



Clinical trial results:

A Phase III, Two-Part, Randomized, Double-Blind, Active Comparator-Controlled, Multicenter Clinical Trial to Study the Relative Efficacy and Tolerability of Two Doses of MK-0663/Etoricoxib in Patients with Ankylosing Spondylitis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-019872-65
Trial protocol	DE HU FI BE AT GB EE SK CZ LT
Global end of trial date	12 November 2014

Results information

Result version number	v1 (current)
This version publication date	02 March 2016
First version publication date	02 March 2016

Trial information

Trial identification

Sponsor protocol code	MK-0663-108
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01208207
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	12 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 November 2014
Global end of trial reached?	Yes
Global end of trial date	12 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to evaluate the efficacy and tolerability of two doses of etoricoxib compared to naproxen in the treatment of ankylosing spondylitis (AS). The primary objectives are to evaluate the improvement in Spinal Pain Intensity over 6 weeks of treatment with etoricoxib 90 mg or 60 mg compared to naproxen; and to evaluate the improvement in Spinal Pain Intensity over 6 weeks of treatment with etoricoxib 90 mg compared with etoricoxib 60 mg. Additionally, the added benefit of increasing the dose of etoricoxib from 60 mg to 90 mg will be assessed in the second part of the study. The primary hypothesis is that the improvement in Spinal Pain Intensity visual analog score (VAS) as measured by the time-weighted average (TWA) change from baseline over 6 weeks of treatment in Part I for etoricoxib 90 mg or 60 mg once daily is not inferior to naproxen 1000 mg.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statuses and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Prior to randomization, participants were allowed to use up to 4 g/day of acetaminophen/paracetamol for severe AS pain. Throughout the treatment period (Part I and II), participants were allowed to use acetaminophen/paracetamol daily as rescue medication for breakthrough pain but were limited to no more than 1.5 g/day. Participants could also take up to 4 g/day of acetaminophen/paracetamol during the 28-day follow-up period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2010
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	Argentina: 6
Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Romania: 213
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Slovakia: 39
Country: Number of subjects enrolled	South Africa: 59
Country: Number of subjects enrolled	Taiwan: 81
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Colombia: 17

Country: Number of subjects enrolled	Czech Republic: 62
Country: Number of subjects enrolled	Estonia: 18
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 63
Country: Number of subjects enrolled	Hungary: 178
Country: Number of subjects enrolled	India: 35
Country: Number of subjects enrolled	Lithuania: 15
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Poland: 68
Worldwide total number of subjects	1015
EEA total number of subjects	707

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)	0
Adults (18-64 years)	961
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1149 participants were screened for inclusion in the study and 1015 of these participants were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Etoricoxib 60 mg (Part I)

Arm description:

One etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.

Arm type	Experimental
Investigational medicinal product name	Etoricoxib 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib 60 mg oral tablet once daily

Investigational medicinal product name	Naproxen-matching placebo 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Naproxen-matching placebo 500 mg oral tablet twice daily

Investigational medicinal product name	Etoricoxib-matching placebo 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib-matching placebo 90 mg oral tablet once daily

Arm title	Etoricoxib 90 mg (Part I)
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Arm description:

One etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.

Arm type	Experimental
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Investigational medicinal product name	Etoricoxib 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib 90 mg oral tablet once daily	
Investigational medicinal product name	Etoricoxib-matching placebo 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 60 mg oral tablet once daily	
Investigational medicinal product name	Naproxen-matching placebo 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Naproxen-matching placebo 500 mg oral tablet twice daily	
Arm title	Naproxen 1000 mg (Part I)
Arm description:	
One naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I.	
Arm type	Active comparator
Investigational medicinal product name	Etoricoxib-matching placebo 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 60 mg oral tablet once daily	
Investigational medicinal product name	Etoricoxib-matching placebo 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 90 mg oral tablet once daily	
Investigational medicinal product name	Naproxen 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Naproxen 500 mg oral tablet twice daily	

Number of subjects in period 1	Etoricoxib 60 mg (Part I)	Etoricoxib 90 mg (Part I)	Naproxen 1000 mg (Part I)
Started	702	156	157
Completed	632	145	142
Not completed	70	11	15
Consent withdrawn by subject	14	4	4
Physician decision	-	1	-
Adverse event, non-fatal	19	2	6
Progressive Disease	1	-	-
Non-Compliance With Study Drug	1	-	1
Lost to follow-up	6	1	-
Lack of efficacy	21	3	2
Protocol deviation	8	-	2

Period 2

Period 2 title	Part II
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)

Arm description:

Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Arm type	Experimental
Investigational medicinal product name	Etoricoxib 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib 60 mg oral tablet once daily

Investigational medicinal product name	Naproxen-matching placebo 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Naproxen-matching placebo 500 mg oral tablet twice daily

Investigational medicinal product name	Etoricoxib-matching placebo 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 90 mg oral tablet once daily	
Arm title	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)

Arm description:

Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Arm type	Experimental
Investigational medicinal product name	Etoricoxib 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib 90 mg oral tablet once daily

Investigational medicinal product name	Etoricoxib-matching placebo 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib-matching placebo 60 mg oral tablet once daily

Investigational medicinal product name	Naproxen-matching placebo 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Naproxen-matching placebo 500 mg oral tablet twice daily

Arm title	Etoricoxib 90 mg / Etoricoxib 90 mg (Part II)
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Arm description:

Participants who received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Arm type	Experimental
Investigational medicinal product name	Etoricoxib 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Etoricoxib 90 mg oral tablet once daily

Investigational medicinal product name	Naproxen-matching placebo 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Naproxen-matching placebo 500 mg oral tablet twice daily	
Investigational medicinal product name	Etoricoxib-matching placebo 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 60 mg oral tablet once daily	
Arm title	Naproxen 1000 mg /Naproxen 1000 mg (Part II)
Arm description:	
Participants who received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 20 weeks in Part II.	
Arm type	Active comparator
Investigational medicinal product name	Naproxen 500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Naproxen 500 mg oral tablet twice daily	
Investigational medicinal product name	Etoricoxib-matching placebo 90 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 90 mg oral tablet once daily	
Investigational medicinal product name	Etoricoxib-matching placebo 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Etoricoxib-matching placebo 60 mg oral tablet once daily	

Number of subjects in period 2	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)	Etoricoxib 90 mg / Etoricoxib 90 mg (Part II)
Started	314	318	145
Completed	282	295	129
Not completed	32	23	16
Consent withdrawn by subject	10	9	3
Physician decision	1	-	2
Adverse event, non-fatal	5	9	4
Technical Problems	1	-	1
Non-Compliance With Study Drug	4	1	1
Lost to follow-up	4	-	2
Lack of efficacy	6	4	3
Protocol deviation	1	-	-

Number of subjects in period 2	Naproxen 1000 mg /Naproxen 1000 mg (Part II)
Started	142
Completed	131
Not completed	11
Consent withdrawn by subject	5
Physician decision	-
Adverse event, non-fatal	2
Technical Problems	-
Non-Compliance With Study Drug	-
Lost to follow-up	1
Lack of efficacy	3
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Etoricoxib 60 mg (Part I)
Reporting group description: One etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.	
Reporting group title	Etoricoxib 90 mg (Part I)
Reporting group description: One etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.	
Reporting group title	Naproxen 1000 mg (Part I)
Reporting group description: One naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I.	

Reporting group values	Etoricoxib 60 mg (Part I)	Etoricoxib 90 mg (Part I)	Naproxen 1000 mg (Part I)
Number of subjects	702	156	157
Age categorical Units: Subjects			
Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	45.4	45.2	44.5
standard deviation	± 12.4	± 11.3	± 12.3
Gender, Male/Female Units: Participants			
Female	209	45	41
Male	493	111	116
Study Specific Characteristic Units: mm VAS			
arithmetic mean	76.7	76.7	77
standard deviation	± 14.2	± 15.2	± 14

Reporting group values	Total		
Number of subjects	1015		
Age categorical Units: Subjects			

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years arithmetic mean standard deviation	-		
Gender, Male/Female Units: Participants			
Female	295		
Male	720		
Study Specific Characteristic Units: mm VAS arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Etoricoxib 60 mg (Part I)
Reporting group description: One etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.	
Reporting group title	Etoricoxib 90 mg (Part I)
Reporting group description: One etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.	
Reporting group title	Naproxen 1000 mg (Part I)
Reporting group description: One naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I.	
Reporting group title	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)
Reporting group description: Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.	
Reporting group title	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)
Reporting group description: Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.	
Reporting group title	Etoricoxib 90 mg / Etoricoxib 90 mg (Part II)
Reporting group description: Participants who received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.	
Reporting group title	Naproxen 1000 mg /Naproxen 1000 mg (Part II)
Reporting group description: Participants who received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 20 weeks in Part II.	
Subject analysis set title	Etoricoxib 60 mg (Part I)
Subject analysis set type	Safety analysis
Subject analysis set description: One etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.	
Subject analysis set title	Etoricoxib 90 mg (Part I)
Subject analysis set type	Safety analysis

Subject analysis set description:

One etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I.

Subject analysis set title	Naproxen 1000 mg (Part I)
Subject analysis set type	Safety analysis

Subject analysis set description:

One naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I.

Subject analysis set title	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Subject analysis set title	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received one etoricoxib 60 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Subject analysis set title	Etoricoxib 90 mg / Etoricoxib 90 mg (Part II)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 6 weeks in Part I received one etoricoxib 90 mg tablet, one 60 mg etoricoxib-matching placebo tablet, and one 500 mg naproxen-matching placebo tablet taken orally in the morning, and one 500 mg naproxen-matching placebo tablet taken orally in the evening for 20 weeks in Part II.

Subject analysis set title	Naproxen 1000 mg /Naproxen 1000 mg (Part II)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 6 weeks in Part I received one naproxen 500 mg tablet, one 90 mg etoricoxib-matching placebo tablet, and one 60 mg etoricoxib-matching placebo tablet taken orally in the morning, and one naproxen 500 mg tablet taken orally in the evening for 20 weeks in Part II.

Primary: Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 90 mg vs. naproxen

End point title	Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 90 mg vs. naproxen ^[1]
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End point description:

Spinal Pain Intensity is measured using a visual analog scale (VAS) from 0-100 mm with a lower value representing a better response. The time-weighted average change is calculated by taking the time between adjacent observations divided by the time from the randomization visit to the last observation in the period of interest, and using it as the weight for computation of the average. Participants were from the Per-Protocol Population which excluded participants due to important protocol deviations that may have had a substantial effect on the result of the primary efficacy endpoint.

End point type	Primary
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End point timeframe:

Baseline and up to Week 6

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistical comparisons between other arms were neither planned nor performed for this primary endpoint.

End point values	Etoricoxib 90 mg (Part I)	Naproxen 1000 mg (Part I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	143		
Units: mm VAS				
least squares mean (confidence interval 95%)	-31.23 (-34.7 to -27.76)	-30.59 (-34.07 to -27.1)		

Statistical analyses

Statistical analysis title	Etoricoxib 90 mg v Naproxen 1000 mg
Comparison groups	Etoricoxib 90 mg (Part I) v Naproxen 1000 mg (Part I)
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.47
upper limit	4.19

Notes:

[2] - The etoricoxib dose (90 mg) will be considered non-inferior to naproxen 1000 mg if the upper bound of the two-sided 95% confidence interval of the between-treatment difference in the least squares (LS) mean (etoricoxib minus naproxen 1000 mg) is no larger than 8 mm VAS (non-inferiority margin).

Primary: Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 60 mg vs. naproxen

End point title	Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 60 mg vs. naproxen ^[3]
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End point description:

Spinal Pain Intensity is measured using a visual analog scale (VAS) from 0-100 mm with a lower value representing a better response. The time-weighted average change is calculated by taking the time between adjacent observations divided by the time from the randomization visit to the last observation in the period of interest, and using it as the weight for computation of the average. Participants were from the Per-Protocol Population which excluded participants due to important protocol deviations that may have had a substantial effect on the result of the primary efficacy endpoint.

End point type	Primary
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End point timeframe:

Baseline and up to Week 6

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistical comparisons between other arms were neither planned nor performed for this primary endpoint.

End point values	Etoricoxib 60 mg (Part I)	Naproxen 1000 mg (Part I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	660	143		
Units: mm VAS				
least squares mean (confidence interval 95%)	-29 (-30.69 to -27.31)	-30.59 (-34.07 to -27.1)		

Statistical analyses

Statistical analysis title	Etoricoxib 60 mg v Naproxen 1000 mg
Comparison groups	Etoricoxib 60 mg (Part I) v Naproxen 1000 mg (Part I)
Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	5.37

Notes:

[4] - The etoricoxib dose (60 mg) will be considered non-inferior to naproxen 1000 mg if the upper bound of the two-sided 95% confidence interval of the between-treatment difference in the LS mean (etoricoxib minus naproxen 1000 mg) is no larger than 8 mm VAS (non-inferiority margin).

Primary: Number of Participants Discontinuing Study Treatment Due to an Adverse Event (AE)

End point title	Number of Participants Discontinuing Study Treatment Due to an Adverse Event (AE) ^[5]
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End point description:

Participants were from the All Participants as Treated (APaT) Population which included the treatment group corresponding to the study treatment they actually received. One participant randomized to Etoricoxib 60 mg in Part II received 90 mg in Part II, and; therefore, was included in the Etoricoxib 60 mg / Etoricoxib 90 mg (Part II) arm.

End point type	Primary
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End point timeframe:

Up to 26 weeks

Notes:

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

Justification: No statistical analysis was planned for this primary endpoint.

End point values	Etoricoxib 60 mg (Part I)	Etoricoxib 90 mg (Part I)	Naproxen 1000 mg (Part I)	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	702	155	156	313
Units: Participants	22	2	6	3

End point values	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)	Etoricoxib 90 mg / Etoricoxib 90 mg (Part II)	Naproxen 1000 mg /Naproxen 1000 mg (Part II)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	319	145	142	
Units: Participants	9	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 90 mg vs. etoricoxib 60 mg

End point title	Time-Weighted Average Change From Baseline in the Spinal Pain Intensity in Study Part 1: etoricoxib 90 mg vs. etoricoxib 60 mg ^[6]
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End point description:

Spinal Pain Intensity is measured using a visual analog scale (VAS) from 0-100 mm with a lower value representing a better response. The time-weighted average change is calculated by taking the time between adjacent observations divided by the time from the randomization visit to the last observation in the period of interest, and using it as the weight for computation of the average. Participants were from the Modified Intent-to-Treat (mITT) Population in Part I which consisted of all randomized participants who received at least 1 dose of study treatment, had at least 1 measurement of interest post-randomization that was collected within 3 days of the last dose of study medication taken in Part I, and had baseline data.

End point type	Secondary
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End point timeframe:

Baseline and up to Week 6

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistical comparisons between other arms were neither planned nor performed for this primary endpoint.

End point values	Etoricoxib 60 mg (Part I)	Etoricoxib 90 mg (Part I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	694	153		
Units: mm VAS				
least squares mean (confidence interval 95%)	-28.94 (-30.58 to -27.29)	-30.51 (-33.87 to -27.15)		

Statistical analyses

Statistical analysis title	Etoricoxib 60 mg v Etoricoxib 90 mg
Comparison groups	Etoricoxib 60 mg (Part I) v Etoricoxib 90 mg (Part I)

Number of subjects included in analysis	847
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.396
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-1.58
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-3.96
upper limit	0.81

Secondary: Average Change From Week 6 in the Spinal Pain Intensity Over Weeks 10 and 12 in Study Part 2: etoricoxib 60/90 mg vs. etoricoxib 60 mg (non-responders from Part I)

End point title	Average Change From Week 6 in the Spinal Pain Intensity Over Weeks 10 and 12 in Study Part 2: etoricoxib 60/90 mg vs. etoricoxib 60 mg (non-responders from Part I)
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End point description:

Spinal Pain Intensity is measured using a visual analog scale (VAS) from 0-100 mm with a lower value representing a better response. Average change was calculated as the average VAS value over Weeks 10 and 12 minus the VAS at Week 6. Participants were from the Modified Intent-to-Treat (mITT) Population in Part I which consisted of all randomized participants who received at least 1 dose of study treatment, had at least 1 measurement of interest post-randomization that was collected within 3 days of the last dose of study medication taken in Part I, and had baseline data.

End point type	Secondary
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End point timeframe:

Week 6 to Week 10 and Week 12

End point values	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II)	Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	178		
Units: mm VAS				
least squares mean (confidence interval 95%)	-7.26 (-9.73 to -4.8)	-9.97 (-12.42 to -7.51)		

Statistical analyses

Statistical analysis title	Etoricoxib 60 mg/60 mg v 60 mg/90 mg
Comparison groups	Etoricoxib 60 mg / Etoricoxib 60 mg (Part II) v Etoricoxib 60 mg / Etoricoxib 90 mg (Part II)

Number of subjects included in analysis	353
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	ANCOVA
Parameter estimate	Difference in Least Squares Mean
Point estimate	-2.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4.88
upper limit	-0.52

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 30 (including up to 28 days after last dose of study drug)

Adverse event reporting additional description:

AE's were collected for the All Patients as Treated Population. Participants were included in the treatment group corresponding to the study treatment they actually received. One participant randomized to Etoricoxib 60 mg in Part II received Etoricoxib 90 mg in Part II, and; therefore, was included in the Etoricoxib 60mg / 90mg (Part II) arm.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Etoricoxib 90 mg / Etoricoxib 90 mg
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Reporting group description:

Participants who received Etoricoxib 90 mg in Part I and at least one dose of Etoricoxib 90 mg in Part II.

Reporting group title	Etoricoxib 60 mg / Etoricoxib 90 mg
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Reporting group description:

Participants who received Etoricoxib 60 mg in Part I and at least one dose of Etoricoxib 90 mg in Part II.

Reporting group title	Etoricoxib 60 mg / Etoricoxib 60 mg
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Reporting group description:

Participants who received Etoricoxib 60 mg in Part I and at least one dose of Etoricoxib 60 mg in Part II.

Reporting group title	Etoricoxib 90 mg
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Reporting group description:

Participants who received at least one dose of Etoricoxib 90 mg in Part I, but no drug in Part II.

Reporting group title	Etoricoxib 60 mg
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Reporting group description:

Participants who received at least one dose of Etoricoxib 60 mg in Part I, but no drug in Part II.

Reporting group title	Naproxen 1000 mg
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Reporting group description:

Participants who received at least one dose of Naproxen 1000 mg in Part I, but no drug in Part II.

Reporting group title	Naproxen 1000 mg / Naproxen 1000 mg
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Reporting group description:

Participants who received Naproxen 1000 mg in Part I and at least one dose of Naproxen 1000 mg in Part II.

Serious adverse events	Etoricoxib 90 mg / Etoricoxib 90 mg	Etoricoxib 60 mg / Etoricoxib 90 mg	Etoricoxib 60 mg / Etoricoxib 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 145 (4.14%)	7 / 319 (2.19%)	1 / 313 (0.32%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ear neoplasm			
alternative dictionary used:			

MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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			
Death			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Non-cardiac chest pain			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 145 (1.38%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Cardiac disorders			
Angina pectoris			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular hypertrophy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Headache			

subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Eye disorders			
Glaucoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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
Appendicitis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 145 (0.69%)	0 / 319 (0.00%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sialoadenitis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	0 / 313 (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	Etoricoxib 90 mg	Etoricoxib 60 mg	Naproxen 1000 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	5 / 70 (7.14%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Ear neoplasm alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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 cell carcinoma alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Vascular disorders			
Deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Hypertensive crisis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Non-cardiac chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Reproductive system and breast disorders			
Prostatitis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Psychiatric disorders			
Depression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Rib fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Skin abrasion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Hip fracture			

subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Left ventricular hypertrophy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Cerebral infarction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 70 (1.43%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

<p>Glaucoma</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 70 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Gastrointestinal disorders</p> <p>Gastric ulcer</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 70 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Gastric ulcer haemorrhage</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 70 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>Ankylosing spondylitis</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>1 / 70 (1.43%)</p> <p>0 / 1</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Rotator cuff syndrome</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 70 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Infections and infestations</p> <p>Abscess</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 10 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 70 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>	<p>0 / 14 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>
<p>Appendicitis</p>			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Diverticulitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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
Sialoadenitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (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	Naproxen 1000 mg / Naproxen 1000 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 142 (1.41%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ear neoplasm			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cell carcinoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin abrasion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Left ventricular hypertrophy alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

<p>Gastric ulcer</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 142 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>		
<p>Gastric ulcer haemorrhage</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 142 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Ankylosing spondylitis</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 142 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>		
<p>Rotator cuff syndrome</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 142 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>		
<p>Infections and infestations</p> <p>Abscess</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 142 (0.70%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Appendicitis</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>0 / 142 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p>		
<p>Diverticulitis</p>			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sialoadenitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Etoricoxib 90 mg / Etoricoxib 90 mg	Etoricoxib 60 mg / Etoricoxib 90 mg	Etoricoxib 60 mg / Etoricoxib 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 145 (16.55%)	50 / 319 (15.67%)	55 / 313 (17.57%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 145 (0.00%)	7 / 319 (2.19%)	9 / 313 (2.88%)
occurrences (all)	0	7	10
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 145 (5.52%)	15 / 319 (4.70%)	18 / 313 (5.75%)
occurrences (all)	8	16	21
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 145 (0.00%)	0 / 319 (0.00%)	2 / 313 (0.64%)
occurrences (all)	0	0	2
Tachyarrhythmia			
subjects affected / exposed	0 / 145 (0.00%)	1 / 319 (0.31%)	0 / 313 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed occurrences (all)	9 / 145 (6.21%) 11	13 / 319 (4.08%) 18	10 / 313 (3.19%) 15
Anosmia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	4 / 319 (1.25%) 10	1 / 313 (0.32%) 1
Dysgeusia subjects affected / exposed occurrences (all)	3 / 145 (2.07%) 3	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	2 / 313 (0.64%) 2
General disorders and administration site conditions Drug withdrawal syndrome subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Gastrointestinal disorders Abdominal pain upper alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 2	8 / 319 (2.51%) 12	15 / 313 (4.79%) 28
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	7 / 319 (2.19%) 8	4 / 313 (1.28%) 4
Abdominal pain subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	3 / 319 (0.94%) 3	3 / 313 (0.96%) 3
Diarrhoea subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 2	8 / 319 (2.51%) 8	7 / 313 (2.24%) 7
Nausea subjects affected / exposed occurrences (all)	3 / 145 (2.07%) 3	3 / 319 (0.94%) 4	5 / 313 (1.60%) 5

Retching subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	2 / 319 (0.63%) 2	2 / 313 (0.64%) 2
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	6 / 319 (1.88%) 6	1 / 313 (0.32%) 1
Dry throat subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Throat tightness subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	0 / 319 (0.00%) 0	0 / 313 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 319 (0.31%) 1	2 / 313 (0.64%) 2
Rash subjects affected / exposed occurrences (all)	0 / 145 (0.00%) 0	1 / 319 (0.31%) 1	4 / 313 (1.28%) 5
Urticaria subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1	1 / 319 (0.31%) 1	1 / 313 (0.32%) 1
Infections and infestations Nasopharyngitis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	7 / 145 (4.83%) 7	21 / 319 (6.58%) 21	17 / 313 (5.43%) 19

Non-serious adverse events	Etoricoxib 90 mg	Etoricoxib 60 mg	Naproxen 1000 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	18 / 70 (25.71%)	9 / 14 (64.29%)
Investigations			

Blood pressure increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 70 (1.43%) 1	0 / 14 (0.00%) 0
Vascular disorders Hypertension alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	4 / 70 (5.71%) 4	2 / 14 (14.29%) 2
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Tachyarrhythmia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Nervous system disorders Headache alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	4 / 70 (5.71%) 13	1 / 14 (7.14%) 1
Anosmia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 70 (2.86%) 2	1 / 14 (7.14%) 1
Dysgeusia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
General disorders and administration site conditions Drug withdrawal syndrome			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Gastrointestinal disorders			
Abdominal pain upper alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	3 / 70 (4.29%) 6	0 / 14 (0.00%) 0
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Abdominal pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 70 (1.43%) 1	0 / 14 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	4 / 70 (5.71%) 6	1 / 14 (7.14%) 1
Nausea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	4 / 70 (5.71%) 4	2 / 14 (14.29%) 2
Retching subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 70 (1.43%) 1	1 / 14 (7.14%) 1
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 70 (0.00%) 0	0 / 14 (0.00%) 0
Dry throat subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Throat tightness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 70 (0.00%) 0	1 / 14 (7.14%) 1
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	2 / 70 (2.86%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	2 / 70 (2.86%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Urticaria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 70 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 10 (0.00%)	0 / 70 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Naproxen 1000 mg / Naproxen 1000 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 142 (17.61%)		
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 142 (5.63%)		
occurrences (all)	8		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Tachyarrhythmia			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	5 / 142 (3.52%)		
occurrences (all)	5		
Anosmia			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Drug withdrawal syndrome			
subjects affected / exposed	0 / 142 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain upper			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	10 / 142 (7.04%)		
occurrences (all)	10		
Abdominal discomfort			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 142 (2.82%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences (all)	1		

Retching subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Dry throat subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Throat tightness subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	2 / 142 (1.41%) 2		
Rash subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1		
Urticaria subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0		
Infections and infestations Nasopharyngitis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	4 / 142 (2.82%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2013	The exclusion criteria was updated to exclude participants with an active duodenal ulcer or with any degree of hepatic insufficiency.
13 November 2013	The sample size was reduced from 1300 participants to approximately 900 participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported