Clinical trial results:
Efficacy, Safety, and Tolerability of Fosmetpantotenate (RE-024), a Phosphopantothenate Replacement Therapy, in Patients With Pantothenate Kinase-Associated Neurodegeneration (PKAN): A Randomized, Double-Blind, Placebo-Controlled Study With an Open-Label Extension

Summary

EudraCT number	2016-001955-29
Trial protocol	DE ES GB CZ NO FR PL IT
Global end of trial date	30 December 2019

Results information

Result version number	v1
This version publication date	10 September 2020
First version publication date	10 September 2020

Trial information

Trial identification

Sponsor protocol code	024PKAN15004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03041116
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Retrophin, Inc.
Sponsor organisation address	3721 Valley Centre Drive, Suite 200, San Diego, United States, 92130
Public contact	Clinical Trial Information Desk, Retrophin Inc., +1 877-659-5518,
Scientific contact	Clinical Trial Information Desk, Retrophin Inc., +1 877-659-5518,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002036-PIP01-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety, and tolerability of fosmetpantotenate over 24 weeks in subjects with Pantothenate Kinase-associated Neurodegeneration (PKAN).

Protection of trial subjects:

At each study site, the protocol and associated informed consent form (ICF), participant information sheet, any information provided to the subject, and the investigator's brochure (IB), reviewed and approved by Institutional Review Board (IRB)/ Independent Ethics Committee (IEC). Amendments to the protocol and ICF were reviewed and approved in the same manner before being implemented. This study was conducted in accordance with Good Clinical Practice (GCP) as required by the International Council for Harmonisation (ICH) guidelines and in accordance with country-specific laws and regulations governing clinical studies of investigational products. Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki (1996). The study progress in accordance with the protocol, GCP, and local regulations were monitored periodically by Sponsor representative or by its designee. During the conduct of the study, the data monitoring committee (DMC) periodically reviewed safety study results and evaluated treatment groups for excess adverse events (AEs), and the paediatric subjects were enrolled only after 8 adult subjects had been enrolled, completed 3 weeks of study treatment, and safety data from adult subjects were reviewed by the DMC. All study findings and documents were regarded as confidential. Each subject or parent or legal guardians were given full and adequate oral and written information about the nature, purpose, possible risks, and benefits of the study as well as potential treatment alternatives.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United States: 24

Worldwide total number of subjects	84
EEA total number of subjects	57

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	17
Adolescents (12-17 years)	13
Adults (18-64 years)	54
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Spain, United States, Canada, Czech Republic, France, Germany, Italy, Norway, and Poland from 17Jul2017 to 23Dec2019. In total 91 subjects were screened. Of these 84 subjects were randomised in the double blind period and 78 subjects completed the double blind period.

Pre-assignment

Screening details:

The study consisted of a screening period of up to 29 days. All assessments at screening were done as per the schedule of assessments.

Period 1

Period 1 title	Double-blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

This was double-blind clinical study. The identity of the treatments were concealed by the use of study drugs that are identical in packaging, labeling, and schedule of administration, appearance, taste, and odor. During the open-label extension, subjects (including parents or legal guardians of subjects <18 years of age) and site personnel remained blinded to the subject’s randomized treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Each randomized subject received oral dose of placebo matched to fosmetpantotenate (RE-024) with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject’s age and weight at screening for 24 Weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered orally once on Day 1, two times a day on Days 2 and 3, TID on Day 4, then continued till Week 24. Subject’s aged 18 to 65 years and 6 to <18 years weighing >= 40 kg: received 300 mg dose on Day 1, 300 mg twice a day on Days 2 and 3, 300 mg TID on Day 4; subject’s aged 6 to <18 years weighing >=20 kg but <40 kg: received 150 mg dose on Day 1, 150 mg twice a day on Days 2 and 3, 150 mg TID on Day 4; subject’s aged 6 to <18 years weighing <20 kg: received 75 mg dose on Day 1, 75 mg twice a day on Days 2 and 3, 75 mg TID on Day 4.

Arm title	Fosmetpantotenate

Arm description:

Each randomized subject received oral dose of fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject’s age and weight at screening for 24 Weeks.

