Clinical trial results:
An Open Label, Actual Use Study in Consumers Taking an Extended-Release Over-the-Counter NSAID in a Naturalistic Setting

Summary

EudraCT number	2014-005268-13
Trial protocol	Outside EU/EEA
Global end of trial date	14 November 2008

Results information

Result version number	v2 (current)
This version publication date	07 September 2016
First version publication date	15 July 2015
Version creation reason	• New data added to full data set Bayer sponsor contact information to be updated

Trial information

Trial identification

Sponsor protocol code	BAYH6689/13129

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00751400
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 November 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess subjects' patterns of use of the extended release (ER) naproxen sodium product.

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 and/or their legally authorized representative 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	31 July 2008
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: 562
Worldwide total number of subjects	562
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)	2
Adults (18-64 years)	444
From 65 to 84 years	109

85 years and over	7

Subject disposition

Recruitment

Recruitment details:

Recruitment for the study was conducted using newspaper ads, direct mailing, in-store pharmacy posters, and flyers. Potential subjects who learned about the study through local advertising were directed to call a toll-free number (call center at the contract research organization [CRO]) where minimal screening questions were asked.

Pre-assignment

Screening details:

Once at the pharmacy, if the screening criteria were met, subjects were given an (empty) over-the-counter (OTC) package and were allowed as much time as needed to review the label. They were then told the cost of the investigational product and asked if they would like to purchase it for their own use.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Naproxen Sodium ER (BAYH6689)

Arm description:

Subjects received 1 tablet of naproxen sodium ER every 24 hours while symptoms lasted for no more than 10 consecutive days for pain and no more than 3 consecutive days for fever.

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:

Subjects received 1 tablet of naproxen sodium ER every 24 hours while symptoms lasted for no more than 10 consecutive days for pain and no more than 3 consecutive days for fever.

Number of subjects in period 1	Naproxen Sodium ER (BAYH6689)
Started	497
Subjects Provided Drug	497
Subjects Consumed Drug	485 [1]
Subjects Provided Detailed Use Data	467 [2]
Completed	487
Not completed	10
Lost to follow-up	10

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: A few subjects had used product outside of both 5-day interview windows but considered

as study completers (subjects who completed at least 1 interview), as planned. Hence, the number of subjects at this milestone differs with the number of subjects in the arm.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: A few subjects did not use study product but considered as study completers (subjects who completed at least 1 interview), as planned. Hence, the number of subjects at this milestone differs with the number of subjects in the arm.

Baseline characteristics

Reporting groups[1]	
Reporting group title	Naproxen Sodium ER (BAYH6689)

Reporting group description:

Subjects received 1 tablet of naproxen sodium ER every 24 hours while symptoms lasted for no more than 10 consecutive days for pain and no more than 3 consecutive days for fever.

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: Not all the enrolled subjects were provided with study drugs. As baseline included only subjects who were provided with the study drug, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period.

Reporting group values	Naproxen Sodium ER (BAYH6689)	Total	
Number of subjects	497	497	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.8		
standard deviation	± 15.1	-	
Gender categorical Units: subjects			
Male	205	205	
Female	292	292	
Education Units: Subjects			
8th grade or less	6	6	
Some high school	21	21	
High school graduate, GED, or certificate	119	119	
Some college or technical school	185	185	
College graduate	117	117	
Post-graduate degree	49	49	
Missing	0	0	
Literacy			
Rapid Estimate of Adult Literacy in Medicine (REALM) scores ranged from 0-66 (single scale): a score of 61 or greater is considered normal literacy; a score of 60 or less is considered low literacy.			
Units: Subjects			
Normal	437	437	
Low	56	56	
No REALM Score	4	4	
Prior Analgesic Use			
Heavy analgesic user: 30 or more doses of OTC analgesics per month (self reported based on categorical responses). Regular analgesic user: 5 to 29 doses of OTC analgesics per month (self reported based on categorical responses).			
Units: Subjects			
Heavy	148	148	
Regular	349	349	
Race Units: Subjects			

White	399	399	
Black	56	56	
Hispanic	3	3	
Asian	8	8	
Other	31	31	
Missing	0	0	

End points

End points reporting groups

Reporting group title	Naproxen Sodium ER (BAYH6689)

Reporting group description:

Subjects received 1 tablet of naproxen sodium ER every 24 hours while symptoms lasted for no more than 10 consecutive days for pain and no more than 3 consecutive days for fever.

Primary: Use Days With One or More Misuse Occasions

End point title	Use Days With One or More Misuse Occasions[1]

End point description:

Misuse occasion: any reported use of 2 or more tablets within a 22 hour period (included use of 2 tablets in 1 dose or the use of 1 tablet at one time and 1+ tablets at a later time within the same 22 hour period). Use-days were calculated based on days in which there was subject-reported product consumption, meaning that if a tablet was consumed on a day this resulted in 1 use-day. If a subject reported product consumption on 3 different days this resulted in 3 use-days. The cumulative expression of use-days is the total number of use-days reported by all subjects with follow up data. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Primary

End point timeframe:

1 month

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)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: days				
use days without a misuse occasion	2112			
use days with a misuse occasion	294			

Statistical analyses

No statistical analyses for this end point

Secondary: Dosing Occasions With One and More Than One Tablet Taken

End point title	Dosing Occasions With One and More Than One Tablet Taken

End point description:

Dosing occasion means a single occasion in which a subject reported consuming the study drug. Multiple dosing occasions were possible throughout one use-day. For example, if a subject took one tablet at 6 anti-meridian (am), this would result in one dosing occasion. If the same subject took one tablet later that same day at 8 post-meridian (pm), this would result in a second dosing occasion. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: dosing occasions				
number (not applicable)				
only one tablet taken	2500			
more than one tablet taken	66			

Statistical analyses

No statistical analyses for this end point

Secondary: Use Days With and Without Next Dose Less Than 22 Hours Later

End point title	Use Days With and Without Next Dose Less Than 22 Hours Later

End point description:

Use-days were calculated based on days in which there was subject-reported product consumption, meaning that if a tablet was consumed on a day this resulted in one use-day. If a subject reported product consumption on three different days this resulted in three use-days. The cumulative expression of use-days is the total number of use-days reported by all subjects with follow up data. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: days				
number (not applicable)				
no dose less than 22 hours later	2175			
at least one dose less than 22 hours later	231			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With and Without More Than One Tablet Taken Per Dose

End point title	Number of Subjects With and Without More Than One Tablet Taken Per Dose

End point description:

Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: subjects				
never took more than one tablet per dose	440			
took more than one tablet per dose	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With and Without Next Dose Less Than 22 Hours Later

End point title	Number of Subjects With and Without Next Dose Less Than 22 Hours Later

End point description:

This endpoint is a measure of subjects while endpoint titled "Use Days With and Without Next Dose Less Than 22 Hours Later" provides the outcome as a measure of cumulative number of use-days for all subjects involved. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: subjects				
no doses less than 22 hours later	359			
at least one dose less than 22 hours later	108			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With and Without More Than 660 milligram (mg) at Least Once

End point title	Number of Subjects With and Without More Than 660 milligram (mg) at Least Once

End point description:

This measure refers to number of subjects that exceeded 660 mg of naproxen sodium per day at least once during the reporting period. The maximum dose (660 mg) may have been exceeded with one dose (if a subject consumed two tablets in one dosing occasion) or may have been exceeded throughout the course of a use-day (if a subject took one tablet in one dosing occasion and then later in the same day took one or more tablets in another dosing occasion). Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: subjects				
not more than 660 mg	344			
more than 660 mg at least once	123			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Daily Dose

End point title	Average Daily Dose

End point description:

Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: milligram (mg)				
arithmetic mean (standard deviation)	722 (± 233.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects That Have Taken Study Drug on More Than 10 Consecutive Days and Not on More Than 10 Consecutive Days

End point title	Number of Subjects That Have Taken Study Drug on More Than 10 Consecutive Days and Not on More Than 10 Consecutive Days

End point description:

This endpoint is reporting how many subjects exceeded the label limit for consecutive days of study drug dosing. Here, "Number of subjects analysed" reflects number of subjects reporting at least one tablet taken at any point during study.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	485			
Units: subjects				
not more than 10 consecutive days	376			
more than 10 consecutive days	109			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Total Dosing Occasions Per Subject

End point title	Number of Total Dosing Occasions Per Subject

End point description:

Dosing occasion means a single occasion in which a subject reported consuming the study drug. Multiple dosing occasions were possible throughout one use-day. For example, if a subject took one tablet at 6 am this would result in one dosing occasion. If the same subject took one tablet later that same day at 8 pm this would result in a second dosing occasion. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: dosing occasions				
arithmetic mean (standard deviation)	5.5 (± 3.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Dosing Occasions Per Subject That Exceeded 660 milligram (mg)

End point title	Number of Dosing Occasions Per Subject That Exceeded 660 milligram (mg)

End point description:

Dosing occasion means a single occasion in which a subject reported consuming the study drug. Multiple dosing occasions were possible throughout one use-day. For example, if a subject took one tablet at 6 am this would result in one dosing occasion. If the same subject took one tablet later that same day at 8 pm this would result in a second dosing occasion. Here, "Number of subjects analysed" reflects subjects that completed at least one interview and provided use information for the previous 5 days.

End point type	Secondary

End point timeframe:

1 month

End point values	Naproxen Sodium ER (BAYH6689)			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: dosing occasions				
arithmetic mean (standard deviation)	0.6 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the date of informed consent signed until the end of 28-day follow-up period	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	Naproxen Sodium ER (BAYH6689)

Reporting group description:

Single dose (1 tablet) of naproxen sodium ER 660 mg every 24 hours while symptoms lasted for not more than 10 consecutive days for pain and not more than 3 consecutive days for fever.

Serious adverse events	Naproxen Sodium ER (BAYH6689)		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 485 (0.62%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Naproxen Sodium ER (BAYH6689)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 485 (23.09%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Irritability			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Sluggishness			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Seasonal allergy			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Cough			

subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 485 (0.62%)		
occurrences (all)	5		
Abnormal dreams			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Investigations			
Blood iron decreased			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Ankle fracture			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Feeding tube complication			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	3		
Hand fracture			

subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Foreign body in eye			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Tooth fracture			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Wrist fracture			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	3		
Syncope			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	10 / 485 (2.06%)		
occurrences (all)	10		
Migraine			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Eye disorders			
Eye disorder			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	6 / 485 (1.24%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	7 / 485 (1.44%)		
occurrences (all)	7		
Dental discomfort			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	7 / 485 (1.44%)		
occurrences (all)	8		
Dyspepsia			
subjects affected / exposed	10 / 485 (2.06%)		
occurrences (all)	12		
Flatulence			
subjects affected / exposed	4 / 485 (0.82%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	8 / 485 (1.65%)		
occurrences (all)	8		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Stomach discomfort			

subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Oesophagitis			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 485 (1.03%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	4 / 485 (0.82%)		
occurrences (all)	5		
Muscle spasms			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Musculoskeletal pain			

subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	6 / 485 (1.24%)		
occurrences (all)	6		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Gingival infection			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	4 / 485 (0.82%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	2 / 485 (0.41%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 485 (0.21%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	4 / 485 (0.82%)		
occurrences (all)	4		

Sinusitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 3 / 485 (0.62%) 3 2 / 485 (0.41%) 2		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	 2 / 485 (0.41%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 June 2008	The protocol was amended to reflect changes requested by the Food and Drug Administration (FDA). 1. Dose of 440 mg was administered within the first hour 2. Clarified details about periodic follow-up interviews 3. Moderate OTC analgesic users had self-reported taking at least 5 doses per month 4. Study was conducted in 3 parts: screening, enrolment and use phase, and clarifications were provided on these phases 5. Tracking of recruitment was briefly explained 6. Subjects who had inquired about the study were excluded in the enrolment phase if they had participated in an OTC analgesic-related study in the last 12 months, healthcare and related professionals, history of known allergies to non-steroidal antiinflammatory drugs, heart surgery in the last 60 days or plans for it in the next 60 days, female pregnant or breast-feeding 7. Eligibility screener period was included as an assessment period 8. The primary endpoint was updated as the proportion of the total number of use days with a misuse occasion among all use-days in the User population. A cut point of 22 hours had been established in order to account for some variability in the reporting of exact dosing timing by subjects during follow-up interviews. 9. The following secondary endpoints were included: a) average daily dose of naproxen on use days in the user population; b) number/percentage of subjects in the safety population who took Aleve 24 Hour more than 10 consecutive days; c) total number of dosing occasions during use days per subject among the user population. All analyses were performed for the heavy, regular, normal and low literate use cohorts.
17 June 2008	The following statement was included under phone eligibility screener section: "The purpose of this study was to collect information about how an investigational dose of an approved medication was used by consumers".
02 July 2008	The drug label was updated with revised expiry date and a statement that product might take longer to work if taken with food.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

No control group, detailed data collected for up to 10 days during 1 month follow-up, data recall by subjects may vary.

Notes: