



Clinical trial results:

A Phase III Randomized Double-Blind Placebo Controlled Trial to Evaluate the Efficacy and Safety of Nitazoxanide and Nitazoxanide plus Oseltamivir in the Treatment of Acute Uncomplicated Influenza

Summary

EudraCT number	2013-003933-14
Trial protocol	BE
Global end of trial date	16 April 2015

Results information

Result version number	v1 (current)
This version publication date	09 July 2021
First version publication date	09 July 2021

Trial information

Trial identification

Sponsor protocol code	RM08-3002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01610245
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Romark Laboratories, L.C.
Sponsor organisation address	3000 Bayport Dr., Tampa, United States, 33607
Public contact	Yelen Concepcion, Romark Laboratories L.C., +1 813282 8544, Yelen.Concepcion@romark.com
Scientific contact	Matthew Bardin, Romark Laboratories L.C., +1 813282 8544, matthew.bardin@romark.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	28 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2015
Global end of trial reached?	Yes
Global end of trial date	16 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Evaluate the effect of nitazoxanide administered 600 mg orally b.i.d. for 5 days on time to alleviation of symptoms of acute uncomplicated influenza compared to that of a placebo.
- Evaluate the effect of combination therapy with nitazoxanide 600 mg plus oseltamivir 75 mg administered orally b.i.d. for 5 days on time to alleviation of symptoms of acute uncomplicated influenza compared to that of monotherapy with nitazoxanide 600 mg b.i.d. for 5 days and monotherapy with oseltamivir 75 mg b.i.d. for 5 days

Protection of trial subjects:

There were no specific measures that were put in place to protect trial subjects beyond those in accordance with the protocol, current International Conference in Harmonization (ICH) guidelines on Good Clinical Practice (GCP), and applicable regulatory and country-specific requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 March 2013
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	Belgium: 8
Country: Number of subjects enrolled	Australia: 117
Country: Number of subjects enrolled	New Zealand: 47
Country: Number of subjects enrolled	Canada: 48
Country: Number of subjects enrolled	United States: 1721
Worldwide total number of subjects	1941
EEA total number of subjects	8

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)	0
Adolescents (12-17 years)	119
Adults (18-64 years)	1810
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was a multicenter, randomized, factorial, double-blind, placebo controlled study. Patients were selected according to the inclusion and exclusion criteria outlined in the protocol. 13 investigators in Australia, 7 investigators in New Zealand, 1 investigator in Belgium, 14 investigators in Canada and 132 investigators in the US.

Pre-assignment

Screening details:

The population studied included adults and adolescents aged 13 to 69 years of age with presence of clinical signs and/or symptoms consistent with an acute illness compatible with influenza infection. Confirmation of influenza A or B infection by one of 4 means. Onset of illness no more than 48 hours before presentation.

Pre-assignment period milestones

Number of subjects started	2072 ^[1]
Number of subjects completed	1941

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Failed screening.: 131
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Notes:

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

Justification: Subject was considered enrolled if he met inclusion/exclusion criteria. The pre-assignment period was the screening period.

Period 1

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

Blinding implementation details:

An independent third party prepared the master randomization list and maintained the blinding of the study. Randomization was performed in blocks of four. Blocks of blinded study medication were assigned to each investigator. Each investigator then sequentially assigned treatment numbers to patients who qualified for the study. The treatment numbers appeared on the bottles containing the blinded study medication.

Arms

Are arms mutually exclusive?	Yes
Arm title	Nitazoxanide 600 b.i.d.

Arm description:

Two nitazoxanide 300 mg tablets and one placebo capsule b.i.d. for 5 days.

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

Dosage and administration details:

Two NTZ 300 mg tablets and one placebo capsule b.i.d. for 5 days

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule b.i.d. for 5 days.

Arm title	Oseltamivir 75 mg b.i.d.
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Arm description:

One oseltamivir 75 mg capsule and two placebo tablets b.i.d. for 5 days.

Arm type	Active comparator
Investigational medicinal product name	oseltamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One OST 75 mg capsule and two placebo tablets b.i.d. for 5 days.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two placebo tablets b.i.d. for 5 days

Arm title	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d
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Arm description:

Two nitazoxanide 300 mg tablets and one oseltamivir 75 mg capsule b.i.d. for 5 days

Arm type	Experimental
Investigational medicinal product name	nitazoxanide and oseltamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Two NTZ 300 mg tablets and one OST 75 mg capsule b.i.d. for 5 days

Arm title	Placebo
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Arm description:

Two placebo tablets and one placebo capsule b.i.d. for 5 days

Arm type	Placebo
Investigational medicinal product name	N/A
Investigational medicinal product code	
Other name	placebo tablets, placebo capsule
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Two placebo tablets and one placebo capsule b.i.d. for 5 days

Number of subjects in period 1	Nitazoxanide 600 b.i.d.	Oseltamivir 75 mg b.i.d.	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d
Started	484	481	488
Completed	448	450	449
Not completed	36	31	39
Consent withdrawn by subject	18	10	13
Physician decision	-	-	1
Adverse event, non-fatal	2	2	2
Lost to follow-up	13	17	19
non-compliant with study drug	3	-	3
unable to attend follow up appointments	-	2	1

Number of subjects in period 1	Placebo
Started	488
Completed	454
Not completed	34
Consent withdrawn by subject	15
Physician decision	1
Adverse event, non-fatal	2
Lost to follow-up	11
non-compliant with study drug	3
unable to attend follow up appointments	2

Baseline characteristics

Reporting groups

Reporting group title	Nitazoxanide 600 b.i.d.
Reporting group description: Two nitazoxanide 300 mg tablets and one placebo capsule b.i.d. for 5 days.	
Reporting group title	Oseltamivir 75 mg b.i.d.
Reporting group description: One oseltamivir 75 mg capsule and two placebo tablets b.i.d. for 5 days.	
Reporting group title	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d
Reporting group description: Two nitazoxanide 300 mg tablets and one oseltamivir 75 mg capsule b.i.d. for 5 days	
Reporting group title	Placebo
Reporting group description: Two placebo tablets and one placebo capsule b.i.d. for 5 days	

Reporting group values	Nitazoxanide 600 b.i.d.	Oseltamivir 75 mg b.i.d.	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d
Number of subjects	484	481	488
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)	28	23	28
Adults (18-64 years)	449	457	458
From 65-84 years	7	1	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	35.3	35.8	34.8
full range (min-max)	13 to 68	13 to 65	13 to 68
Gender categorical Units: Subjects			
Female	274	287	295
Male	210	194	193
Race Units: Subjects			
Asian	10	5	13
Black	77	75	77
White	277	284	282
Other	120	117	116
Smoking History Units: Subjects			

Current smoker	93	68	85
Past smoker	45	55	46
Never smoked	346	358	357
Height			
Units: cm			
arithmetic mean	169.5	168.4	168.1
full range (min-max)	144 to 201	145 to 201	140 to 193
Weight			
Units: kg			
arithmetic mean	79.9	79.9	80.41
full range (min-max)	36.8 to 152.9	39.9 to 140.6	40.8 to 129.7
BMI			
Units: kg/m2			
arithmetic mean	27.7	28.1	28.4
full range (min-max)	15.8 to 47.7	16.6 to 39.9	16.5 to 47.2

Reporting group values	Placebo	Total	
Number of subjects	488	1941	
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)	40	119	
Adults (18-64 years)	446	1810	
From 65-84 years	2	12	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	35.9		
full range (min-max)	13 to 69	-	
Gender categorical			
Units: Subjects			
Female	305	1161	
Male	183	780	
Race			
Units: Subjects			
Asian	4	32	
Black	74	303	
White	278	1121	
Other	132	485	
Smoking History			
Units: Subjects			
Current smoker	90	336	
Past smoker	58	204	
Never smoked	340	1401	

Height			
Units: cm			
arithmetic mean	167.9		
full range (min-max)	130 to 202	-	
Weight			
Units: kg			
arithmetic mean	79.22		
full range (min-max)	41.3 to 142.9	-	
BMI			
Units: kg/m2			
arithmetic mean	28.0		
full range (min-max)	16.1 to 41.2	-	

End points

End points reporting groups

Reporting group title	Nitazoxanide 600 b.i.d.
Reporting group description: Two nitazoxanide 300 mg tablets and one placebo capsule b.i.d. for 5 days.	
Reporting group title	Oseltamivir 75 mg b.i.d.
Reporting group description: One oseltamivir 75 mg capsule and two placebo tablets b.i.d. for 5 days.	
Reporting group title	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d
Reporting group description: Two nitazoxanide 300 mg tablets and one oseltamivir 75 mg capsule b.i.d. for 5 days	
Reporting group title	Placebo
Reporting group description: Two placebo tablets and one placebo capsule b.i.d. for 5 days	

Primary: Reduce time to alleviation of all clinical symptoms of influenza

End point title	Reduce time to alleviation of all clinical symptoms of influenza
End point description: Time to alleviation of all clinical symptoms of influenza (First time at when each symptom was scored as mild or absent and remained so for 24 hours) as reported by patients.	
End point type	Primary
End point timeframe: Baseline through day 28.	

End point values	Nitazoxanide 600 b.i.d.	Oseltamivir 75 mg b.i.d.	Nitazoxanide 600 mg tablet and oseltamivir 75 mg capsule b.i.d	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	185	168	177	180
Units: hours				
median (inter-quartile range (Q1-Q3))	119.1 (81 to 186)	113.7 (64 to 168)	106.9 (61 to 179)	116.5 (72 to 199)

Statistical analyses

Statistical analysis title	Comparison of NTZ to placebo
Statistical analysis description: Time to alleviation of symptoms for the NTZ group was compared to that of the placebo group using the Peto & Peto modification of the Gehan-Wilcoxon test with acetaminophen use included as a factor.	
Comparison groups	Nitazoxanide 600 b.i.d. v Placebo

Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8622
Method	Peto-Peto modification of Gehan-Wilcoxon

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The timeframe for reporting adverse events was baseline through Day 28.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Nitazoxanide 600 mg b.i.d.
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Reporting group description: -

Reporting group title	Oseltamivir 75 mg b.i.d.
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Reporting group description: -

Reporting group title	Nitazoxanide 600 mg + Oseltamivir 75 mg b.i.d.
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Reporting group description: -

Reporting group title	Placebo 600 mg b.i.d
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Reporting group description: -

Serious adverse events	Nitazoxanide 600 mg b.i.d.	Oseltamivir 75 mg b.i.d.	Nitazoxanide 600 mg + Oseltamivir 75 mg b.i.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 484 (1.24%)	1 / 481 (0.21%)	3 / 488 (0.61%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (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
Joint dislocation			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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
Pregnancy, puerperium and perinatal conditions			
Abortion of etopic pregnancy			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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			
Adverse drug reaction			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (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
Pyrexia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (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
Crohn's Disease			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal perforation			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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

Pancreatitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (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
Diarrhoea infectious			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (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
Cryptosporidiosis infection			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	0 / 488 (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
Haemochromatosis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (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	Placebo 600 mg b.i.d		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 488 (1.02%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion of etopic pregnancy			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's Disease			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis Acute			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal perforation			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cryptosporidiosis infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemochromatosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Nitazoxanide 600 mg b.i.d.	Oseltamivir 75 mg b.i.d.	Nitazoxanide 600 mg + Oseltamivir 75 mg b.i.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 484 (26.45%)	141 / 481 (29.31%)	155 / 488 (31.76%)
Vascular disorders			
Capillary fragility			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	2 / 488 (0.41%)
occurrences (all)	0	1	2
Surgical and medical procedures			
Dental operation			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Oophorectomy			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ophthalmic fluid drainage			

subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	2 / 484 (0.41%)	2 / 481 (0.42%)	2 / 488 (0.41%)
occurrences (all)	2	3	2
Device failure			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Feeling abnormal			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Hernia pain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Non-cardiac chest pain			

subjects affected / exposed	2 / 484 (0.41%)	3 / 481 (0.62%)	0 / 488 (0.00%)
occurrences (all)	2	3	0
Oedema mucosal			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	1	1	1
Vessel puncture site haematoma			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Multiple allergies			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

Breast tenderness			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Dysmenorrhoea			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Epididymitis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Genital discomfort			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Menstruation delayed			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	3 / 484 (0.62%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	3	0	0
Scrotal mass			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Semen discolouration			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Testicular mass			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0

Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	2	0	1
Dyspnoea			
subjects affected / exposed	2 / 484 (0.41%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	2	2	1
Epistaxis			
subjects affected / exposed	4 / 484 (0.83%)	5 / 481 (1.04%)	4 / 488 (0.82%)
occurrences (all)	4	5	5
Haemoptysis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Increased upper airway secretion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	1	0	2
Nasal congestion			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1
Nasal ulcer			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Pharyngeal erythema			

subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	2	0	1
Pharyngeal oedema			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Pleuritic pain			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Rhinitis seasonal			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	1	2	1
Rhonchi			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Snoring			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Sputum discoloured			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Throat irritation			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract congestion			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	2	0	0
Upper-airway cough syndrome			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	3 / 484 (0.62%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	3	0	1
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Anger			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 484 (0.00%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	0	2	1
Bipolar I disorder			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Delirium			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 484 (0.21%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	1	2	1
Disorientation			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	8 / 484 (1.65%)	8 / 481 (1.66%)	4 / 488 (0.82%)
occurrences (all)	8	9	4

Middle insomnia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Post-traumatic stress disorder subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Restlessness subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	2 / 488 (0.41%) 2
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	2 / 481 (0.42%) 2	5 / 488 (1.02%) 5
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	1 / 481 (0.21%) 1	1 / 488 (0.20%) 1
Basophil count increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	2 / 488 (0.41%) 2
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	3 / 488 (0.61%) 3
Blood glucose increased subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	2 / 481 (0.42%) 2	2 / 488 (0.41%) 2
Blood potassium decreased			

subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Blood potassium increased			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Blood pressure increased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Blood pressure systolic increased			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Blood sodium increased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	5 / 484 (1.03%)	3 / 481 (0.62%)	5 / 488 (1.02%)
occurrences (all)	5	3	5
Blood urea decreased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	4 / 488 (0.82%)
occurrences (all)	1	0	4
Haemoglobin decreased			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
High density lipoprotein decreased			
subjects affected / exposed	3 / 484 (0.62%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	3	0	2
Lipids increased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0

Liver function test abnormal subjects affected / exposed occurrences (all)	3 / 484 (0.62%) 3	2 / 481 (0.42%) 2	1 / 488 (0.20%) 1
Low density lipoprotein increased subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Lymphocyte count increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Monocyte count increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 2	2 / 488 (0.41%) 2
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Platelet count increased subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Total cholesterol/HDL ratio increased subjects affected / exposed occurrences (all)	3 / 484 (0.62%) 3	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	2 / 488 (0.41%) 2
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	2 / 484 (0.41%) 2	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Facial bones fracture subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Fall			

subjects affected / exposed	0 / 484 (0.00%)	2 / 481 (0.42%)	0 / 488 (0.00%)
occurrences (all)	0	2	0
Hand fracture			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Heat exhaustion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Laceration			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Muscle strain			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Procedural nausea			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Road traffic accident			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Seroma			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Soft tissue injury			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Spinal column injury			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Thermal burn			

subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Cardiac disorders			
Palpitations subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	1 / 488 (0.20%) 1
Anosmia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	2 / 488 (0.41%) 2
Autonomic nervous system imbalance subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Burning sensation subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Convulsion subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	12 / 484 (2.48%) 16	15 / 481 (3.12%) 16	15 / 488 (3.07%) 16
Dizziness postural			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	2 / 484 (0.41%)	3 / 481 (0.62%)	3 / 488 (0.61%)
occurrences (all)	3	3	3
Headache			
subjects affected / exposed	3 / 484 (0.62%)	3 / 481 (0.62%)	4 / 488 (0.82%)
occurrences (all)	3	6	5
Hypoaesthesia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Hypogeusia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Sinus headache			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	2 / 488 (0.41%)
occurrences (all)	1	1	2
Somnolence			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	4 / 488 (0.82%)
occurrences (all)	0	2	4
Syncope			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Tension headache			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Tremor			

subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Leukocytosis			
subjects affected / exposed	1 / 484 (0.21%)	4 / 481 (0.83%)	2 / 488 (0.41%)
occurrences (all)	1	4	2
Lymph node pain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	2 / 484 (0.41%)	1 / 481 (0.21%)	2 / 488 (0.41%)
occurrences (all)	2	1	2
Lymphopenia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ear canal erythema			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Ear congestion			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Ear discomfort			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Ear disorder			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	3 / 484 (0.62%)	6 / 481 (1.25%)	2 / 488 (0.41%)
occurrences (all)	3	7	2
Hypoacusis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Middle ear effusion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Motion sickness			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane disorder			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Tympanic membrane hyperaemia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	3 / 484 (0.62%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	3	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2

Eye pain			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Eye pruritus			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	6 / 488 (1.23%)
occurrences (all)	1	1	6
Abdominal distension			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	3 / 488 (0.61%)
occurrences (all)	0	1	3
Abdominal pain			
subjects affected / exposed	4 / 484 (0.83%)	4 / 481 (0.83%)	7 / 488 (1.43%)
occurrences (all)	5	5	7
Abdominal pain lower			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	10 / 484 (2.07%)	4 / 481 (0.83%)	11 / 488 (2.25%)
occurrences (all)	10	4	11
Abdominal tenderness			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Change of bowel habit			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Cheilosis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	4 / 484 (0.83%)	2 / 481 (0.42%)	2 / 488 (0.41%)
occurrences (all)	4	2	2
Diarrhoea			
subjects affected / exposed	30 / 484 (6.20%)	12 / 481 (2.49%)	19 / 488 (3.89%)
occurrences (all)	30	16	20
Dry mouth			
subjects affected / exposed	3 / 484 (0.62%)	0 / 481 (0.00%)	3 / 488 (0.61%)
occurrences (all)	3	0	3
Dyspepsia			
subjects affected / exposed	2 / 484 (0.41%)	2 / 481 (0.42%)	4 / 488 (0.82%)
occurrences (all)	2	2	4
Dysphagia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Eructation			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	4 / 484 (0.83%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	4	0	1
Frequent bowel movements			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Gastric dilatation			

subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Gingival pain			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Gingival swelling			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1
Irritable bowel syndrome			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Mouth ulceration			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	19 / 484 (3.93%)	21 / 481 (4.37%)	31 / 488 (6.35%)
occurrences (all)	19	22	33
Oral disorder			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Oral mucosal erythema			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Post-tussive vomiting			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Rectal spasm			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Tooth impacted			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 484 (0.00%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	0	2	1
Vomiting			
subjects affected / exposed	11 / 484 (2.27%)	20 / 481 (4.16%)	31 / 488 (6.35%)
occurrences (all)	11	21	31
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Jaundice			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Dermatitis contact			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			

subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	1	1	0
Erythema			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	2	0	0
Heat rash			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	4 / 484 (0.83%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	4	2	1
Night sweats			
subjects affected / exposed	3 / 484 (0.62%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	3	2	1
Pruritus			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Pruritus generalised			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	2 / 484 (0.41%)	2 / 481 (0.42%)	2 / 488 (0.41%)
occurrences (all)	2	2	2
Rash macular			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Seborrhoea			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	25 / 484 (5.17%)	0 / 481 (0.00%)	27 / 488 (5.53%)
occurrences (all)	26	0	29

Dysuria			
subjects affected / exposed	4 / 484 (0.83%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	4	0	1
Glycosuria			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	3 / 484 (0.62%)	2 / 481 (0.42%)	4 / 488 (0.82%)
occurrences (all)	3	2	4
Leukocyturia			
subjects affected / exposed	1 / 484 (0.21%)	2 / 481 (0.42%)	1 / 488 (0.20%)
occurrences (all)	1	2	1
Pollakiuria			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Pyuria			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1
Renal pain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 484 (0.21%)	3 / 481 (0.62%)	1 / 488 (0.20%)
occurrences (all)	1	3	1
Back disorder			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Back pain			

subjects affected / exposed	1 / 484 (0.21%)	3 / 481 (0.62%)	5 / 488 (1.02%)
occurrences (all)	1	3	5
Costochondritis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc disorder			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Metatarsalgia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	2	0	1
Muscle tightness			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	3 / 484 (0.62%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	2	0	1
Musculoskeletal stiffness			

subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	2 / 484 (0.41%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	2	0	0
Neck mass			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	1	1	1
Pain in extremity			
subjects affected / exposed	2 / 484 (0.41%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	2	2	1
Pain in jaw			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Sensation of heaviness			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis viral			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	2 / 488 (0.41%)
occurrences (all)	0	1	2
Gingivitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0

Herpes simplex			
subjects affected / exposed	1 / 484 (0.21%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	1	1	1
Herpes zoster			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	1	0	0
Infected dermal cyst			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Infectious mononucleosis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	0 / 488 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	1 / 488 (0.20%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	3 / 484 (0.62%)	4 / 481 (0.83%)	3 / 488 (0.61%)
occurrences (all)	3	4	3
Otitis externa			
subjects affected / exposed	1 / 484 (0.21%)	0 / 481 (0.00%)	2 / 488 (0.41%)
occurrences (all)	1	0	2
Paronychia			
subjects affected / exposed	0 / 484 (0.00%)	0 / 481 (0.00%)	0 / 488 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 481 (0.21%)	1 / 488 (0.20%)
occurrences (all)	0	1	1

Pharyngitis streptococcal subjects affected / exposed occurrences (all)	2 / 484 (0.41%) 2	1 / 481 (0.21%) 1	2 / 488 (0.41%) 2
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Skin infection subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Tinea cruris subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Tinea pedis subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	3 / 484 (0.62%) 3	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Tonsillitis bacterial subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Tooth abscess subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Tooth infection subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	2 / 481 (0.42%) 2	0 / 488 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	3 / 481 (0.62%) 3	3 / 488 (0.61%) 3

Vaginitis bacterial subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Herpes simplex ophthalmic subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	4 / 484 (0.83%) 4	2 / 481 (0.42%) 2	3 / 488 (0.61%) 3
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	1 / 488 (0.20%) 1
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	1 / 481 (0.21%) 1	0 / 488 (0.00%) 0
Hyperlipidaemia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 484 (0.00%) 0	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0
Diabetes mellitus subjects affected / exposed occurrences (all)	1 / 484 (0.21%) 1	0 / 481 (0.00%) 0	0 / 488 (0.00%) 0

Non-serious adverse events	Placebo 600 mg b.i.d		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	141 / 488 (28.89%)		
Vascular disorders			

Capillary fragility subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
Haematoma subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
Hot flush subjects affected / exposed occurrences (all)	1 / 488 (0.20%) 1		
Hypertension subjects affected / exposed occurrences (all)	1 / 488 (0.20%) 1		
Surgical and medical procedures Dental operation subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
Oophorectomy subjects affected / exposed occurrences (all)	1 / 488 (0.20%) 1		
Ophthalmic fluid drainage subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 488 (0.20%) 1		
Chest discomfort subjects affected / exposed occurrences (all)	2 / 488 (0.41%) 2		
Chest pain subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 488 (0.00%) 0		
Device failure			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Feeling abnormal			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hernia pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Oedema mucosal			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Thirst			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Vessel puncture site haematoma			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Xerosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Multiple allergies			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Epididymitis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Erectile dysfunction			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Genital discomfort			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Menstruation delayed			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Metrorrhagia			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Scrotal mass			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Semen discolouration			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Testicular mass			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Vaginal discharge			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Vaginal haemorrhage			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	6 / 488 (1.23%)		
occurrences (all)	6		
Epistaxis			
subjects affected / exposed	6 / 488 (1.23%)		
occurrences (all)	6		
Haemoptysis			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Increased upper airway secretion			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Nasal discomfort			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Nasal mucosal disorder			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Nasal ulcer			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Pharyngeal erythema			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Pharyngeal oedema			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Pleuritic pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Rhinitis seasonal			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Rhonchi			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Sinus congestion			

subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Snoring			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Sputum discoloured			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Upper respiratory tract congestion			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Anger			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Bipolar I disorder			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

Confusional state			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	3		
Delirium			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Disorientation			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Hallucination			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	6 / 488 (1.23%)		
occurrences (all)	6		
Middle insomnia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Post-traumatic stress disorder			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Restlessness			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 488 (0.82%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Basophil count increased			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood potassium decreased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood potassium increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Blood pressure systolic increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood sodium increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood triglycerides increased			
subjects affected / exposed	6 / 488 (1.23%)		
occurrences (all)	6		
Blood urea decreased			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Haemoglobin decreased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
High density lipoprotein decreased			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Lipids increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Liver function test abnormal			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Low density lipoprotein increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Lymphocyte count increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Monocyte count increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Neutrophil count increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

Platelet count increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Total cholesterol/HDL ratio increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Facial bones fracture			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Heat exhaustion			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Ligament sprain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Procedural nausea			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Road traffic accident			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Seroma			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Soft tissue injury			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Spinal column injury			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Tooth fracture			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Ventricular extrasystoles			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ageusia			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Anosmia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Burning sensation			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Convulsion			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	5 / 488 (1.02%)		
occurrences (all)	5		
Dizziness postural			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 488 (0.82%)		
occurrences (all)	5		
Hypoaesthesia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hypogeusia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

Paraesthesia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Sinus headache			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Syncope			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Tension headache			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Lymph node pain			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Lymphopenia			

subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Ear canal erythema			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Ear congestion			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Ear discomfort			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Ear disorder			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Ear pain			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	3		
Hypoacusis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Middle ear effusion			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Motion sickness			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		

Tinnitus			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Tympanic membrane disorder			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Tympanic membrane hyperaemia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Ocular hyperaemia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Vision blurred			

subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	5 / 488 (1.02%)		
occurrences (all)	5		
Abdominal distension			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Abdominal pain lower			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	6 / 488 (1.23%)		
occurrences (all)	7		
Abdominal tenderness			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Change of bowel habit			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Cheilosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	24 / 488 (4.92%)		
occurrences (all)	24		
Dry mouth			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		

Dyspepsia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Epigastric discomfort			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Eructation			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	3 / 488 (0.61%)		
occurrences (all)	3		
Frequent bowel movements			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gastric dilatation			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Gingival pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gingival swelling			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Irritable bowel syndrome			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

Lip dry			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	26 / 488 (5.33%)		
occurrences (all)	28		
Oral disorder			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Oral mucosal erythema			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Post-tussive vomiting			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Rectal spasm			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Tooth impacted			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	13 / 488 (2.66%)		
occurrences (all)	13		
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Jaundice			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Ecchymosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Heat rash			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		

Pruritus generalised			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	4 / 488 (0.82%)		
occurrences (all)	4		
Rash macular			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Seborrhoea			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Dysuria			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Leukocyturia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Pyuria			

subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Renal failure			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Renal pain			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	2		
Back disorder			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	4 / 488 (0.82%)		
occurrences (all)	5		
Costochondritis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Intervertebral disc disorder			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Joint range of motion decreased			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Joint swelling			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Metatarsalgia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	3		
Muscle tightness			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Neck mass			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 488 (0.41%)		
occurrences (all)	2		
Pain in jaw			

subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Sensation of heaviness			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Conjunctivitis viral			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Infected dermal cyst			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Infectious mononucleosis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

Laryngitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	2		
Otitis externa			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Pharyngitis streptococcal			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Tinea cruris			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		

Tinea pedis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Tonsillitis bacterial			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Tooth abscess			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Vaginitis bacterial			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Herpes simplex ophthalmic			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		
Hyperlipidaemia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 488 (0.20%)		
occurrences (all)	1		
Diabetes mellitus			
subjects affected / exposed	0 / 488 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Methods for collecting patient-reported symptom data and measuring symptoms lacked validity. "Alleviation of symptoms" endpoint was not supported by evidence of meaningfulness to patients. Validated methods in this research area are needed.
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Notes: