Clinical trial results:
A Double-Blind, Randomized, Crossover Study to Assess Menstrual Cramp Pain Associated with Primary Dysmenorrhea

Summary

EudraCT number	2017-005031-17
Trial protocol	Outside EU/EEA
Global end of trial date	05 September 2018

Results information

Result version number	v1 (current)
This version publication date	17 March 2019
First version publication date	17 March 2019

Trial information

Trial identification

Sponsor protocol code	BAY117031/19737

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03448536
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the analgesic efficacy of a maximum single dose of two tablets of Aleve (2 x naproxen sodium 220 mg; total dose 440 mg) as compared to two caplets of Tylenol Extra Strength (2 x acetaminophen 500 mg; total dose 1000 mg) for the treatment of menstrual cramping pain associated with primary dysmenorrhea.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 2018
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	United States: 201
Worldwide total number of subjects	201
EEA total number of subjects	0

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)	18

Adults (18-64 years)	183
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at multiple centers in the US between 05 April 2018 (first patient first visit) and 05 September 2018 (last patient last visit).

Pre-assignment

Screening details:

Overall, 242 subjects were screened. Of them, 201 subjects were randomized, and 196 received study treatment.

Period 1

Period 1 title	Randomization
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Naproxen Sodium : Acetaminophen

Arm description:

Subjects received one single oral dose of 440 mg naproxen sodium in treatment period 1, followed by one single oral dose of 1000 mg acetaminophen in treatment period 2

Arm type	Experimental
Investigational medicinal product name	Naproxen sodium
Investigational medicinal product code	BAY117031
Other name	Aleve
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

220 mg *2 tablets, orally, single dose

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	Tylenol Extra Strength
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg *2 caplets, orally, single dose

Arm title	Acetaminophen : Naproxen Sodium

Arm description:

Subjects received one single oral dose of 1000 mg acetaminophen in treatment period 1, followed by one single oral dose of 440 mg naproxen sodium in treatment period 2

Arm type	Experimental
Investigational medicinal product name	Naproxen sodium
Investigational medicinal product code	BAY117031
Other name	Aleve
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

220 mg *2 tablets, orally, single dose

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	Tylenol Extra Strength
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg *2 caplets, orally, single dose

Number of subjects in period 1	Naproxen Sodium : Acetaminophen	Acetaminophen : Naproxen Sodium
Started	100	101
Completed	96	100
Not completed	4	1
Consent withdrawn by subject	-	1
Pregnancy	1	-
Lost to follow-up	2	-
Protocol deviation	1	-

Period 2

Period 2 title	Treatment
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Naproxen Sodium : Acetaminophen

Arm description:

Subjects received one single oral dose of 440 mg naproxen sodium in treatment period 1, followed by one single oral dose of 1000 mg acetaminophen in treatment period 2

Arm type	Experimental
Investigational medicinal product name	Naproxen sodium
Investigational medicinal product code	BAY117031
Other name	Aleve
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

220 mg *2 tablets, orally, single dose

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	Tylenol Extra Strength
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg *2 caplets, orally, single dose

Arm title	Acetaminophen : Naproxen Sodium

Arm description:

Subjects received one single oral dose of 1000 mg acetaminophen in treatment period 1, followed by one single oral dose of 440 mg naproxen sodium in treatment period 2

Arm type	Experimental
Investigational medicinal product name	Naproxen sodium
Investigational medicinal product code	BAY117031
Other name	Aleve
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

220 mg *2 tablets, orally, single dose

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	Tylenol Extra Strength
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg *2 caplets, orally, single dose

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Five subjects were never treated, therefore, baseline data were analysed for Safety Population (N=196).

Number of subjects in period 2[2]	Naproxen Sodium : Acetaminophen	Acetaminophen : Naproxen Sodium
Started	96	100
Completed	88	97
Not completed	8	3
Physician decision	1	-
Consent withdrawn by subject	1	1
Other	3	-
Lost to follow-up	1	2
Inadequate pain reporter	1	-
Protocol deviation	1	-

Notes:

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

Justification: Five subjects were never treated, therefore, baseline data were analysed for Safety Population (N=196).

Baseline characteristics

Reporting groups	
Reporting group title	Naproxen Sodium : Acetaminophen
Reporting group description:	
Subjects received one single oral dose of 440 mg naproxen sodium in treatment period 1, followed by one single oral dose of 1000 mg acetaminophen in treatment period 2	
Reporting group title	Acetaminophen : Naproxen Sodium
Reporting group description:	
Subjects received one single oral dose of 1000 mg acetaminophen in treatment period 1, followed by one single oral dose of 440 mg naproxen sodium in treatment period 2	

Reporting group values	Naproxen Sodium : Acetaminophen	Acetaminophen : Naproxen Sodium	Total
Number of subjects	96	100	196
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	24.7	25.0	
standard deviation	± 5.60	± 5.77	-
Gender categorical			
Units: Subjects			
Female	96	100	196
Male	0	0	0
Race			
Units: Subjects			
White	66	68	134
Black or African American	23	27	50
Asian	6	2	8
American Indian or Alaska Native	1	0	1
Native Hawaiian or Other Pacific Islander	0	1	1
Mutiple	0	2	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	13	14	27
Not Hispanic or Latino	83	85	168
Unknown	0	1	1
At least moderate pain intensity during 4 of last 6 menstrual cycles			
Pain intensity was measured using Categorical Pain Intensity (0 = none, 1 = mild, 2 = moderate, 3 = severe).			
Units: Subjects			
Yes	96	100	196
No	0	0	0

End points

End points reporting groups

Reporting group title	Naproxen Sodium : Acetaminophen
Reporting group description:	
Subjects received one single oral dose of 440 mg naproxen sodium in treatment period 1, followed by one single oral dose of 1000 mg acetaminophen in treatment period 2	
Reporting group title	Acetaminophen : Naproxen Sodium
Reporting group description:	
Subjects received one single oral dose of 1000 mg acetaminophen in treatment period 1, followed by one single oral dose of 440 mg naproxen sodium in treatment period 2	
Reporting group title	Naproxen Sodium : Acetaminophen
Reporting group description:	
Subjects received one single oral dose of 440 mg naproxen sodium in treatment period 1, followed by one single oral dose of 1000 mg acetaminophen in treatment period 2	
Reporting group title	Acetaminophen : Naproxen Sodium
Reporting group description:	
Subjects received one single oral dose of 1000 mg acetaminophen in treatment period 1, followed by one single oral dose of 440 mg naproxen sodium in treatment period 2	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Included all randomized subjects who took at least one dose of investigational medicinal product (IMP).	
Subject analysis set title	Intent to treat (ITT) population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Included all subjects who were randomized and provided at least one measure of an efficacy parameter after the first dose of IMP.	
Subject analysis set title	Per protocol (PP) population
Subject analysis set type	Per protocol
Subject analysis set description:	
Included all subjects in ITT who did not have any major protocol violations.	
Subject analysis set title	Naproxen Sodium
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received one single oral dose of 440 mg naproxen sodium	
Subject analysis set title	Acetaminophen
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received one single oral dose of 1000 mg acetaminophen	

Primary: Sum of Total Pain Relief (TOTPAR) over 0-12 hours

End point title	Sum of Total Pain Relief (TOTPAR) over 0-12 hours
End point description:	
Pain relief was measured using Categorical Pain Relief Rating Scale (0 = No relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief). Total pain relief scores (TOTPARs) were calculated by multiplying the pain relief score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.	
End point type	Primary
End point timeframe:	
Up to 12 hours post-dose	

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[1]	160[2]		
Units: Scores on a scale * hours				
least squares mean (standard error)	29.18 (± 1.003)	24.87 (± 1.029)		

Notes:

[1] - Per protocol (PP) population

[2] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	TOTPAR over 0-12 hours
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	4.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.06
upper limit	6.56

Secondary: Summed Pain Intensity Difference (SPID) over 0-12 hours

End point title	Summed Pain Intensity Difference (SPID) over 0-12 hours

End point description:

Pain intensity was measured using Numerical Rating Scale (from 0 to 10: 0 = no pain, 10 = worst possible pain). For each postdose time point, pain intensity differences (PIDs) were derived by subtracting the pain intensity at the postdose time point from the baseline intensity score (baseline score – post-baseline score). A positive difference was indicative of improvement. Time-weighted summed pain intensity differences (SPIDs) were calculated by multiplying the PID score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.

End point type	Secondary

End point timeframe:

Up to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[3]	160[4]		
Units: Scores on a scale * hours				
least squares mean (standard error)	53.62 (± 1.931)	43.82 (± 1.977)		

Notes:

[3] - Per protocol (PP) population

[4] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	SPID over 0-12 hours
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.75
upper limit	13.85

Secondary: SPID over 0-6 hours

End point title	SPID over 0-6 hours

End point description:

Pain intensity was measured using Numerical Rating Scale (from 0 to 10: 0 = no pain, 10 = worst possible pain). For each postdose time point, pain intensity differences (PIDs) were derived by subtracting the pain intensity at the postdose time point from the baseline intensity score (baseline score – post-baseline score). A positive difference was indicative of improvement. Time-weighted summed pain intensity differences (SPIDs) were calculated by multiplying the PID score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.

End point type	Secondary

End point timeframe:

Up to 6 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[5]	160[6]		
Units: Scores on a scale * hours				
least squares mean (standard error)	23.47 (± 0.902)	21.94 (± 0.925)		

Notes:

[5] - Per protocol (PP) population

[6] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	SPID over 0-6 hours
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.129
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	3.49

Secondary: SPID over 6-12 hours

End point title	SPID over 6-12 hours

End point description:

Pain intensity was measured using Numerical Rating Scale (from 0 to 10: 0 = no pain, 10 = worst possible pain). For each postdose time point, pain intensity differences (PIDs) were derived by subtracting the pain intensity at the postdose time point from the baseline intensity score (baseline score – post-baseline score). A positive difference was indicative of improvement. Time-weighted summed pain intensity differences (SPIDs) were calculated by multiplying the PID score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.

End point type	Secondary

End point timeframe:

From 6 hours to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[7]	160[8]		
Units: Scores on a scale * hours				
least squares mean (standard error)	30.15 (± 1.252)	21.88 (± 1.280)		

Notes:

[7] - Per protocol (PP) population

[8] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	SPID over 6-12 hours
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	8.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.76
upper limit	10.78

Secondary: TOTPAR over 0-6 hours

End point title	TOTPAR over 0-6 hours

End point description:

Pain relief was measured using Categorical Pain Relief Rating Scale (0 = No relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief). Total pain relief scores (TOTPARs) were calculated by multiplying the pain relief score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.

End point type	Secondary

End point timeframe:

Up to 6 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[9]	160[10]		
Units: Scores on a scale * hours				
least squares mean (standard error)	13.46 (± 0.451)	12.90 (± 0.463)		

Notes:

[9] - Per protocol (PP) population

[10] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	TOTPAR over 0-6 hours
Comparison groups	Naproxen Sodium v Acetaminophen

Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.307
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	1.64

Secondary: TOTPAR 6-12 hours

End point title	TOTPAR 6-12 hours

End point description:

Pain relief was measured using Categorical Pain Relief Rating Scale (0 = No relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief). Total pain relief scores (TOTPARs) were calculated by multiplying the pain relief score at each postdose time point by the duration (in hours) since the preceding time point and then summing these values.

End point type	Secondary

End point timeframe:

From 6 hours to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[11]	160[12]		
Units: Scores on a scale * hours				
least squares mean (standard error)	15.72 (± 0.661)	11.97 (± 0.677)		

Notes:

[11] - Per protocol (PP) population

[12] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	TOTPAR 6-12 hours
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	3.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.34
upper limit	5.16

Secondary: Time to first intake of rescue medication

End point title	Time to first intake of rescue medication

End point description:

Time to first intake of rescue medication was defined as the number of hours elapsed between time of dose and time of rescue medication in each treatment period. Subjects would be censored at time of last pain assessment. '99999' denotes that value could not be calculated due to censored data.

End point type	Secondary

End point timeframe:

Up to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[13]	160[14]		
Units: Hours				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[13] - Per protocol (PP) population

[14] - Per protocol (PP) population

Statistical analyses

Statistical analysis title	Time to first intake of rescue medication
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Pain Intensity Difference (PID) scores by evaluation

End point title	Pain Intensity Difference (PID) scores by evaluation

End point description:

Pain intensity was measured using Numerical Rating Scale (from 0 to 10: 0 = no pain, 10 = worst possible pain). For each postdose time point, pain intensity differences (PIDs) were derived by subtracting the pain intensity at the postdose time point from the baseline intensity score (baseline score – post-baseline score). A positive difference was indicative of improvement.

End point type	Secondary

End point timeframe:

Up to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: Scores on a scale				
arithmetic mean (standard deviation)				
30 minutes	0.8 (± 1.47)	0.9 (± 1.61)		
1 hour	1.9 (± 1.93)	2.1 (± 2.01)		
3 hours	4.1 (± 2.40)	4.0 (± 2.68)		
6 hours	5.1 (± 2.59)	4.3 (± 2.90)		
9 hours	4.9 (± 2.93)	3.6 (± 3.13)		
12 hours	5.0 (± 2.97)	3.5 (± 3.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects by Global Evaluation Scores

End point title	Number of Subjects by Global Evaluation Scores

End point description:

Global evaluation was performed either at 12 hours post-dose or immediately at the first intake of rescue medication. Global Evaluation Score was based on the question 'Overall, I would rate the effectiveness of the study medication in relieving my menstrual pain as: 0=Poor, 1=Fair, 2=Good, 3=Very Good, 4=Excellent.'

End point type	Secondary

End point timeframe:

Up to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	156[15]	156[16]		
Units: Subjects				
Poor	10	13		
Fair	26	42		
Good	25	38		
Very Good	60	38		
Excellent	35	25		

Notes:

[15] - Subjects assessed for this endpoint in Per protocol (PP) population (n=170)

[16] - Subjects assessed for this endpoint in Per protocol (PP) population (n=160)

Statistical analyses

Statistical analysis title	Number of Subjects by Global Evaluation Scores
Comparison groups	Naproxen Sodium v Acetaminophen
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel

Secondary: Pain relief scores by evaluation

End point title	Pain relief scores by evaluation

End point description:

Pain relief was measured using Categorical Pain Relief Rating Scale (0 = No relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief).

End point type	Secondary

End point timeframe:

Up to 12 hours post-dose

End point values	Naproxen Sodium	Acetaminophen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170[17]	160[18]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
30 minutes	0.9 (± 0.98)	0.9 (± 1.01)		
1 hour	1.4 (± 1.06)	1.6 (± 1.12)		
3 hours	2.3 (± 1.17)	2.3 (± 1.32)		
6 hours	2.7 (± 1.45)	2.4 (± 1.50)		
9 hours	2.6 (± 1.52)	2.0 (± 1.57)		
12 hours	2.7 (± 1.60)	1.9 (± 1.69)		

Notes:

[17] - Per protocol (PP) population

[18] - Per protocol (PP) population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The observation phase for AEs started with signing the informed consent form and ended in general with the last visit of follow-up. After the end of follow-up there was no requirement to actively collect AEs.

Adverse event reporting additional description:

In case of ongoing AEs after the last follow-up visit – especially when related to treatment with the study medication – the respective AE was followed until resolution, if possible.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Naproxen Sodium

Reporting group description:

Subjects received one single oral dose of 440 mg naproxen sodium

Reporting group title	Acetaminophen

Reporting group description:

Subjects received one single oral dose of 1000 mg acetaminophen

Serious adverse events	Naproxen Sodium	Acetaminophen	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 192 (0.00%)	0 / 185 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Naproxen Sodium	Acetaminophen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 192 (6.25%)	9 / 185 (4.86%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Facial bones fracture			

subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Laceration			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Nail avulsion			
subjects affected / exposed	0 / 192 (0.00%)	1 / 185 (0.54%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye pruritus			
subjects affected / exposed	1 / 192 (0.52%)	1 / 185 (0.54%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 192 (1.04%)	1 / 185 (0.54%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 192 (0.00%)	1 / 185 (0.54%)	
occurrences (all)	0	1	
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 192 (0.00%)	1 / 185 (0.54%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 192 (0.52%)	0 / 185 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Pharyngitis streptococcal			
subjects affected / exposed	1 / 192 (0.52%)	2 / 185 (1.08%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	3 / 192 (1.56%)	0 / 185 (0.00%)	
occurrences (all)	3	0	
Urinary tract infection			
subjects affected / exposed	0 / 192 (0.00%)	1 / 185 (0.54%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 192 (0.00%)	1 / 185 (0.54%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2018	Amendment 1 (integrated protocol Version 2.0) specified the following key modifications: positive drug screen at visit 2 was added in Exclusion criteria; time point/frame of measurement for primary variable was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported