Clinical trial results:
A Randomized, Double-Blind, Placebo Controlled Trial to Assess the Analgesic Efficacy and Safety of Extended Release Naproxen Sodium Tablets in Postsurgical Dental Pain

Summary

EudraCT number	2014-005272-28
Trial protocol	Outside EU/EEA
Global end of trial date	01 September 2011

Results information

Result version number	v2 (current)
This version publication date	07 September 2016
First version publication date	21 June 2015
Version creation reason	• New data added to full data set • Correction of full data set Bayer sponsor contact information to be updated

Trial information

Trial identification

Sponsor protocol code	BAYH6689/15142

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01389284
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368, Leverkusen, Germany,
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 September 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective was to evaluate pain relief of the extended release (ER) naproxen sodium 660 milligram (mg) tablet compared to commercial naproxen sodium 220 mg tablet over 24 hours in subjects with postsurgical dental pain.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects and/or their legally authorized representative. 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	15 June 2011
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: 300
Worldwide total number of subjects	300
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)	0

Adults (18-64 years)	300
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at one trial site in the United States between 15 June 2011 (first subject first visit) and 01 September 2011 (last subject last visit).

Pre-assignment

Screening details:

Overall, a total of 392 subjects were screened, out of which 300 subjects were randomized and treated, and 299 subjects completed the study.

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, Carer

Arms

Are arms mutually exclusive?	No
Arm title	Naproxen Sodium ER (BAYH6689)

Arm description:

1 naproxen sodium ER 660 mg tablet and 1 naproxen sodium immediate release (IR) 220 mg placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).

Arm type	Experimental
Investigational medicinal product name	Naproxen Sodium ER
Investigational medicinal product code	BAYH6689
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Naproxen sodium ER tablet 660 mg, orally administered once daily for 24 hours.

Investigational medicinal product name	Naproxen Sodium IR Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of 220 mg naproxen sodium IR (Aleve) for 24 hours.

Arm title	Naproxen Sodium IR (Aleve, BAYH6689)

Arm description:

1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg tablet initially followed by 1 naproxen sodium IR 220 mg tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg tablet at hour 16 (± 15 minutes).

Arm type	Active comparator
Investigational medicinal product name	Naproxen Sodium ER Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:	
Matching placebo of 660 mg naproxen sodium ER for 24 hours.	
Investigational medicinal product name	Naproxen Sodium IR
Investigational medicinal product code	BAYH6689
Other name	Aleve
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Naproxen sodium IR tablet 220 mg, orally administered 3 times daily for 24 hours.	
Arm title	Placebo
Arm description:	
1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg matching placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).	
Arm type	Placebo
Investigational medicinal product name	Naproxen Sodium ER Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo of 660 mg naproxen sodium ER for 24 hours.	
Investigational medicinal product name	Naproxen Sodium IR Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Matching placebo of 220 mg naproxen sodium IR (Aleve) for 24 hours.	

Number of subjects in period 1	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo
Started	120	120	60
Completed	120	119	60
Not completed	0	1	0
Consent withdrawn by subject	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Naproxen Sodium ER (BAYH6689)
Reporting group description:	
1 naproxen sodium ER 660 mg tablet and 1 naproxen sodium immediate release (IR) 220 mg placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).	
Reporting group title	Naproxen Sodium IR (Aleve, BAYH6689)
Reporting group description:	
1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg tablet initially followed by 1 naproxen sodium IR 220 mg tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg tablet at hour 16 (± 15 minutes).	
Reporting group title	Placebo
Reporting group description:	
1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg matching placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).	

Reporting group values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo
Number of subjects	120	120	60
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	24	23	25
standard deviation	± 5.05	± 4.67	± 6.56
Gender categorical			
Units: subjects			
Female	70	71	41
Male	50	49	19
Pain Intensity Score			
Pain intensity was evaluated using a 4-point Categorical Pain Intensity Rating Scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe			
Units: Subjects			
0 = None	0	0	0
1 = Mild	0	0	0
2 = Moderate	96	97	53
3 = Severe	24	23	7

Reporting group values	Total		
Number of subjects	300		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: subjects			
Female	182		
Male	118		
Pain Intensity Score			
Pain intensity was evaluated using a 4-point Categorical Pain Intensity Rating Scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe			
Units: Subjects			
0 = None	0		
1 = Mild	0		
2 = Moderate	246		
3 = Severe	54		

End points

End points reporting groups

Reporting group title	Naproxen Sodium ER (BAYH6689)

Reporting group description:

1 naproxen sodium ER 660 mg tablet and 1 naproxen sodium immediate release (IR) 220 mg placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).

Reporting group title	Naproxen Sodium IR (Aleve, BAYH6689)

Reporting group description:

1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg tablet initially followed by 1 naproxen sodium IR 220 mg tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg tablet at hour 16 (± 15 minutes).

Reporting group title	Placebo

Reporting group description:

1 naproxen sodium ER 660 mg matching placebo tablet and 1 naproxen sodium IR 220 mg matching placebo tablet initially followed by 1 naproxen sodium IR 220 mg matching placebo tablet at hour 8 (± 15 minutes), and 1 naproxen sodium IR 220 mg matching placebo tablet at hour 16 (± 15 minutes).

Subject analysis set title	Intent-to-treat (ITT) Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

A subject was included in the ITT population if he/she was randomized to a treatment group, took at least one dose of the investigational product, and provided at least one estimate of an efficacy parameter after the first dose of the investigational product. The ITT population was used for all efficacy analyses.

Primary: Summed, Time-weighted Pain Intensity Difference From 0 to 24 Hours Postdose (SPID0-24)

End point title	Summed, Time-weighted Pain Intensity Difference From 0 to 24 Hours Postdose (SPID0-24)[1]

End point description:

SPID0-24 was calculated by multiplying the pain intensity difference score at each post-dose timepoint by the duration (in hours) since the preceding timepoint and then summing these values over 0 to 24 hours. Pain intensity was measured at baseline, 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 8, 12, 16, 20 and 24 hours using the 4-point categorical pain intensity scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe. SPID0-24 can vary from -24 to 72. The positive SPID value indicates improvement of pain relief. The higher the SPID value, the more improvement of pain relief.

End point type	Primary

End point timeframe:

From 0 to 24 hours post-dose

Notes:

[1] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[2]	120[3]	60[4]	
Units: Score on the scale				
arithmetic mean (standard error)	23.2 (± 2.01)	23.6 (± 2.01)	-0.6 (± 2.85)	

Notes:

[2] - ITT population.

[3] - ITT population.

[4] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Summed, Time-weighted Pain Intensity Differences (SPID)

End point title	Summed, Time-weighted Pain Intensity Differences (SPID)

End point description:

Pain intensity was measured at baseline, 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 8, 12, 16, 20 and 24 hours using the 4-point categorical pain intensity scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe. The total possible score ranges of SPIDs were SPID0-6: -6 to 18, SPID0-8: -8 to 24, SPID0-12: -12 to 36, SPID0-16: -16 to 48, SPID16-24: -8 to 24. The positive SPID value indicates improvement of pain relief. The higher the SPID value, the more improvement of pain relief.
LS Mean=Least squares mean.

End point type	Secondary

End point timeframe:

0-6, 0-8, 0-12, 0-16 and 16-24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[5]	120[6]	60[7]	
Units: Score on the scale				
arithmetic mean (confidence interval 95%)				
From 0 to 6 hours, LS Mean	5.3 (4.5 to 6.1)	5.3 (4.5 to 6.1)	-0.5 (-1.6 to 0.7)	
From 0 to 8 hours, LS Mean	7 (5.9 to 8.1)	6.9 (5.7 to 8)	-0.8 (-2.3 to 0.8)	
From 0 to 12 hours, LS Mean	10.9 (9.1 to 12.7)	10.9 (9.2 to 12.7)	-0.9 (-3.4 to 1.6)	
From 0 to 16 hours, LS Mean	14.7 (12.3 to 17.2)	15 (12.5 to 17.5)	-1 (-4.5 to 2.6)	
From 16 to 24 hours, LS Mean	8.5 (6.9 to 10)	8.6 (7.1 to 10.1)	0.4 (-1.8 to 2.6)	

Notes:

[5] - ITT population.

[6] - ITT population.

[7] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Summed, Time-weighted Total Pain Relief Scores (TOTPARs)

End point title	Summed, Time-weighted Total Pain Relief Scores (TOTPARs)

End point description:

TOTPARs were derived by multiplying the pain relief score at each post-dose timepoint by the duration (in hours) since the preceding timepoint and then summing these values over the specified interval. Pain Relief was evaluated at 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 8, 12, 16, 20 and 24 hours postdose, using the 5-point overall pain relief scale: 0 = No relief, 1 = A little relief, 2 = Some relief, 3 = A lot of relief, 4 = Complete relief. The possible total score ranges of TOTPARs are: TOTPAR0-6: 0 to 18, TOTPAR0-8: 0 to 24, TOTPAR0-12: 0 to 36, TOTPAR0-16: 0 to 48, TOTPAR0-24: 0 to 72, TOTPAR16-24: 0 to 24.

End point type	Secondary

End point timeframe:

0-6, 0-8, 0-12, 0-16, 0-24, and 16-24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[8]	120[9]	60[10]	
Units: Score on the scale				
arithmetic mean (confidence interval 95%)				
From 0 to 6 hours	13.1 (11.9 to 14.3)	12.8 (11.6 to 14)	4.7 (2.9 to 6.4)	
From 0 to 8 hours	17.4 (15.7 to 19.1)	16.8 (15.1 to 18.5)	6.1 (3.8 to 8.5)	
From 0 to 12 hours	26.5 (23.9 to 29.2)	26.4 (23.7 to 29)	9.7 (5.9 to 13.5)	
From 0 to 16 hours	35.5 (31.8 to 39.2)	35.8 (32 to 39.5)	13.4 (8.1 to 18.6)	
From 0 to 24 hours	54.5 (48.6 to 60.4)	55.1 (49.2 to 61)	21.8 (13.4 to 30.2)	
From 16 to 24 hours	19 (16.7 to 21.3)	19.4 (17.1 to 21.6)	8.4 (5.2 to 11.6)	

Notes:

[8] - ITT population.

[9] - ITT population.

[10] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Intensity Differences (PIDs) by Time From Initial Dose

End point title	Pain Intensity Differences (PIDs) by Time From Initial Dose

End point description:

Pain intensity was evaluated using a 4-point Categorical Pain Intensity Rating Scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe.

End point type	Secondary

End point timeframe:

At 0, 0.25, 0.5, 0.75, 1, 2, 3, 4 ,5 ,6, 8, 12, 16, 20 and 24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[11]	120[12]	60[13]	
Units: Score on the scale				
arithmetic mean (confidence interval 95%)				
0.25 hours, LS Mean	1.9 (1.8 to 2)	2 (1.9 to 2.1)	2 (1.9 to 2.2)	
0.5 hours, LS Mean	1.7 (1.6 to 1.8)	1.7 (1.6 to 1.8)	1.9 (1.8 to 2.1)	
0.75 hours, LS Mean	1.4 (1.3 to 1.6)	1.5 (1.4 to 1.6)	2 (1.8 to 2.2)	
1 hours, LS Mean	1.2 (1.1 to 1.4)	1.4 (1.3 to 1.5)	2.1 (1.9 to 2.3)	
2 hours, LS Mean	1.2 (1.1 to 1.4)	1.2 (1 to 1.3)	2.3 (2.1 to 2.5)	
3 hours, LS Mean	1.2 (1.1 to 1.4)	1.2 (1 to 1.3)	2.3 (2.1 to 2.6)	
4 hours, LS Mean	1.2 (1 to 1.3)	1.2 (1.1 to 1.4)	2.3 (2.1 to 2.5)	
5 hours, LS Mean	1.3 (1.1 to 1.4)	1.2 (1.1 to 1.4)	2.3 (2.1 to 2.5)	
6 hours, LS Mean	1.3 (1.1 to 1.4)	1.3 (1.1 to 1.4)	2.3 (2.1 to 2.5)	
8 hours, LS Mean	1.3 (1.2 to 1.5)	1.4 (1.2 to 1.6)	2.3 (2.1 to 2.6)	
12 hours, LS Mean	1.2 (1 to 1.4)	1.2 (1 to 1.3)	2.2 (2 to 2.5)	
16 hours, LS Mean	1.2 (1 to 1.4)	1.2 (1 to 1.4)	2.2 (1.9 to 2.5)	
20 hours, LS Mean	1.2 (1 to 1.4)	1.1 (1 to 1.3)	2.2 (1.9 to 2.5)	
24 hours, LS Mean	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)	2.1 (1.8 to 2.3)	

Notes:

[11] - ITT population.

[12] - ITT population.

[13] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Relief From Initial Dose

End point title	Pain Relief From Initial Dose

End point description:

Pain relief was evaluated using the 5-point overall pain relief scale: 0 = No relief, 1 = A little relief, 2 = Some relief, 3 = A lot of relief, 4 = Complete relief.
LS Mean=Least squares mean.

End point type	Secondary

End point timeframe:

At 0.25, 0.5, 0.75, 1, 2, 3, 4 ,5 ,6, 8, 12, 16, 20 and 24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[14]	120[15]	60[16]	
Units: Score on the scale				
arithmetic mean (standard deviation)				
0.25 hours	0.9 (± 0.96)	0.8 (± 0.92)	0.6 (± 0.75)	
0.5 hours	1.5 (± 1.08)	1.3 (± 1.02)	0.8 (± 0.94)	

0.75 hours	2 (± 1.21)	1.7 (± 1.14)	0.9 (± 0.96)	
1 hour	2.2 (± 1.29)	2 (± 1.17)	0.9 (± 1.02)	
2 hours	2.3 (± 1.3)	2.3 (± 1.29)	0.8 (± 1.02)	
3 hours	2.3 (± 1.33)	2.4 (± 1.39)	0.7 (± 1.03)	
4 hours	2.4 (± 1.41)	2.2 (± 1.43)	0.9 (± 1.2)	
5 hours	2.3 (± 1.35)	2.2 (± 1.49)	0.9 (± 1.23)	
6 hours	2.2 (± 1.37)	2.2 (± 1.53)	0.8 (± 1.28)	
8 hours	2.1 (± 1.4)	2 (± 1.5)	0.8 (± 1.23)	
12 hours	2.3 (± 1.51)	2.4 (± 1.57)	0.9 (± 1.46)	
16 hours	2.2 (± 1.52)	2.3 (± 1.61)	1 (± 1.47)	
20 hours	2.3 (± 1.58)	2.3 (± 1.63)	1 (± 1.5)	
24 hours	2.4 (± 1.63)	2.5 (± 1.68)	1.2 (± 1.73)	

Notes:

[14] - ITT population.

[15] - ITT population.

[16] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to First Intake of Rescue Medication

End point title	Median Time to First Intake of Rescue Medication

End point description:

Time to first use of rescue medication was estimated using Kaplan-Meier method and analyzed by a logrank test stratified by baseline pain intensity. If at least 50% of subjects in a treatment group took rescue medication, the median time to first rescue was determined for that treatment group.
'99999' indicates that the median time to rescue medication was not computable because less than 50% of the subjects took rescue medication.

End point type	Secondary

End point timeframe:

Up to 24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[17]	120[18]	60[19]	
Units: Hours				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)	2.9 (1 to 12)	

Notes:

[17] - ITT population.

[18] - ITT population.

[19] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Percentage of Subjects Who Took Rescue Medication

End point title	Cumulative Percentage of Subjects Who Took Rescue Medication

End point description:

End point type	Secondary

End point timeframe:

At 0.25, 0.5, 0.75, 1, 2, 3, 4 ,5 ,6, 8, 12, 16, 20 and 24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[20]	120[21]	60[22]	
Units: Percentage of subjects				
number (not applicable)				
0.25 hours	0	0	0	
0.5 hours	0	0	0	
0.75 hours	0	0	0	
1 hour	0	0	0	
2 hours	7.5	7.5	30	
3 hours	12.5	13.3	50	
4 hours	16.7	16.7	55	
5 hours	18.3	20	58.3	
6 hours	20	23.3	60	
8 hours	20.8	25	63.3	
12 hours	22.5	25.8	66.7	
16 hours	25	27.5	66.7	
20 hours	26.7	27.5	66.7	
24 hours	26.7	27.5	66.7	

Notes:

[20] - ITT population.

[21] - ITT population.

[22] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Times the Subjects Took Rescue Medication Over the 24-hour Period

End point title	Number of Times the Subjects Took Rescue Medication Over the 24-hour Period

End point description:

End point type	Secondary

End point timeframe:

24 hours postdose

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[23]	120[24]	60[25]	
Units: Rescue medication intakes				
arithmetic mean (standard deviation)	0.5 (± 0.86)	0.6 (± 1.02)	1.4 (± 1.2)	

Notes:

[23] - ITT population.

[24] - ITT population.

[25] - ITT population.

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of the Investigational Product as a Pain Reliever

End point title	Global Assessment of the Investigational Product as a Pain Reliever

End point description:

Global assessment of investigational product as a pain reliever was rated on a 5-point categorical scale: 0 = poor, 1 = fair, 2 = good, 3 = very good, 4 = excellent.

End point type	Secondary

End point timeframe:

24 hours postdose or immediately before the first intake of rescue medication

End point values	Naproxen Sodium ER (BAYH6689)	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120[26]	120[27]	60[28]	
Units: subjects				
number (not applicable)				
0 - Poor	16	18	34	
1 - Fair	14	12	5	
2 - Good	22	20	5	
3 - Very good	33	43	12	
4 - Excellent	35	27	4	

Notes:

[26] - ITT population.

[27] - ITT population.

[28] - ITT population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded throughout the treatment period through 5 days after investigational products administration. All serious adverse events were collected through about 30 days after the last dose of investigational product or placebo.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Naproxen Sodium IR (Aleve, BAYH6689)

Reporting group description:

1 matching tablet of IR 220 mg, 1 tablet of IR 220 mg, and 1 tablet of IR 220 mg at hours 0, 8, and 16 (± 15 minutes), respectively.

Reporting group title	Placebo

Reporting group description:

1 matching tablet of placebo, 1 tablet of placebo, and 1 tablet of placebo at hours 0, 8, and 16 (± 15 minutes), respectively.

Reporting group title	Naproxen Sodium ER (BAYH6689)

Reporting group description:

1 matching tablet of ER 660 mg, 1 tablet of placebo, and 1 tablet of placebo at hours 0, 8, and 16 (± 15 minutes), respectively.

Serious adverse events	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	Naproxen Sodium ER (BAYH6689)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	0 / 120 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Naproxen Sodium IR (Aleve, BAYH6689)	Placebo	Naproxen Sodium ER (BAYH6689)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 120 (28.33%)	23 / 60 (38.33%)	27 / 120 (22.50%)
Injury, poisoning and procedural complications			
Operative haemorrhage			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Nervous system disorders			

Dizziness			
subjects affected / exposed	6 / 120 (5.00%)	2 / 60 (3.33%)	2 / 120 (1.67%)
occurrences (all)	6	3	3
Headache			
subjects affected / exposed	13 / 120 (10.83%)	12 / 60 (20.00%)	11 / 120 (9.17%)
occurrences (all)	13	12	11
Hypoaesthesia			
subjects affected / exposed	4 / 120 (3.33%)	3 / 60 (5.00%)	2 / 120 (1.67%)
occurrences (all)	4	3	2
Paraesthesia			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	2 / 120 (1.67%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Tenderness			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 120 (1.67%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	1	0	1
Dental discomfort			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	9 / 120 (7.50%)	8 / 60 (13.33%)	10 / 120 (8.33%)
occurrences (all)	9	8	10
Paraesthesia oral			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	3 / 120 (2.50%)	2 / 60 (3.33%)	4 / 120 (3.33%)
occurrences (all)	3	2	4
Reproductive system and breast disorders			
Vulvovaginal pruritus			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	3 / 120 (2.50%)	2 / 60 (3.33%)	1 / 120 (0.83%)
occurrences (all)	3	2	1
Epistaxis			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 120 (0.00%)	2 / 60 (3.33%)	1 / 120 (0.83%)
occurrences (all)	0	2	1
Nasal congestion			

subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	1	0	1
Urticaria			
subjects affected / exposed	1 / 120 (0.83%)	0 / 60 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 120 (0.00%)	0 / 60 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Muscle twitching			
subjects affected / exposed	0 / 120 (0.00%)	1 / 60 (1.67%)	0 / 120 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported