (0.9%)	0	1:1 (0.7%)

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System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.7.1
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Safety Population

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Hepatobiliary disorders	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Cholelithiasis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Immune system disorders	3:3 (2.8%)	2:1 (2.3%)	5:4 (2.7%)
Seasonal allergy	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Hypersensitivity	1:1 (0.9%)	0	1:1 (0.7%)
Infections and infestations	160:70 (66.0%)	90:36 (83.7%)	250:106 (71.1%)
Corona virus infection	56:49 (46.2%)	25:22 (51.2%)	81:71 (47.7%)
Upper respiratory tract infection	26:18 (17.0%)	18:12 (27.9%)	44:30 (20.1%)
Influenza	14:11 (10.4%)	4:4 (9.3%)	18:15 (10.1%)
Nasopharyngitis	8:6 (5.7%)	9:7 (16.3%)	17:13 (8.7%)
Urinary tract infection	6:6 (5.7%)	6:5 (11.6%)	12:11 (7.4%)
Bronchitis	6:6 (5.7%)	1:1 (2.3%)	7:7 (4.7%)
Sinusitis	7:4 (3.8%)	2:2 (4.7%)	9:6 (4.0%)
Viral infection	2:1 (0.9%)	2:2 (4.7%)	4:3 (2.0%)
Gastroenteritis viral	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Rhinitis	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Pilonidal cyst	0	4:2 (4.7%)	4:2 (1.3%)
Tonsillitis	3:2 (1.9%)	0	3:2 (1.3%)

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Infections and infestations, continued...			
Paronychia	0	2:2 (4.7%)	2:2 (1.3%)
Chlamydial infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Ear infection	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Gastroenteritis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Pneumonia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Viral rhinitis	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Eye infection	2:2 (1.9%)	0	2:2 (1.3%)
Lower respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Respiratory tract infection	2:2 (1.9%)	0	2:2 (1.3%)
Otitis externa	4:1 (0.9%)	0	4:1 (0.7%)
Rash pustular	2:1 (0.9%)	0	2:1 (0.7%)
Tinea versicolour	2:1 (0.9%)	0	2:1 (0.7%)
Body tinea	0	1:1 (2.3%)	1:1 (0.7%)
Escherichia infection	0	1:1 (2.3%)	1:1 (0.7%)
Fungal infection	0	1:1 (2.3%)	1:1 (0.7%)
Laryngitis	0	1:1 (2.3%)	1:1 (0.7%)
Localised infection	0	1:1 (2.3%)	1:1 (0.7%)
Pharyngitis	0	1:1 (2.3%)	1:1 (0.7%)
Postoperative wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Purulence	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal mycotic infection	0	1:1 (2.3%)	1:1 (0.7%)

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Infections and infestations, continued...			
Wound infection	0	1:1 (2.3%)	1:1 (0.7%)
Furuncle	1:1 (0.9%)	0	1:1 (0.7%)
Gastroenteritis norovirus	1:1 (0.9%)	0	1:1 (0.7%)
Gastrointestinal infection	1:1 (0.9%)	0	1:1 (0.7%)
Hordeolum	1:1 (0.9%)	0	1:1 (0.7%)
Onychomycosis	1:1 (0.9%)	0	1:1 (0.7%)
Otitis media	1:1 (0.9%)	0	1:1 (0.7%)
Staphylococcal infection	1:1 (0.9%)	0	1:1 (0.7%)
Tinea cruris	1:1 (0.9%)	0	1:1 (0.7%)
Tooth abscess	1:1 (0.9%)	0	1:1 (0.7%)
Injury, poisoning and procedural complications	167:71 (67.0%)	74:26 (60.5%)	241:97 (65.1%)
Contusion	26:18 (17.0%)	10:5 (11.6%)	36:23 (15.4%)
Excoriation	27:17 (16.0%)	7:4 (9.3%)	34:21 (14.1%)
Ligament sprain	22:18 (17.0%)	7:3 (7.0%)	29:21 (14.1%)
Laceration	16:13 (12.3%)	8:6 (14.0%)	24:19 (12.8%)
Vaccination complication	18:11 (10.4%)	10:7 (16.3%)	28:18 (12.1%)
Joint injury	4:4 (3.8%)	4:4 (9.3%)	8:8 (5.4%)
Foot fracture	5:5 (4.7%)	1:1 (2.3%)	6:6 (4.0%)
Joint dislocation	2:2 (1.9%)	3:3 (7.0%)	5:5 (3.4%)
Concussion	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)

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Injury, poisoning and procedural complications, continued...			
Tooth fracture	3:3 (2.8%)	2:2 (4.7%)	5:5 (3.4%)
Hand fracture	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Muscle strain	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Periorbital haematoma	2:2 (1.9%)	2:1 (2.3%)	4:3 (2.0%)
Limb injury	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Procedural pain	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Wound	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Traumatic haematoma	3:3 (2.8%)	0	3:3 (2.0%)
Ankle fracture	3:2 (1.9%)	0	3:2 (1.3%)
Ligament rupture	0	2:2 (4.7%)	2:2 (1.3%)
Eye injury	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Head injury	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Arthropod bite	2:2 (1.9%)	0	2:2 (1.3%)
Avulsion fracture	2:2 (1.9%)	0	2:2 (1.3%)
Fibula fracture	2:2 (1.9%)	0	2:2 (1.3%)
Injury	2:2 (1.9%)	0	2:2 (1.3%)
Clavicle fracture	0	1:1 (2.3%)	1:1 (0.7%)
Facial bones fracture	0	1:1 (2.3%)	1:1 (0.7%)
Mouth injury	0	1:1 (2.3%)	1:1 (0.7%)
Post-traumatic neck syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Rib fracture	0	1:1 (2.3%)	1:1 (0.7%)

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Injury, poisoning and procedural complications, continued...			
Spinal column injury	0	1:1 (2.3%)	1:1 (0.7%)
Sunburn	0	1:1 (2.3%)	1:1 (0.7%)
Upper limb fracture	0	1:1 (2.3%)	1:1 (0.7%)
Anaemia postoperative	1:1 (0.9%)	0	1:1 (0.7%)
Back injury	1:1 (0.9%)	0	1:1 (0.7%)
Chillblains	1:1 (0.9%)	0	1:1 (0.7%)
Humerus fracture	1:1 (0.9%)	0	1:1 (0.7%)
Lower limb fracture	1:1 (0.9%)	0	1:1 (0.7%)
Soft tissue injury	1:1 (0.9%)	0	1:1 (0.7%)
Stress fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tendon rupture	1:1 (0.9%)	0	1:1 (0.7%)
Thermal burn	1:1 (0.9%)	0	1:1 (0.7%)
Tibia fracture	1:1 (0.9%)	0	1:1 (0.7%)
Tooth injury	1:1 (0.9%)	0	1:1 (0.7%)
Wrist fracture	1:1 (0.9%)	0	1:1 (0.7%)
Investigations	71:39 (36.8%)	21:12 (27.9%)	92:51 (34.2%)
Alanine aminotransferase increased	27:24 (22.6%)	6:4 (9.3%)	33:28 (18.8%)
Aspartate aminotransferase increased	13:10 (9.4%)	1:1 (2.3%)	14:11 (7.4%)
Weight decreased	4:4 (3.8%)	4:4 (9.3%)	8:8 (5.4%)
Brain natriuretic peptide increased	4:4 (3.8%)	1:1 (2.3%)	5:5 (3.4%)

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Investigations, continued...			
Vitamin D decreased	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Serum ferritin decreased	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Gamma-glutamyltransferase increased	3:3 (2.8%)	0	3:3 (2.0%)
Blood glucose increased	0	2:2 (4.7%)	2:2 (1.3%)
Blood cholesterol increased	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Blood creatine phosphokinase increased	2:2 (1.9%)	0	2:2 (1.3%)
N-terminal prohormone brain natriuretic peptide increased	2:2 (1.9%)	0	2:2 (1.3%)
Troponin increased	2:1 (0.9%)	0	2:1 (0.7%)
Blood alkaline phosphatase increased	0	1:1 (2.3%)	1:1 (0.7%)
Ceruloplasmin increased	0	1:1 (2.3%)	1:1 (0.7%)
Serum ferritin increased	0	1:1 (2.3%)	1:1 (0.7%)
White blood cell count decreased	0	1:1 (2.3%)	1:1 (0.7%)
Blood folate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Blood triglycerides increased	1:1 (0.9%)	0	1:1 (0.7%)
Blood urea increased	1:1 (0.9%)	0	1:1 (0.7%)
Electrocardiogram T wave inversion	1:1 (0.9%)	0	1:1 (0.7%)
Glomerular filtration rate decreased	1:1 (0.9%)	0	1:1 (0.7%)
Glucose tolerance test abnormal	1:1 (0.9%)	0	1:1 (0.7%)
Heart rate increased	1:1 (0.9%)	0	1:1 (0.7%)
Weight increased	1:1 (0.9%)	0	1:1 (0.7%)

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Metabolism and nutrition disorders	19:15 (14.2%)	7:6 (14.0%)	26:21 (14.1%)
Vitamin D deficiency	4:4 (3.8%)	2:2 (4.7%)	6:6 (4.0%)
Decreased appetite	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Dehydration	3:3 (2.8%)	0	3:3 (2.0%)
Hypercholesterolaemia	3:3 (2.8%)	0	3:3 (2.0%)
Iron deficiency	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Vitamin B12 deficiency	2:2 (1.9%)	0	2:2 (1.3%)
Abnormal loss of weight	0	1:1 (2.3%)	1:1 (0.7%)
Folate deficiency	0	1:1 (2.3%)	1:1 (0.7%)
Type 2 diabetes mellitus	0	1:1 (2.3%)	1:1 (0.7%)
Diabetes mellitus	1:1 (0.9%)	0	1:1 (0.7%)
Dyslipidaemia	1:1 (0.9%)	0	1:1 (0.7%)
Increased appetite	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal and connective tissue disorders	101:48 (45.3%)	34:21 (48.8%)	135:69 (46.3%)
Arthralgia	24:20 (18.9%)	6:6 (14.0%)	30:26 (17.4%)
Muscle spasms	23:16 (15.1%)	3:3 (7.0%)	26:19 (12.8%)
Back pain	16:9 (8.5%)	8:7 (16.3%)	24:16 (10.7%)
Pain in extremity	7:7 (6.6%)	3:3 (7.0%)	10:10 (6.7%)
Musculoskeletal pain	7:6 (5.7%)	2:2 (4.7%)	9:8 (5.4%)

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Musculoskeletal and connective tissue disorders, continued...			
Myalgia	5:4 (3.8%)	3:2 (4.7%)	8:6 (4.0%)
Musculoskeletal chest pain	0	3:3 (7.0%)	3:3 (2.0%)
Pain in jaw	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Muscle tightness	2:1 (0.9%)	1:1 (2.3%)	3:2 (1.3%)
Neck pain	3:2 (1.9%)	0	3:2 (1.3%)
Bursitis	2:2 (1.9%)	0	2:2 (1.3%)
Limb discomfort	2:1 (0.9%)	0	2:1 (0.7%)
Muscular weakness	0	1:1 (2.3%)	1:1 (0.7%)
Rotator cuff syndrome	0	1:1 (2.3%)	1:1 (0.7%)
Scoliosis	0	1:1 (2.3%)	1:1 (0.7%)
Sensation of heaviness	0	1:1 (2.3%)	1:1 (0.7%)
Arthritis	1:1 (0.9%)	0	1:1 (0.7%)
Flank pain	1:1 (0.9%)	0	1:1 (0.7%)
Intervertebral disc protrusion	1:1 (0.9%)	0	1:1 (0.7%)
Muscle atrophy	1:1 (0.9%)	0	1:1 (0.7%)
Musculoskeletal stiffness	1:1 (0.9%)	0	1:1 (0.7%)
Osteoporosis	1:1 (0.9%)	0	1:1 (0.7%)
Spinal disorder	1:1 (0.9%)	0	1:1 (0.7%)
Synovial cyst	1:1 (0.9%)	0	1:1 (0.7%)

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Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5:4 (3.8%)	4:4 (9.3%)	9:8 (5.4%)
Skin papilloma	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Benign neoplasm of eyelid	0	1:1 (2.3%)	1:1 (0.7%)
Haemangioma of skin	0	1:1 (2.3%)	1:1 (0.7%)
Uterine leiomyoma	0	1:1 (2.3%)	1:1 (0.7%)
Morton's neuroma	1:1 (0.9%)	0	1:1 (0.7%)
Pituitary tumour benign	1:1 (0.9%)	0	1:1 (0.7%)
Nervous system disorders	84:34 (32.1%)	24:18 (41.9%)	108:52 (34.9%)
Headache	50:20 (18.9%)	7:6 (14.0%)	57:26 (17.4%)
Dizziness	8:6 (5.7%)	3:3 (7.0%)	11:9 (6.0%)
Migraine	6:4 (3.8%)	0	6:4 (2.7%)
Muscle spasticity	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Neuropathy peripheral	0	3:3 (7.0%)	3:3 (2.0%)
Restless legs syndrome	1:1 (0.9%)	2:2 (4.7%)	3:3 (2.0%)
Loss of consciousness	3:2 (1.9%)	0	3:2 (1.3%)
Hypoaesthesia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Presyncope	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Ataxia	2:2 (1.9%)	0	2:2 (1.3%)
Dysgeusia	2:2 (1.9%)	0	2:2 (1.3%)

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System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Nervous system disorders, continued...			
Speech disorder	2:2 (1.9%)	0	2:2 (1.3%)
Disturbance in attention	0	1:1 (2.3%)	1:1 (0.7%)
Hyperaesthesia	0	1:1 (2.3%)	1:1 (0.7%)
Syncope	0	1:1 (2.3%)	1:1 (0.7%)
Tremor	0	1:1 (2.3%)	1:1 (0.7%)
Balance disorder	1:1 (0.9%)	0	1:1 (0.7%)
Convulsion	1:1 (0.9%)	0	1:1 (0.7%)
Migraine with aura	1:1 (0.9%)	0	1:1 (0.7%)
Neuralgia	1:1 (0.9%)	0	1:1 (0.7%)
Paraesthesia	1:1 (0.9%)	0	1:1 (0.7%)
Post-traumatic headache	1:1 (0.9%)	0	1:1 (0.7%)
Somnolence	1:1 (0.9%)	0	1:1 (0.7%)
Psychiatric disorders	25:19 (17.9%)	15:10 (23.3%)	40:29 (19.5%)
Depression	8:8 (7.5%)	6:6 (14.0%)	14:14 (9.4%)
Insomnia	6:5 (4.7%)	2:1 (2.3%)	8:6 (4.0%)
Anxiety	5:5 (4.7%)	0	5:5 (3.4%)
Attention deficit/hyperactivity disorder	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Initial insomnia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Confusional state	0	1:1 (2.3%)	1:1 (0.7%)
Delirium	0	1:1 (2.3%)	1:1 (0.7%)

The summaries provided are represented by the format: x:y (p%) where x refers to the number of treatment-emergent adverse events, y refers to the number of patients experiencing one or more adverse events, and p is the percent of patients for the given treatment.
The number of patients who experienced at least one adverse event is summarized in each row.
Events collected with relationship other than UNRELATED or UNLIKELY RELATED are considered RELATED.
System organ classes are presented alphabetically. Preferred terms within system organ classes are presented by decreasing frequency count.

Note: Adverse Events are coded using MedDRA® (Medical Dictionary for Regulatory Activities) Version 14.1

Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Psychiatric disorders, continued...			
Mood swings	0	1:1 (2.3%)	1:1 (0.7%)
Suicidal behaviour	0	1:1 (2.3%)	1:1 (0.7%)
Suicidal ideation	0	1:1 (2.3%)	1:1 (0.7%)
Abnormal dreams	1:1 (0.9%)	0	1:1 (0.7%)
Bipolar disorder	1:1 (0.9%)	0	1:1 (0.7%)
Insomnia related to another mental condition	1:1 (0.9%)	0	1:1 (0.7%)
Libido decreased	1:1 (0.9%)	0	1:1 (0.7%)
Renal and urinary disorders	21:15 (14.2%)	8:5 (11.6%)	29:20 (13.4%)
Micturition urgency	6:6 (5.7%)	3:3 (7.0%)	9:9 (6.0%)
Nephrolithiasis	6:5 (4.7%)	0	6:5 (3.4%)
Urinary incontinence	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Incontinence	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Renal cyst	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Glycosuria	0	1:1 (2.3%)	1:1 (0.7%)
Nocturia	0	1:1 (2.3%)	1:1 (0.7%)
Haematuria	1:1 (0.9%)	0	1:1 (0.7%)
Pollakiuria	1:1 (0.9%)	0	1:1 (0.7%)
Renal colic	1:1 (0.9%)	0	1:1 (0.7%)
Urinary retention	1:1 (0.9%)	0	1:1 (0.7%)
Urine odour abnormal	1:1 (0.9%)	0	1:1 (0.7%)

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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Reproductive system and breast disorders	19:13 (12.3%)	10:8 (18.6%)	29:21 (14.1%)
Dysmenorrhoea	5:2 (1.9%)	2:1 (2.3%)	7:3 (2.0%)
Ovarian cyst	3:2 (1.9%)	1:1 (2.3%)	4:3 (2.0%)
Menstruation irregular	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Menorrhagia	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Vaginal laceration	2:2 (1.9%)	0	2:2 (1.3%)
Breast tenderness	0	1:1 (2.3%)	1:1 (0.7%)
Erectile dysfunction	0	1:1 (2.3%)	1:1 (0.7%)
Polymenorrhoea	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal burning sensation	0	1:1 (2.3%)	1:1 (0.7%)
Vulvovaginal pruritus	0	1:1 (2.3%)	1:1 (0.7%)
Amenorrhoea	1:1 (0.9%)	0	1:1 (0.7%)
Mammary duct ectasia	1:1 (0.9%)	0	1:1 (0.7%)
Metrorrhagia	1:1 (0.9%)	0	1:1 (0.7%)
Pelvic pain	1:1 (0.9%)	0	1:1 (0.7%)
Polycystic ovaries	1:1 (0.9%)	0	1:1 (0.7%)
Prostatitis	1:1 (0.9%)	0	1:1 (0.7%)

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The number of patients who experienced at least one adverse event is summarized in each row.
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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Respiratory, thoracic and mediastinal disorders	37:24 (22.6%)	13:8 (18.6%)	50:32 (21.5%)
Cough	10:10 (9.4%)	4:3 (7.0%)	14:13 (8.7%)
Epistaxis	7:6 (5.7%)	1:1 (2.3%)	8:7 (4.7%)
Nasal congestion	3:3 (2.8%)	0	3:3 (2.0%)
Oropharyngeal pain	3:3 (2.8%)	0	3:3 (2.0%)
Dyspnoea	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rhinorrhoea	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Sleep apnoea syndrome	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rhinitis allergic	2:2 (1.9%)	0	2:2 (1.3%)
Asthma	0	2:1 (2.3%)	2:1 (0.7%)
Wheezing	0	2:1 (2.3%)	2:1 (0.7%)
Nasal disorder	2:1 (0.9%)	0	2:1 (0.7%)
Choking	0	1:1 (2.3%)	1:1 (0.7%)
Dysphonia	1:1 (0.9%)	0	1:1 (0.7%)
Nasal obstruction	1:1 (0.9%)	0	1:1 (0.7%)
Nasal septum deviation	1:1 (0.9%)	0	1:1 (0.7%)
Nasal turbinate hypertrophy	1:1 (0.9%)	0	1:1 (0.7%)
Pulmonary congestion	1:1 (0.9%)	0	1:1 (0.7%)
Sinus congestion	1:1 (0.9%)	0	1:1 (0.7%)
Upper-airway cough syndrome	1:1 (0.9%)	0	1:1 (0.7%)

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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders	31:27 (25.5%)	24:13 (30.2%)	55:40 (26.8%)
Eczema	3:3 (2.8%)	5:3 (7.0%)	8:6 (4.0%)
Acne	1:1 (0.9%)	3:3 (7.0%)	4:4 (2.7%)
Alopecia	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Night sweats	2:2 (1.9%)	1:1 (2.3%)	3:3 (2.0%)
Hyperhidrosis	3:3 (2.8%)	0	3:3 (2.0%)
Urticaria	3:3 (2.8%)	0	3:3 (2.0%)
Rash macular	4:2 (1.9%)	0	4:2 (1.3%)
Psoriasis	1:1 (0.9%)	2:1 (2.3%)	3:2 (1.3%)
Pruritus	0	2:2 (4.7%)	2:2 (1.3%)
Dermatitis contact	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Rash maculo-papular	1:1 (0.9%)	1:1 (2.3%)	2:2 (1.3%)
Dandruff	0	1:1 (2.3%)	1:1 (0.7%)
Dermal cyst	0	1:1 (2.3%)	1:1 (0.7%)
Erythema	0	1:1 (2.3%)	1:1 (0.7%)
Heat rash	0	1:1 (2.3%)	1:1 (0.7%)
Nail discolouration	0	1:1 (2.3%)	1:1 (0.7%)
Petechiae	0	1:1 (2.3%)	1:1 (0.7%)
Pruritus generalised	0	1:1 (2.3%)	1:1 (0.7%)
Rosacea	0	1:1 (2.3%)	1:1 (0.7%)

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Table 14.3.1.7.1
Overall Non-Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo - Omaveloxolone (N=106)	Omaveloxolone - Omaveloxolone (N=43)	Overall Omaveloxolone (N=149)
Skin and subcutaneous tissue disorders, continued...			
Blister	1:1 (0.9%)	0	1:1 (0.7%)
Dermatitis psoriasiform	1:1 (0.9%)	0	1:1 (0.7%)
Dry skin	1:1 (0.9%)	0	1:1 (0.7%)
Ecchymosis	1:1 (0.9%)	0	1:1 (0.7%)
Ingrowing nail	1:1 (0.9%)	0	1:1 (0.7%)
Milia	1:1 (0.9%)	0	1:1 (0.7%)
Skin disorder	1:1 (0.9%)	0	1:1 (0.7%)
Skin swelling	1:1 (0.9%)	0	1:1 (0.7%)
Skin ulcer	1:1 (0.9%)	0	1:1 (0.7%)
Swelling face	1:1 (0.9%)	0	1:1 (0.7%)
Vascular disorders	6:6 (5.7%)	3:3 (7.0%)	9:9 (6.0%)
Haematoma	3:3 (2.8%)	1:1 (2.3%)	4:4 (2.7%)
Deep vein thrombosis	0	2:2 (4.7%)	2:2 (1.3%)
Hypertension	2:2 (1.9%)	0	2:2 (1.3%)
Hypotension	1:1 (0.9%)	0	1:1 (0.7%)

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Table 14.3.2.1
Death

Subject ID (Sex/Age)	Treatment Start Date	Treatment End Date	Death Date

NO PATIENTS MET THE CRITERIA OF THIS REPORT