Arm type	Experimental
Investigational medicinal product name	Fosmetpantotenate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered orally once on Day 1, two times a day on Days 2 and 3, TID on Day 4, then continued till Week 24. Subject's aged 18 to 65 years and 6 to <18 years weighing >= 40 kg: received 300 mg dose on Day 1, 300 mg twice a day on Days 2 and 3, 300 mg TID on Day 4; subject's aged 6 to <18 years weighing >=20 kg but <40 kg: received 150 mg dose on Day 1, 150 mg twice a day on Days 2 and 3, 150 mg TID on Day 4; subject's aged 6 to <18 years weighing <20 kg: received 75 mg dose on Day 1, 75 mg twice a day on Days 2 and 3, 75 mg TID on Day 4.

Number of subjects in period 1	Placebo	Fosmetpantotenate
Started	43	41
Completed	37	41
Not completed	6	0
Withdrawal of Subject/Guardian Assent/Consent	4	-
Death	2	-

Period 2

Period 2 title	Open-label
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Each randomized subject received oral dose of placebo matched to fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose TID from Day 4, based on the subject's age and weight at screening for 24 Weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered orally once on Day 1, two times a day on Days 2 and 3, TID on Day 4, then continued till Week 24. Subject's aged 18 to 65 years and 6 to <18 years weighing >= 40 kg: received 300 mg dose on Day 1, 300 mg twice a day on Days 2 and 3, 300 mg TID on Day 4; subject's aged 6 to <18 years weighing >=20 kg but <40 kg: received 150 mg dose on Day 1, 150 mg twice a day on Days 2 and 3, 150 mg TID on Day 4; subject's aged 6 to <18 years weighing <20 kg: received 75 mg dose on Day 1, 75 mg twice a day on Days 2 and 3, 75 mg TID on Day 4.

Arm title	Fosmetpantotenate

Arm description:

Each randomized subject received oral dose of fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose TID from Day 4, based on the subject's age and weight at screening for 24 Weeks. No dose escalation was required for the open-label period. All subjects (including placebo

group subjects from the double-blind period initiating fosmetpantotenate treatment) started treatment with fosmetpantotenate in the open-label period according to the dose of study medication they were receiving at the end of the double-blind period.

Arm type	Experimental
Investigational medicinal product name	Fosmetpantotenate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered orally once on Day 1, two times a day on Days 2 and 3, TID on Day 4, then continued till Week 24. Subject's aged 18 to 65 years and 6 to <18 years weighing >= 40 kg: received 300 mg dose on Day 1, 300 mg twice a day on Days 2 and 3, 300 mg TID on Day 4; subject's aged 6 to <18 years weighing >=20 kg but <40 kg: received 150 mg dose on Day 1, 150 mg twice a day on Days 2 and 3, 150 mg TID on Day 4; subject's aged 6 to <18 years weighing <20 kg: received 75 mg dose on Day 1, 75 mg twice a day on Days 2 and 3, 75 mg TID on Day 4.

Number of subjects in period 2	Placebo	Fosmetpantotenate
Started	37	41
Completed	0	0
Not completed	37	41
Withdrawal of Subject/Guardian Assent/Consent	-	1
Death	-	1
Termination of the Study by Sponsor	37	39

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Each randomized subject received oral dose of placebo matched to fosmetpantotenate (RE-024) with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject's age and weight at screening for 24 Weeks.	
Reporting group title	Fosmetpantotenate
Reporting group description:	
Each randomized subject received oral dose of fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject's age and weight at screening for 24 Weeks.	

Reporting group values	Placebo	Fosmetpantotenate	Total
Number of subjects	43	41	84
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	9	8	17
Adolescents (12-17 years)	7	6	13
Adults (18-64 years)	27	27	54
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	23.1	22.6	
standard deviation	± 13.56	± 10.61	-
Gender categorical Units: Subjects			
Female	19	20	39
Male	24	21	45

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Each randomized subject received oral dose of placebo matched to fosmetpantotenate (RE-024) with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject's age and weight at screening for 24 Weeks.

Reporting group title	Fosmetpantotenate

Reporting group description:

Each randomized subject received oral dose of fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose three times a day (TID) from Day 4, based on the subject's age and weight at screening for 24 Weeks.

Reporting group title	Placebo

Reporting group description:

Each randomized subject received oral dose of placebo matched to fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose TID from Day 4, based on the subject's age and weight at screening for 24 Weeks.

Reporting group title	Fosmetpantotenate

Reporting group description:

Each randomized subject received oral dose of fosmetpantotenate with dose escalation for Days 1 through 3, followed by the full dose TID from Day 4, based on the subject's age and weight at screening for 24 Weeks. No dose escalation was required for the open-label period. All subjects (including placebo group subjects from the double-blind period initiating fosmetpantotenate treatment) started treatment with fosmetpantotenate in the open-label period according to the dose of study medication they were receiving at the end of the double-blind period.

Primary: Change from baseline in the Pantothenate Kinase-Associated Neurodegeneration–Activities of Daily Living (PKAN-ADL) total score to the end of the 24-week double-blind period

End point title	Change from baseline in the Pantothenate Kinase-Associated Neurodegeneration–Activities of Daily Living (PKAN-ADL) total score to the end of the 24-week double-blind period

End point description:

Change from baseline to Week 24 activities of daily living was assessed on the PKAN-ADL scale based on the Unified Parkinson's Disease Rating Scale (UPDRS) Part II.

End point type	Primary

End point timeframe:

At Baseline (Day -1), and Week 24

End point values	Placebo	Fosmetpantotenate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Unit on a Scale				
least squares mean (standard error)				
Week 24	-1.3 (± 0.58)	-1.3 (± 0.56)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 24
Comparison groups	Placebo v Fosmetpantotenate
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9115 [1]
Method	Mixed models analysis
Parameter estimate	Difference in LS Mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	1.51
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[1] - p-value is derived from test of contrast between treatment effects using LSM estimate, adjusted for baseline score and age group from Type III analysis. The test of contrast at week 24 is considered the primary comparison.

Primary: Number of subjects with at least 1 (≥1) treatment-emergent adverse events (TEAEs) and treatment-emergent serious adverse events (TESAEs)

End point title	Number of subjects with at least 1 (≥1) treatment-emergent adverse events (TEAEs) and treatment-emergent serious adverse events (TESAEs)[2]

End point description:

An adverse event (AE) is any untoward medical occurrence associated with the use of the investigational product (IP; active or placebo) in a subject, without regard to possibility of causal relationship with IP. A serious adverse event (SAE) is an AE resulting in any of the following outcomes: death; initial or prolonged inpatient hospitalization ; life threatening experience (immediate risk of death from AE); persistent or significant disability/incapacity; congenital anomaly/birth defect; other medically important serious medical events. The TEAEs in double-blind period are defined as AEs that are new or are a worsening of an existing condition that begins from day of first dose of IP until day after last dose for double-blind treatment period.

End point type	Primary

End point timeframe:

From Screening until end of treatment (Approximately 29 Months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was available for this end point.

End point values	Placebo	Fosmetpantotenate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Count of Subjects				
number (not applicable)				
≥1 AE	36	34		
≥1 TEAE	35	34		
≥1 TESAE	6	8		
≥1 TEAE leading to IP discontinuation	2	0		
Mild TEAE	15	15		
Moderate TEAE	12	16		
Severe TEAE	8	3		
TEAE not related to IP	11	12		
TEAE unlikely related to IP	5	7		
Possibly related to IP	14	10		
Related to IP	5	5		
TEAE with outcome of death	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in the Unified Parkinson's Disease Rating Scale Part 3 (UPDRS-III) total score to the end of the 24-week double-blind period

End point title	Absolute change from baseline in the Unified Parkinson's Disease Rating Scale Part 3 (UPDRS-III) total score to the end of the 24-week double-blind period

End point description:

The UPDRS is a comprehensive assessment of the burden and severity of signs and symptoms of parkinsonism captured via systematic interview and neurological examination.

End point type	Secondary

End point timeframe:

At Baseline (Day -1), and Week 24

End point values	Placebo	Fosmetpantotenate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Unit on a Scale				
arithmetic mean (standard deviation)				
Week 24 (n= 35, 40)	-1.0 (± 6.81)	0.7 (± 5.25)		

Statistical analyses

Statistical analysis title	Statistical analysis for Week 24
Comparison groups	Placebo v Fosmetpantotenate
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1421 [3]
Method	Mixed models analysis
Parameter estimate	Difference in LS Mean
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4.78
Variability estimate	Standard error of the mean
Dispersion value	1.38

Notes:

[3] - p-value is derived from the test of contrast between treatment effects using the LSM estimate, adjusted for baseline score and age group from the Type III analysis. The test of contrast at week 24 is considered the primary comparison.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Screening until end of treatment (Approximately 29 Months)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Fosmetpantotenate Treatment-Placebo
Reporting group description: -	
Reporting group title	Fosmetpantotenate Treatment-Fosmetpantotenate
Reporting group description: -	
Reporting group title	Double-Blind- Placebo
Reporting group description: -	
Reporting group title	Double-Blind- Fosmetpantotenate
Reporting group description: -	
Reporting group title	Open-label-Placebo
Reporting group description: -	
Reporting group title	Open-label-Fosmetpantotenate
Reporting group description: -	

Serious adverse events	Fosmetpantotenate Treatment-Placebo	Fosmetpantotenate Treatment-Fosmetpantotenate	Double-Blind-Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 37 (24.32%)	9 / 41 (21.95%)	6 / 43 (13.95%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	2
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shunt malfunction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Fracture treatment			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 37 (10.81%)	4 / 41 (9.76%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 5	1 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin lesion			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Skin Infections			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis streptococcal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double-Blind-Fosmetpantotenate	Open-label-Placebo	Open-label-Fosmetpantotenate
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 41 (19.51%)	9 / 37 (24.32%)	4 / 41 (9.76%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt malfunction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Fracture treatment			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 41 (4.88%)	4 / 37 (10.81%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	1 / 3	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin lesion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Skin Infections			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis streptococcal			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Fosmetpantotenate Treatment-Placebo	Fosmetpantotenate Treatment-Fosmetpantotenate	Double-Blind-Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 37 (67.57%)	35 / 41 (85.37%)	34 / 43 (79.07%)
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	7 / 41 (17.07%)	4 / 43 (9.30%)
occurrences (all)	1	8	4
Discomfort			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
General physical health deterioration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Generalised oedema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Medical device site inflammation			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Medical device site rash			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Seasonal allergy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Apnoea			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Bronchial secretion retention			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Choking			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Obstructive airways disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pharyngeal erythema			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Insomnia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Sleep disorder			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0

Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Affect lability			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Product issues			
Product taste abnormal			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	2 / 43 (4.65%)
occurrences (all)	0	2	2
Device failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Device occlusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	4 / 41 (9.76%)	2 / 43 (4.65%)
occurrences (all)	1	4	4
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 37 (8.11%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	3	1	2
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Haemoglobin decreased			

subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	2 / 43 (4.65%)
occurrences (all)	0	1	2
Alanine aminotransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Bacterial test positive			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Blood cholesterol increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Blood glucose decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Cardiac murmur			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Coagulation time prolonged			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Crystal urine present			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	2 / 43 (4.65%)
occurrences (all)	0	1	3
Culture throat positive			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Haemoglobin urine present			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	2 / 43 (4.65%)
occurrences (all)	1	1	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0

Monocyte count increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Monocyte percentage increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Neutrophil count increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Nitrite urine present			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Platelet count increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Urine leukocyte esterase positive			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
White blood cell count decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
White blood cell count increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Cortisol decreased			

subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Platelet count decreased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Prothrombin time prolonged			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Urine leukocyte esterase			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Gastrostomy tube site complication			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	3 / 41 (7.32%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Laceration			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	1 / 41 (2.44%)	2 / 43 (4.65%)
occurrences (all)	2	1	4
Fall			
subjects affected / exposed	1 / 37 (2.70%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
Hand fracture			
subjects affected / exposed	1 / 37 (2.70%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
Skin abrasion			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Arthropod bite			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0

Contusion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Face injury			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
Foetal exposure during pregnancy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Traumatic haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Animal scratch			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Eyelid contusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Scar			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Traumatic fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1

Joint dislocation			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 37 (8.11%)	7 / 41 (17.07%)	8 / 43 (18.60%)
occurrences (all)	3	11	9
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 37 (8.11%)	4 / 41 (9.76%)	5 / 43 (11.63%)
occurrences (all)	3	4	9
Oromandibular dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	2	1	1
Dizziness			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	2 / 43 (4.65%)
occurrences (all)	0	2	3
Paraesthesia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Drooling			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Dyskinesia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Muscle spasticity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Neuralgia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Nystagmus			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	2 / 43 (4.65%)
occurrences (all)	0	1	2
Multiple sclerosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Nerve compression			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Epilepsy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Opisthotonus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Parkinsonism			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Restless legs syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Hyperkinesia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	2
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Dark circles under eyes			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Eczema eyelids			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Optic atrophy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 37 (5.41%)	8 / 41 (19.51%)	4 / 43 (9.30%)
occurrences (all)	2	11	6
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	5 / 41 (12.20%)	0 / 43 (0.00%)
occurrences (all)	1	5	0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	8 / 41 (19.51%)	5 / 43 (11.63%)
occurrences (all)	2	12	6
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	4 / 41 (9.76%)	2 / 43 (4.65%)
occurrences (all)	2	5	2
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	4 / 41 (9.76%)	7 / 43 (16.28%)
occurrences (all)	0	4	13
Dyspepsia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 37 (2.70%)	2 / 41 (4.88%)	2 / 43 (4.65%)
occurrences (all)	1	2	3
Dry mouth			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Faecaloma			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Faeces soft			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Haematochezia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Hyperchlorhydria			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Parotid gland enlargement			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Tongue disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Abdominal pain lower			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrointestinal hypermotility			

subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
Dermal cyst			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Rash generalised			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Acne			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2

Rash pruritic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Endocrine disorders			
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Arthralgia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Knee deformity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Osteopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0

Muscle tightness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Posture abnormal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Infections and infestations			
Ear infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	3 / 41 (7.32%)	0 / 43 (0.00%)
occurrences (all)	1	3	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	3 / 41 (7.32%)	0 / 43 (0.00%)
occurrences (all)	1	4	0
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	5 / 41 (12.20%)	2 / 43 (4.65%)
occurrences (all)	1	7	2
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	6 / 41 (14.63%)	0 / 43 (0.00%)
occurrences (all)	2	6	0
Bronchitis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	1	2	0
Genital candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Skin infection			
subjects affected / exposed	0 / 37 (0.00%)	2 / 41 (4.88%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Clostridium difficile infection			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Gastrointestinal infection			
subjects affected / exposed	1 / 37 (2.70%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Helminthic infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Oral candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Stoma site infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Pneumonia influenzal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	2	0	1
Ear lobe infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	3 / 41 (7.32%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Iron deficiency			
subjects affected / exposed	0 / 37 (0.00%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	1 / 37 (2.70%)	0 / 41 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 41 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2

Non-serious adverse events	Double-Blind-Fosmetpantotenate	Open-label-Placebo	Open-label-Fosmetpantotenate

Total subjects affected by non-serious adverse events subjects affected / exposed	34 / 41 (82.93%)	25 / 37 (67.57%)	25 / 41 (60.98%)
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 41 (12.20%)	1 / 37 (2.70%)	2 / 41 (4.88%)
occurrences (all)	6	1	2
Discomfort			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Feeling cold			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
General physical health deterioration			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Generalised oedema			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Medical device site inflammation			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Medical device site rash			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Drug hypersensitivity			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Apnoea			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Bronchial secretion retention			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1
Nasal congestion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Choking			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Obstructive airways disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Sleep disorder			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Affect lability			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Product issues			
Product taste abnormal			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Device failure			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Device occlusion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 41 (9.76%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	4	1	0
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	3 / 37 (8.11%)	1 / 41 (2.44%)
occurrences (all)	0	3	1
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	2 / 37 (5.41%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Haemoglobin decreased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences (all)	0	1	1

Bacterial test positive			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Blood cholesterol increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Blood glucose decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Coagulation time prolonged			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Crystal urine present			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Culture throat positive			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Haemoglobin urine present			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Monocyte count increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Monocyte percentage increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0

Neutrophil count increased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Nitrite urine present			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Platelet count increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
White blood cell count decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
White blood cell count increased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Blood urea increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Cortisol decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
White blood cells urine positive			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Prothrombin time prolonged			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Gastrostomy tube site complication			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1
Laceration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 41 (0.00%)	2 / 37 (5.41%)	1 / 41 (2.44%)
occurrences (all)	0	2	1
Fall			
subjects affected / exposed	2 / 41 (4.88%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Hand fracture			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences (all)	1	1	1
Skin abrasion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Arthropod bite			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Face injury			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Foetal exposure during pregnancy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1

Limb injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Traumatic haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Animal scratch			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Eyelid contusion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Scar			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Traumatic fracture			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 41 (14.63%)	3 / 37 (8.11%)	1 / 41 (2.44%)
occurrences (all)	10	3	1
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 41 (4.88%)	3 / 37 (8.11%)	2 / 41 (4.88%)
occurrences (all)	2	3	2
Oromandibular dystonia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	2 / 37 (5.41%)	0 / 41 (0.00%)
occurrences (all)	1	2	0
Dizziness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Drooling			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Dyskinesia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Muscle spasticity			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Nystagmus			

subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	2
Somnolence			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Nerve compression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Opisthotonus			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Parkinsonism			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperkinesia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0

Normochromic normocytic anaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dark circles under eyes			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Eczema eyelids			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Optic atrophy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 41 (12.20%)	2 / 37 (5.41%)	3 / 41 (7.32%)
occurrences (all)	5	2	6
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 41 (9.76%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences (all)	4	1	1
Vomiting			
alternative assessment type:			

Systematic			
subjects affected / exposed	4 / 41 (9.76%)	2 / 37 (5.41%)	4 / 41 (9.76%)
occurrences (all)	8	2	4
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 41 (7.32%)	2 / 37 (5.41%)	2 / 41 (4.88%)
occurrences (all)	3	2	2
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences (all)	2	0	2
Dyspepsia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	1 / 41 (2.44%)
occurrences (all)	1	1	1
Dry mouth			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Faecaloma			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Faeces soft			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Haematochezia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0

Hyperchlorhydria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Parotid gland enlargement			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Tongue disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	3	0	1
Dermal cyst			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Dermatitis diaper			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Ingrowing nail			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Rash generalised			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Acne			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0

Urine odour abnormal			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Knee deformity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Posture abnormal			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Ear infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 41 (7.32%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	3	1	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 41 (7.32%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	4	1	0
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 41 (7.32%)	1 / 37 (2.70%)	2 / 41 (4.88%)
occurrences (all)	4	1	3
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 41 (2.44%)	2 / 37 (5.41%)	5 / 41 (12.20%)
occurrences (all)	1	2	5
Bronchitis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	2	1	0
Genital candidiasis			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	3
Skin infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	3
Clostridium difficile infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Gastroenteritis viral			

subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	1 / 41 (2.44%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Helminthic infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Stoma site infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			

subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Pneumonia influenzal			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Ear lobe infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 41 (4.88%)	0 / 37 (0.00%)	1 / 41 (2.44%)
occurrences (all)	2	0	1
Iron deficiency			
subjects affected / exposed	1 / 41 (2.44%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 37 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2018	Amendment 1 (Version 2): The following changes were made to the protocol- Changed lower age limit for classification as an adult from 19 to 18 years of age. Excluded subjects with history of metastasized or ongoing malignancy. Prohibited changing deep brain stimulation (DBS) settings during the study. Clarified that a dose escalation was not required for subjects once they rolled over from the double-blind period and that all subjects should start the open-label period according to the dose of study medication they were receiving at the end of the double-blind period. Clarified that, for subjects 6 to <18 years of age, in the open-label extension period, the initial dose may be adjusted, if needed, based on the subject's weight at the end of the double-blind period. In addition, the reasons for permanent discontinuation of study medication were updated to be Clinical Data Interchange Standards Consortium (CDISC)-compliant and text was added to clarify that subjects who discontinue study medication early should be encouraged to continue study visits through Week 120. An additional visit, End of Treatment, was added. Added guidance for follow-up management of subjects who presented with suicidality on the Columbia Suicide Severity Rating Scale (C-SSRS). Provided option for subjects to have some study visits performed at home at the discretion of the Investigator. Added text to clarify that the bitter taste of the study medication was not to be captured as an AE, although reactions to the taste such as vomiting, and gagging could be reported as AEs. Added elevations in liver enzymes as an AE of interest. Clarified that male subjects were to report if their female partner became pregnant and that female subjects would be discontinued from study medication (not the study) if they became pregnant.
06 February 2019	Amendment 2 (Version 3: US version only): Extended open-label extension period from 96 weeks to 276 weeks. Added an exploratory assessment for research.
23 May 2019	Amendment 3 (Global Version 4): Clarified that the open-label extension period should have been 278 weeks (instead of 276). Clarified circumstances for which routine electrocardiograms may be waived for subjects using DBS devices. Added flexibility to waive the C-SSRS assessment based on the Polish's principal investigator, judgement. Reduced the number of blood draws for exploratory assessment for research. Added analysis of PKAN-ADL at Week 3 to align with the statistical analysis plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 December 2019	The sponsor made the decision to terminate the open label extension of the study after the results of the double blind period were analyzed and did not show efficacy. The primary efficacy endpoint was neither statistically significant nor clinically different between treatment and placebo.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In the double-blind period, fosmetpantotenate did not show statistically significant effects or clinical benefits; hence, the open-label period of the study was terminated. So, only endpoints for double-blind period are presented.

Notes: