



Clinical trial results:

Randomized, Double-Blind, Multicenter, Placebo-Controlled, Safety and Efficacy Study of RDEA594 Versus Placebo in the Treatment of Hyperuricemia in Patients with Gout

Summary

EudraCT number	2009-013055-30
Trial protocol	ES DE GB CZ BG
Global end of trial date	06 September 2011

Results information

Result version number	v1 (current)
This version publication date	05 February 2017
First version publication date	05 February 2017

Trial information

Trial identification

Sponsor protocol code	RDEA594-202
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ardea Biosciences, Inc.
Sponsor organisation address	9390 Towne Centre Drive, San Diego, United States, 92121
Public contact	Maple Fung, MD, Ardea Biosciences, Inc., 1 8586526500 x,
Scientific contact	Maple Fung, MD, Ardea Biosciences, Inc., 1 8586526500 x, mfung@ardeabio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 March 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2010
Global end of trial reached?	Yes
Global end of trial date	06 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group.

Protection of trial subjects:

This study was conducted in accordance with the protocol, International Conference on

Harmonisation (ICH) E6 Good Clinical Practice (GCP), the Declaration of Helsinki (2008), and

all other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 August 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 39
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Georgia: 15
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	143
EEA total number of subjects	82

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	124
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were to be screened within 28 days prior to the first dose of study drug (Day 0) and up to 14 days before initiation of colchicine treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	lesinurad 200 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	lesinurad 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	lesinurad 400 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	lesinurad 400 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg

Arm title	lesinurad 600 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	lesinurad 600 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg

Arm title	Placebo
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Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
N/A	

Number of subjects in period 1^[1]	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg
Started	31	33	32
Completed	28	27	30
Not completed	3	6	2
Consent withdrawn by subject	3	2	-
N/A	-	1	-
Adverse event, non-fatal	-	2	-
Lost to follow-up	-	1	1
Protocol deviation	-	-	1

Number of subjects in period 1^[1]	Placebo
Started	27
Completed	23
Not completed	4
Consent withdrawn by subject	1
N/A	-
Adverse event, non-fatal	-
Lost to follow-up	2
Protocol deviation	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Subjects were withdrawn prior to dosing of study medication.

Period 2

Period 2 title	Open Label Extension
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Arm title	Pooled
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	lesinurad 200 mg, 400 mg, 600 mg, Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg, 400 mg, 600 mg

Number of subjects in period 2^[2]	Pooled
Started	50
Completed	8
Not completed	42
Discharged after study closure	4
Consent withdrawn by subject	9
N/A	3
Adverse event, non-fatal	6
Investigator Judgment	1
Site Closures	14
Lost to follow-up	1
Protocol deviation	4

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects were withdrawn prior to dosing of study medication.

Baseline characteristics

Reporting groups

Reporting group title	lesinurad 200 mg
Reporting group description: -	
Reporting group title	lesinurad 400 mg
Reporting group description: -	
Reporting group title	lesinurad 600 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg
Number of subjects	31	33	32
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	29	27
From 65-84 years	3	4	5
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	51	52.8	53.4
standard deviation	± 11.3	± 9.2	± 12.6
Gender, Male/Female			
Units: Participants			
Male	31	32	31
Female	0	1	1
Region of Enrollment			
Units: Subjects			
Bulgaria	8	10	7
Canada	6	10	12
Czech Republic	1	1	3
Germany	2	2	1
Poland	7	5	3
Republic of Georgia	3	4	4
USA	4	1	2
Age, Customized			
Units: Subjects			
<65	28	29	27
>=65	3	4	5

Reporting group values	Placebo	Total	
Number of subjects	27	123	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	23	107	
From 65-84 years	4	16	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	49.9		
standard deviation	± 11.2	-	
Gender, Male/Female Units: Participants			
Male	27	121	
Female	0	2	
Region of Enrollment Units: Subjects			
Bulgaria	8	33	
Canada	8	36	
Czech Republic	2	7	
Germany	0	5	
Poland	6	21	
Republic of Georgia	3	14	
USA	0	7	
Age, Customized Units: Subjects			
<65	23	107	
>=65	4	16	

End points

End points reporting groups

Reporting group title	lesinurad 200 mg
Reporting group description: -	
Reporting group title	lesinurad 400 mg
Reporting group description: -	
Reporting group title	lesinurad 600 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Pooled
Reporting group description: -	

Primary: To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group.

End point title	To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group.
End point description:	
End point type	Primary
End point timeframe:	28 Days

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	21
Units: Number of events				
number (not applicable)	7.7	30.8	38.5	0

Statistical analyses

Statistical analysis title	Number of Subjects with sUA < 6.0 mg/dL
Comparison groups	lesinurad 200 mg v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4949
Method	Fisher exact

Statistical analysis title	Number of Subjects with sUA < 6.0 mg/dL
Comparison groups	lesinurad 600 mg v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0033
Method	Fisher exact

Statistical analysis title	Number of Subjects with sUA < 6.0 mg/dL
Comparison groups	lesinurad 400 mg v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0112
Method	Fisher exact

Secondary: To evaluate the proportion of subjects whose sUA levels are <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL at each weekly study visit during the Double-Blind Period.

End point title	To evaluate the proportion of subjects whose sUA levels are <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL at each weekly study visit during the Double-Blind Period.
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End point description:

End point type	Secondary
End point timeframe:	28 Days

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	27
Units: Number				
number (not applicable)				
<6.0 mg/dL at Day 7	9.7	12.1	13.8	0
<6.0 mg/dL at Day 14	3.4	33.3	33.3	4.5
<6.0 mg/dL at Day 21	3.8	25.9	46.2	0
<6.0 mg/dL at Day 28	7.7	30.8	38.5	0
<5.0 mg/dL at Day 7	0	3	3.4	0
<5.0 mg/dL at Day 14	0	13.3	7.4	0
<5.0 mg/dL at Day 21	0	3.7	23.1	0
<5.0 mg/dL at Day 28	3.8	7.7	15.4	0
<4.0 mg/dL at Day 7	0	3	0	0
<4.0 mg/dL at Day 14	0	0	0	0

<4.0 mg/dL at Day 21	0	0	7.7	0
<4.0 mg/dL at Day 28	0	0	0	0

Statistical analyses

Statistical analysis title	sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL
Comparison groups	lesinurad 200 mg v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Statistical analysis title	sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL
Comparison groups	lesinurad 600 mg v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Statistical analysis title	sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL
Comparison groups	lesinurad 400 mg v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Main Period)

End point title	To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Main Period)
End point description:	
Value provided by randomized treatment	
End point type	Secondary
End point timeframe:	
Up to day 28	

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	27
Units: Number				
number (not applicable)				
Day 7 Absolute reduction from baseline	-2.15	-2.33	-2.46	-0.17
Day 7 Percent reduction from baseline	-21.88	-22.32	-24.33	-0.96
Day 14 Absolute reduction from baseline	-1.67	-2.61	-3.11	-0.15
Day 14 Percent reduction from baseline	-16.87	-25.09	-31.18	-0.37
Day 21 Absolute reduction from baseline	-1.58	-2.34	-3.65	-0.06
Day 21 Percent reduction from baseline	-15.67	-21.96	-36.68	0.52
Day 28 Absolute reduction from baseline	-1.73	-2.92	-2.94	-0.02
Day 28 Percent reduction from baseline	-17.7	-28.92	-29.11	0.75

Statistical analyses

Statistical analysis title	Absolute and percent reduction from baseline
Comparison groups	lesinurad 200 mg v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Absolute and percent reduction from baseline
Comparison groups	lesinurad 600 mg v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.01
Method	ANCOVA

Statistical analysis title	Absolute and percent reduction from baseline
Comparison groups	lesinurad 400 mg v Placebo

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.01
Method	ANCOVA

Secondary: To evaluate the percentage change in 24-hour urine urate level (excretion) from baseline to Day 28.

End point title	To evaluate the percentage change in 24-hour urine urate level (excretion) from baseline to Day 28.
End point description:	
End point type	Secondary
End point timeframe:	
28 Days	

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	27
Units: Number				
number (not applicable)	7.58	1.79	3.21	-10.45

Statistical analyses

Statistical analysis title	Percentage change in 24-hour urine urate level
Comparison groups	lesinurad 200 mg v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4267
Method	ANCOVA

Statistical analysis title	Percentage change in 24-hour urine urate level
Comparison groups	lesinurad 400 mg v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.873
Method	ANCOVA

Statistical analysis title	Percentage change in 24-hour urine urate level
Comparison groups	lesinurad 600 mg v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7872
Method	ANCOVA

Secondary: To evaluate the incidence of gout flares. (Main Period)

End point title	To evaluate the incidence of gout flares. (Main Period)
End point description:	
End point type	Secondary
End point timeframe:	
28 Days	

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	27
Units: Percent				
number (not applicable)	9.7	12.1	12.5	3.7

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Main period)

End point title	To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Main period)
End point description:	
End point type	Secondary
End point timeframe:	
28 Days and through extension	

End point values	lesinurad 200 mg	lesinurad 400 mg	lesinurad 600 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	27
Units: Percent (Subjects with TEAEs)				
number (not applicable)	25.8	45.5	34.4	22.2

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the proportion of subjects whose sUA level decreases to or is maintained at <6.0 mg/dL in the Open-Label Extension Period.

End point title	To evaluate the proportion of subjects whose sUA level decreases to or is maintained at <6.0 mg/dL in the Open-Label Extension Period.
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End point description:

End point type	Secondary
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End point timeframe:

18 Months

End point values	Pooled			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: n/N				
number (not applicable)				
Week 2 - Extension	19.6			
Week 4 - Extension	10.6			
Week 6 - Extension	12.5			
Week 8 - Extension	26.2			
Week 10 - Extension	50			
Week 12 - Extension	37.5			
Week 14 - Extension	31.6			
Week 16 - Extension	34.3			
Week 18 - Extension	37.5			
Week 20 - Extension	37.1			
Week 22 - Extension	50			
Week 28 - Extension	77.8			
Week 36 - Extension	50			
Week 44 - Extension	87.5			
Week 52 - Extension	85.7			
Week 60 - Extension	80			
Week 68 - Extension	100			

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Open-Label Extension)

End point title	To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Open-Label Extension)
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End point description:

Value provided by maximum dose level.

End point type	Secondary
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End point timeframe:

28 Days and through extension

End point values	Pooled			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Number				
number (not applicable)				
Week 2 Absolute reduction from baseline	-1.07			
Week 2 Percent reduction from baseline	-11.3			
Week 4 Absolute reduction from baseline	-0.87			
Week 4 Percent reduction from baseline	-8.47			
Week 6 Absolute reduction from baseline	-1.31			
Week 6 Percent reduction from baseline	-13.27			
Week 8 Absolute reduction from baseline	-1.2			
Week 8 Percent reduction from baseline	-12.29			
Week 10 Absolute reduction from baseline	-1.71			
Week 10 Percent reduction from baseline	-20.75			
Week 12 Absolute reduction from baseline	-1.39			
Week 12 Percent reduction from baseline	-15.18			
Week 14 Absolute reduction from baseline	-1.36			
Week 14 Percent reduction from baseline	-15.43			
Week 16 Absolute reduction from baseline	-1.46			

Week 16 Percent reduction from baseline	-16.89			
Week 18 Absolute reduction from baseline	-2.18			
Week 18 Percent reduction from baseline	-22.33			
Week 20 Absolute reduction from baseline	-1.67			
Week 20 Percent reduction from baseline	-18.41			
Week 22 Absolute reduction from baseline	-2.7			
Week 22 Percent reduction from baseline	-31.94			
Week 28 Absolute reduction from baseline	-2.8			
Week 28 Percent reduction from baseline	-32.22			
Week 36 Absolute reduction from baseline	-2.47			
Week 36 Percent reduction from baseline	-27.96			
Week 44 Absolute reduction from baseline	-2.49			
Week 44 Percent reduction from baseline	-28.11			
Week 52 Absolute reduction from baseline	-2.33			
Week 52 Percent reduction from baseline	-27.55			
Week 60 Absolute reduction from baseline	-2.7			
Week 60 Percent reduction from baseline	-32.3			
Week 68 Absolute reduction from baseline	-2.8			
Week 68 Percent reduction from baseline	-36.84			

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the incidence of gout flares. (Open-label Extension)

End point title	To evaluate the incidence of gout flares. (Open-label Extension)
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End point description:

End point type	Secondary
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End point timeframe:

28 Days and through extension

End point values	Pooled			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Gout Flare Rate (per 28 days)				
number (not applicable)				
Month 1	0.0406			
Month 2	0.1804			
Month 3	0.0962			
Month 4	0.0522			
Month 5	0			
Month 6	0.056			
Month 7	0			
Month 8	0.0996			
Month 9	0			
Month 10	0.1167			
Month 11	0			
Month 12	0.1267			
Month 13	0.2857			
Month 14	0			
Month 15	0			
Month 16	0			
Month 17	0			

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Open-label extension)

End point title	To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Open-label extension)
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End point description:

End point type	Secondary
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End point timeframe:

28 Days and through extension

End point values	Pooled			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Percent (Subjects with AE)				
number (not applicable)	64			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed from the time the subject provided informed consent through the duration of the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	main period 200 mg
Reporting group description: -	
Reporting group title	main period 600 mg
Reporting group description: -	
Reporting group title	main period 400 mg
Reporting group description: -	
Reporting group title	main period placebo
Reporting group description: -	
Reporting group title	open-label extension period maximum dose 200 mg
Reporting group description: -	
Reporting group title	open-label extension period maximum dose 400 mg
Reporting group description: -	
Reporting group title	open-label extension period maximum dose 600 mg
Reporting group description: -	

Serious adverse events	main period 200 mg	main period 600 mg	main period 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (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

Serious adverse events	main period placebo	open-label extension period maximum dose 200 mg	open-label extension period maximum dose 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (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

Serious adverse events	open-label extension period maximum dose 600 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	main period 200 mg	main period 600 mg	main period 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 31 (25.81%)	11 / 32 (34.38%)	15 / 33 (45.45%)
Vascular disorders			
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Sensation of pressure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Investigations			
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Creatinine renal clearance decreased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Renal function test abnormal subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Excoriation subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0

Muscle strain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Periorbital haematoma subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Tendon injury subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 32 (3.13%) 1	1 / 33 (3.03%) 1
Sciatica subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Sensory disturbance subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 32 (3.13%) 1	0 / 33 (0.00%) 0
Ear and labyrinth disorders Otitis media subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 2
Eye disorders			

Conjunctivitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 32 (3.13%) 1	0 / 33 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Abdominal tenderness subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 32 (3.13%) 1	0 / 33 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Dyspepsia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	2 / 33 (6.06%) 2
Melaena subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Nausea			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 2
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Rash subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 32 (3.13%) 1	0 / 33 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Urge incontinence subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	0 / 33 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 32 (3.13%) 1	0 / 33 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 32 (6.25%) 2	0 / 33 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 32 (0.00%) 0	1 / 33 (3.03%) 1
Muscle spasms			

subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	3 / 33 (9.09%)
occurrences (all)	1	1	3
Sinusitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	3 / 31 (9.68%)	8 / 32 (25.00%)	4 / 33 (12.12%)
occurrences (all)	3	10	6
Hypercholesterolaemia			

subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	main period placebo	open-label extension period maximum dose 200 mg	open-label extension period maximum dose 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)	1 / 4 (25.00%)	12 / 15 (80.00%)
Vascular disorders			
Epistaxis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Oedema peripheral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sensation of pressure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	3
Blood creatinine increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 27 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Renal function test abnormal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	6
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Periorbital haematoma			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tendon injury			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	1 / 4 (25.00%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 27 (7.41%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Sciatica			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Otitis media subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 4 (0.00%) 0	1 / 15 (6.67%) 3
Abdominal tenderness subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Dyspepsia			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Melaena subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	1 / 15 (6.67%) 3
Pollakiuria subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Urge incontinence subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 4 (0.00%) 0	0 / 15 (0.00%) 0
Back pain			

subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	6
Bursitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 27 (3.70%)	0 / 4 (0.00%)	7 / 15 (46.67%)
occurrences (all)	2	0	22
Hypercholesterolaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 4 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	open-label extension period maximum dose 600 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 31 (67.74%)		
Vascular disorders			
Epistaxis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Flushing			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	6		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Pyrexia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sensation of pressure</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>3</p> <p>0 / 31 (0.00%)</p> <p>0</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>3</p> <p>0 / 31 (0.00%)</p> <p>0</p>		
<p>Investigations</p> <p>Aspartate aminotransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood creatine phosphokinase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood creatinine increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood triglycerides increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Creatinine renal clearance decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lipase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Liver function test abnormal</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Renal function test abnormal</p>	<p>0 / 31 (0.00%)</p> <p>0</p> <p>1 / 31 (3.23%)</p> <p>3</p> <p>2 / 31 (6.45%)</p> <p>6</p> <p>0 / 31 (0.00%)</p> <p>0</p> <p>2 / 31 (6.45%)</p> <p>6</p> <p>1 / 31 (3.23%)</p> <p>3</p> <p>0 / 31 (0.00%)</p> <p>0</p>		

subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Excoriation			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	6		
Muscle strain			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Periorbital haematoma			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Skin laceration			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Tendon injury			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	2		
Atrial fibrillation			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Sciatica			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Sensory disturbance			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Ear and labyrinth disorders			
Otitis media subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 3		
Vertigo subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Eye disorders			
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 4		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 3		
Abdominal tenderness subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 3		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 6		
Dry mouth subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 3		
Dysgeusia			

subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Melaena			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	9		
Toothache			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Urge incontinence			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	4		
Bursitis			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	6		
Pain in extremity			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	6		
Nasopharyngitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	4		
Sinusitis			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	6		
Tooth abscess			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		
Upper respiratory tract infection			

subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	4		
Viral infection			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	9 / 31 (29.03%)		
occurrences (all)	40		
Hypercholesterolaemia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2009	Changes were made to the protocol to address new safety information from the US FDA about colchicine and the related concerns raised by German Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM).
15 December 2009	The protocol was primarily amended to allow for extended dosing of subjects by adding an optional Open-Label Extension Period for subjects who successfully complete the 4-week Double-Blind Treatment Period and attend the follow-up visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported