



Clinical trial results:

Randomized, Double-Masked, Vehicle Controlled, Clinical Evaluation To Assess The Safety And Efficacy Of Nepafenac Ophthalmic Suspension, 0.3% For Improvement In Clinical Outcomes Among Diabetic Subjects Following Cataract Surgery

Summary

EudraCT number	2013-001874-12
Trial protocol	HU IT DE AT ES
Global end of trial date	28 May 2015

Results information

Result version number	v1 (current)
This version publication date	09 June 2016
First version publication date	09 June 2016

Trial information

Trial identification

Sponsor protocol code	C-12-071
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01872611
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alcon Research, Ltd.
Sponsor organisation address	6201 S. Freeway, Fort Worth, Texas, United States, 76134
Public contact	Head, Pharma, GCRA, Alcon Research, Ltd., +1 888-451-3937, alcon.medinfo@alcon.com
Scientific contact	Head, Pharma, GCRA, Alcon Research, Ltd., +1 888-451-3937, alcon.medinfo@alcon.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 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2015
Global end of trial reached?	Yes
Global end of trial date	28 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate superiority of Nepafenac Ophthalmic Suspension, 0.3% dosed once daily relative to Nepafenac Vehicle based upon clinical outcomes among diabetic subjects following cataract surgery.

Protection of trial subjects:

This study was performed in compliance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice (GCP), including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 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	Spain: 64
Country: Number of subjects enrolled	Austria: 22
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hungary: 70
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Australia: 58
Country: Number of subjects enrolled	Colombia: 47
Country: Number of subjects enrolled	Israel: 67
Country: Number of subjects enrolled	Mexico: 93
Country: Number of subjects enrolled	Peru: 8
Country: Number of subjects enrolled	Philippines: 33
Country: Number of subjects enrolled	Singapore: 18
Country: Number of subjects enrolled	United States: 89
Worldwide total number of subjects	588
EEA total number of subjects	175

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)	185
From 65 to 84 years	394
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 73 investigational centers located in the U.S., Europe, the Middle East, Africa, Latin America, the Caribbean, and the Asia Pacific region.

Pre-assignment

Screening details:

A total of 819 subjects were screened and 605 subjects were randomized to treatment; 17 of the randomized subjects did not receive treatment (one of which died prior to treatment).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nepafenac

Arm description:

With prednisolone acetate standard of care, Nepafenac Ophthalmic Suspension, 0.3%, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Arm type	Experimental
Investigational medicinal product name	Nepafenac Ophthalmic Suspension, 0.3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Investigational medicinal product name	Prednisolone acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ocular use

Dosage and administration details:

1 drop instilled in the operative eye 4 times daily beginning post-operatively on the day of surgery for the first 2 weeks, followed by 2 times daily for the next 2 weeks

Arm title	Vehicle
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Arm description:

With prednisolone acetate standard of care, Nepafenac vehicle, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Investigational medicinal product name	Prednisolone acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ocular use

Dosage and administration details:

1 drop instilled in the operative eye 4 times daily beginning post-operatively on the day of surgery for the first 2 weeks, followed by 2 times daily for the next 2 weeks

Number of subjects in period 1	Nepafenac	Vehicle
Started	293	295
Full Analysis Set	289	293
Completed	277	292
Not completed	16	3
Adverse event, non-fatal	3	1
Death	-	1
Lost to follow-up	8	-
Reason not specified	-	1
Withdrawal by subject	5	-

Baseline characteristics

Reporting groups

Reporting group title	Nepafenac
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Reporting group description:

With prednisolone acetate standard of care, Nepafenac Ophthalmic Suspension, 0.3%, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Reporting group title	Vehicle
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Reporting group description:

With prednisolone acetate standard of care, Nepafenac vehicle, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.

Reporting group values	Nepafenac	Vehicle	Total
Number of subjects	293	295	588
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	67.9 ± 8.6	68.1 ± 8.3	-
Gender categorical Units: Subjects			
Female	151	149	300
Male	142	146	288

Subject analysis sets

Subject analysis set title	Nepafenac
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set, defined as all randomized subjects who completed implant surgery and had at least one on-therapy postsurgical visit.

Subject analysis set title	Vehicle
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set, defined as all randomized subjects who completed implant surgery and had at least one on-therapy postsurgical visit.

Reporting group values	Nepafenac	Vehicle	
Number of subjects	289	293	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	67.7 ± 8.5	68.1 ± 8.4	

Gender categorical			
Units: Subjects			
Female	149	149	
Male	140	144	

End points

End points reporting groups

Reporting group title	Nepafenac
Reporting group description: With prednisolone acetate standard of care, Nepafenac Ophthalmic Suspension, 0.3%, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.	
Reporting group title	Vehicle
Reporting group description: With prednisolone acetate standard of care, Nepafenac vehicle, 1 drop instilled in the operative eye 1 day prior to surgery, continuing on the day of surgery, and for 90 days following surgery. An additional 1 drop will be administered 30 to 120 minutes prior to surgery.	
Subject analysis set title	Nepafenac
Subject analysis set type	Full analysis
Subject analysis set description: Full analysis set, defined as all randomized subjects who completed implant surgery and had at least one on-therapy postsurgical visit.	
Subject analysis set title	Vehicle
Subject analysis set type	Full analysis
Subject analysis set description: Full analysis set, defined as all randomized subjects who completed implant surgery and had at least one on-therapy postsurgical visit.	

Primary: Percentage of Participants With Best-corrected Visual Acuity (BCVA) Improvement of ≥ 15 Letters From Preoperative Baseline to Day 14 and Maintained Through Day 90

End point title	Percentage of Participants With Best-corrected Visual Acuity (BCVA) Improvement of ≥ 15 Letters From Preoperative Baseline to Day 14 and Maintained Through Day 90
End point description: BCVA (with spectacles or other visual corrective devices) was reported in letters read correctly, using the Early Treatment Diabetic Retinopathy Study (ETDRS) test of 70 letters. Improvement of BCVA was defined as an increase (gain) in the number of letters read, compared to the baseline assessment. One eye (study eye) contributed to the analysis.	
End point type	Primary
End point timeframe: Baseline to Day 14, and maintained through Day 90	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	48.8	50.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Parameter dispersion is the standard error for the odds ratio.	
Comparison groups	Nepafenac v Vehicle
Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.671
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

Primary: Measure Title Percentage of Participants Who Develop Macular Edema Within 90 Days Following Cataract Surgery (Day 0)

End point title	Measure Title Percentage of Participants Who Develop Macular Edema Within 90 Days Following Cataract Surgery (Day 0)
End point description:	
Macular edema was defined as $\geq 30\%$ Increase from pre-operative baseline in central subfield macular thickness, as measured with Spectral Domain Ocular Coherence Tomography (SD-OCT). One eye (study eye) contributed to the analysis.	
End point type	Primary
End point timeframe:	
Day 0 to Day 90	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	5.9	14.3		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Parameter dispersion is the standard error for the odds ratio.	
Comparison groups	Nepafenac v Vehicle

Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.1

Secondary: Percentage of Participants With BCVA Improvement of ≥ 15 Letters From Preoperative Baseline to Day 90

End point title	Percentage of Participants With BCVA Improvement of ≥ 15 Letters From Preoperative Baseline to Day 90
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to Day 90	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	65.4	65.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With BCVA Improvement of ≥ 15 Letters From Preoperative Baseline to Day 60

End point title	Percentage of Participants With BCVA Improvement of ≥ 15 Letters From Preoperative Baseline to Day 60
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to Day 60	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	68.9	62.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a > 5-letter Loss in BCVA From Day 7 to Any Visit

End point title	Percentage of Participants With a > 5-letter Loss in BCVA From Day 7 to Any Visit
End point description:	
End point type	Secondary
End point timeframe:	
Day 7 up to any visit	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	18.7	16.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With With a > 10-letter Loss in BCVA From Day 7 to Any Visit

End point title	Percentage of Participants With With a > 10-letter Loss in BCVA From Day 7 to Any Visit
End point description:	
End point type	Secondary
End point timeframe:	
Day 7 up to any visit	

End point values	Nepafenac	Vehicle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	289	293		
Units: Percentage of participants				
number (not applicable)	10.7	8.9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Reporting of adverse events (AEs) began once informed consent was obtained from the subject and continued through Day 90 (or Day 120, if applicable). Ocular adverse events are presented for both study eye and nonstudy eye combined.

Adverse event reporting additional description:

An AE was defined as any untoward medical occurrence in a subject after signing the informed consent and did not necessarily have to have a causal relationship with the study treatment. AEs were reported as pretreatment, treatment-emergent, and posttreatment. Reports of AEs were obtained through solicited and spontaneous comments from the subject.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Nepafenac
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Reporting group description:

Nepafenac Ophthalmic Suspension, 0.3%

Reporting group title	Vehicle
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Reporting group description:

Nepafenac Ophthalmic Suspension Vehicle

Reporting group title	Posttreatment
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Reporting group description:

All subjects after cessation of study treatment up to study exit

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There are no non-serious events at the 5% threshold.

Serious adverse events	Nepafenac	Vehicle	Posttreatment
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 293 (4.78%)	14 / 295 (4.75%)	4 / 588 (0.68%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Peripheral artery stenosis			

subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Thrombosis			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Intra-ocular injection			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin graft			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Device dislocation			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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			
Acute respiratory failure			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Lumbar vertebral fracture			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Atrial fibrillation			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Atrial flutter			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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 failure			

subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Coronary artery occlusion			
subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 293 (0.68%)	1 / 295 (0.34%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 293 (0.00%)	0 / 295 (0.00%)	1 / 588 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diabetic retinal oedema			
subjects affected / exposed	0 / 293 (0.00%)	0 / 295 (0.00%)	1 / 588 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 293 (0.00%)	0 / 295 (0.00%)	1 / 588 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Posterior capsule rupture subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Gastrointestinal disorders			
Rectal haemorrhage subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (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
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Intervertebral disc degeneration subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Vertebral foraminal stenosis subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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			
Appendicitis subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Cellulitis subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Herpes zoster			

subjects affected / exposed	1 / 293 (0.34%)	0 / 295 (0.00%)	0 / 588 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 293 (0.00%)	1 / 295 (0.34%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 293 (0.00%)	2 / 295 (0.68%)	0 / 588 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 293 (0.00%)	0 / 295 (0.00%)	1 / 588 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nepafenac	Vehicle	Posttreatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 293 (0.00%)	0 / 295 (0.00%)	0 / 588 (0.00%)

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

None reported