Clinical trial results:
A SINGLE-DOSE, RANDOMIZED, TWO-PERIOD, CROSSOVER STUDY TO ASSESS BIOEQUIVALENCE BETWEEN TWO IBUPROFEN 200 MG TABLET FORMULATIONS, IN HEALTHY ADULTS

Summary

EudraCT number	2013-001442-34
Trial protocol	SE
Global end of trial date	24 September 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	03 August 2015

Trial information

Trial identification

Sponsor protocol code	IBUPAI0002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	McNeil AB
Sponsor organisation address	Box 941, Norrbroplatsen 2, Helsingborg, Sweden, SE-251 09
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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	31 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 September 2013
Global end of trial reached?	Yes
Global end of trial date	24 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to show bioequivalence between Ipren film coated tablet 200 mg and Brufen film coated tablet 200 mg, with respect to the single-dose pharmacokinetics of S-(+) ibuprofen. The maximum observed plasma concentrations (Cmax), and the areas under the concentration-vs.-time curve until last measurable concentration (AUCt), were compared to assess bioequivalence.

Protection of trial subjects:

Ethical Conduct of the Study

This study was conducted in accordance with the final protocol and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, including ICH E6. In addition, all local regulatory requirements and laws were followed.

Subject Information and Consent

Written informed consent was obtained before initiation of any protocol-specified activities. The investigator explained the nature, purpose, and possible risks associated with study participation to each subject. Each subject was informed that he/she could withdraw from the study at any time and for any reason. Each subject was given sufficient time to consider the implications of the study before deciding whether to participate. Subjects who chose to participate signed an informed consent document.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 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	Sweden: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 41 subjects screened for entry into the study, 30 healthy subjects were randomized to treatment. After randomization one subject withdrew his consent. Accordingly 29 subjects completed both treatments in the study.

Period 1

Period 1 title	Treatment Period 1 (24 hours)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Sequence 1: Ipren followed by Brufen

Arm description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Arm title	Sequence 2: Brufen followed by Ipren

Arm description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Number of subjects in period 1	Sequence 1: Ipren followed by Brufen	Sequence 2: Brufen followed by Ipren
Started	15	15
Completed	15	15

Period 2

Period 2 title	Washout (48 hours)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Sequence 1: Ipren followed by Brufen

Arm description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Arm title	Sequence 2: Brufen followed by Ipren

Arm description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Number of subjects in period 2	Sequence 1: Ipren followed by Brufen	Sequence 2: Brufen followed by Ipren
Started	15	15
Completed	15	14
Not completed	0	1
Consent withdrawn by subject	-	1

Period 3

Period 3 title	Treatment Period 2 (24 hours)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Sequence 1: Ipren followed by Brufen

Arm description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Arm title	Sequence 2: Brufen followed by Ipren

Arm description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Arm type	Experimental
Investigational medicinal product name	Ipren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Ipren 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Investigational medicinal product name	Brufen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received Brufen 200 milligram (mg) tablet orally once daily on day 1 of each treatment period.

Number of subjects in period 3	Sequence 1: Ipren followed by Brufen	Sequence 2: Brufen followed by Ipren
Started	15	14
Completed	15	14

Baseline characteristics

Reporting groups	
Reporting group title	Sequence 1: Ipren followed by Brufen
Reporting group description:	
Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.	
Reporting group title	Sequence 2: Brufen followed by Ipren
Reporting group description:	
Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.	

Reporting group values	Sequence 1: Ipren followed by Brufen	Sequence 2: Brufen followed by Ipren	Total
Number of subjects	15	15	30
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	15	30
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	29	27.3	
standard deviation	± 9.47	± 6.71	-
Title for Gender Units: subjects			
Female	5	7	12
Male	10	8	18

End points

End points reporting groups

Reporting group title	Sequence 1: Ipren followed by Brufen

Reporting group description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Reporting group title	Sequence 2: Brufen followed by Ipren

Reporting group description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Reporting group title	Sequence 1: Ipren followed by Brufen

Reporting group description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Reporting group title	Sequence 2: Brufen followed by Ipren

Reporting group description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Reporting group title	Sequence 1: Ipren followed by Brufen

Reporting group description:

Participants received Ipren in Treatment Period 1 and Brufen in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Reporting group title	Sequence 2: Brufen followed by Ipren

Reporting group description:

Participants received Brufen in Treatment Period 1 and Ipren in Treatment Period 2. The washout period between the 24 hours treatment periods was at least 48 hours.

Subject analysis set title	Ipren
Subject analysis set type	Full analysis

Subject analysis set description:

This study was an open, single-dose, randomized, two-way cross-over study.Thirty (30) healthy male and female volunteers, aged between 18 and 50 years, inclusive, were included. Single doses of Ipren film coated tablet 200 mg and Brufen film coated tablet 200 mg were administered in a standardized mode, on two separated treatment visits. A washout period of at least 48 hours separated the treatments. After an overnight fast at the clinic, drug administration was started at about 8 am.

Subject analysis set title	Brufen
Subject analysis set type	Full analysis

Subject analysis set description:

This study was an open, single-dose, randomized, two-way cross-over study.Thirty (30) healthy male and female volunteers, aged between 18 and 50 years, inclusive, were included. Single doses of Ipren film coated tablet 200 mg and Brufen film coated tablet 200 mg were administered in a standardized mode, on two separated treatment visits. A washout period of at least 48 hours separated the treatments. After an overnight fast at the clinic, drug administration was started at about 8 am.

Primary: Maximal Observed Plasma Concentration (Cmax) of S-(+) Ibuprofen

End point title	Maximal Observed Plasma Concentration (Cmax) of S-(+) Ibuprofen

End point description:

The Cmax is the maximum observed plasma concentration.

End point type	Primary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: microgram(s)/millilitre (ug/mL)				
arithmetic mean (standard deviation)	7.87 (± 1.83)	9.8 (± 2.22)		

Statistical analyses

Statistical analysis title	Cmax of S-(+) Ibuprofen comparison vs. Brufen

Statistical analysis description:

Point and interval estimates are based on a linear model for ln-transformed Cmax data. Statistical model included covariate adjustments for period and sequence, and subject, nested within sequence as fixed effects. Number of subjects included in the cross-over analysis were 28.

Comparison groups	Ipren v Brufen
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	> 0.05 [2]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.233
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.302
upper limit	-0.164
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[1] - For bioequivalence the 90% CI for the treatment difference (ln-scale), Ipren vs. Brufen, had to be contained in the interval from -0.223 to 0.223.
[2] - Exact value not calculated. Inference based on 90% confidence interval.

Primary: Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Until the Time of the Last Measurable Plasma Concentration (AUCt) of S-(+) Ibuprofen

End point title	Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Until the Time of the Last Measurable Plasma Concentration (AUCt) of S-(+) Ibuprofen

End point description:

The AUCt is the area under the plasma concentration-time curve from time zero to until the last measurable plasma concentration 't'.

End point type	Primary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: microgram/milliliter x hour (ug/mL x h)				
arithmetic mean (standard deviation)	37.67 (± 9.06)	37.98 (± 10.03)		

Statistical analyses

Statistical analysis title	AUCt of S-(+) Ibuprofen comparison vs. Brufen

Statistical analysis description:

Point and interval estimates are based on a linear model for ln-transformed AUCt data. Statistical model included covariate adjustments for period and sequence, and subject, nested within sequence as fixed effects. Number of subjects included in the cross-over analysis were 28.

Comparison groups	Ipren v Brufen
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence[3]
P-value	< 0.05 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.018
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.067
upper limit	0.031
Variability estimate	Standard error of the mean
Dispersion value	0.029

Notes:

[3] - For bioequivalence the 90% CI for the treatment difference (ln-scale), Ipren vs. Brufen, had to be contained in the interval from -0.223 to 0.223.
[4] - Exact value not calculated. Inference based on 90% confidence interval.

Secondary: Maximal Observed Plasma Concentration (Cmax) of R-(-) Ibuprofen and Total Ibuprofen

End point title	Maximal Observed Plasma Concentration (Cmax) of R-(-) Ibuprofen and Total Ibuprofen

End point description:

The Cmax is the maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: microgram/milliliter (ug/mL)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	7.97 (± 2.46)	9.67 (± 2.27)		
Total ibuprofen	15.78 (± 4.04)	19.36 (± 4.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Until the Time of the Last Measurable Plasma Concentration (AUCt) of R-(-) Ibuprofen and Total Ibuprofen

End point title	Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Until the Time of the Last Measurable Plasma Concentration (AUCt) of R-(-) Ibuprofen and Total Ibuprofen

End point description:

The AUCt is the area under the plasma concentration-time curve from time zero to until the last measurable plasma concentration 't'.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: microgram/milliliter x hour (ug/mL x h)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	27.18 (± 7.71)	27.77 (± 6.74)		
Total ibuprofen	65 (± 14.31)	65.66 (± 13.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUCinfinity) for S-(+) Ibuprofen

End point title	Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUCinfinity) for S-(+) Ibuprofen

End point description:

The AUCinfinity is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: microgram/milliliter x hour (ug/mL x h)				
arithmetic mean (standard deviation)	40.27 (± 10.54)	40.12 (± 11.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUCinfinity) for R-(-) Ibuprofen and Total Ibuprofen

End point title	Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUCinfinity) for R-(-) Ibuprofen and Total Ibuprofen

End point description:

The AUCinfinity is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: microgram/milliliter x hour (ug/mL x h)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	27.59 (± 7.75)	28.2 (± 6.75)		
Total ibuprofen	67.66 (± 15.4)	67.8 (± 14.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Extrapolated Part of Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUC[infinity,ex]) for S-(+) Ibuprofen

End point title	Extrapolated Part of Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUC[infinity,ex]) for S-(+) Ibuprofen

End point description:

The AUC[infinity,ex] is calculated by dividing the difference of AUC(0-infinity) and AUC(0-last) by AUC(0-infinity), (AUC[0-infinity] - AUC[0-last])/AUC[0-infinity].

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: percentage (%)				
arithmetic mean (standard deviation)	6 (± 3.5)	5.1 (± 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Extrapolated Part of Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUC[infinity,ex]) for R-(-) Ibuprofen and Total Ibuprofen

End point title	Extrapolated Part of Area Under the Plasma Concentration Versus Time Curve from Start of Drug Administration Extrapolated to Infinity (AUC[infinity,ex]) for R-(-) Ibuprofen and Total Ibuprofen

End point description:

The AUC[infinity,ex] is calculated by dividing the difference of AUC(0-infinity) and AUC(0-last) by AUC(0-infinity), (AUC[0-infinity] - AUC[0-last])/AUC[0-infinity].

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: percentage (%)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	1.6 (± 1)	1.6 (± 1.1)		
Total ibuprofen	3.7 (± 2.4)	3 (± 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time at Which Maximal Plasma Concentration is Observed (Tmax) for S-(+) Ibuprofen

End point title	Time at Which Maximal Plasma Concentration is Observed (Tmax) for S-(+) Ibuprofen

End point description:

The Tmax is defined as actual sampling time to reach maximum observed S-(+) Ibuprofen concentration.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: hours (h)				
median (full range (min-max))	2.5 (1.17 to 4)	1.33 (0.83 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time at Which Maximal Plasma Concentration is Observed (Tmax) for R-(-) Ibuprofen and Total Ibuprofen

End point title	Time at Which Maximal Plasma Concentration is Observed (Tmax) for R-(-) Ibuprofen and Total Ibuprofen

End point description:

The Tmax is defined as actual sampling time to reach maximum observed R-(-) Ibuprofen and Total Ibuprofen concentration.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: hours (h)				
median (full range (min-max))				
R-(-) ibuprofen	2.5 (1.17 to 4)	1.25 (0.83 to 4)		
Total ibuprofen	2.5 (1.17 to 4)	1.25 (0.83 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half Life (t1/2) of S-(+) Ibuprofen

End point title	Terminal Half Life (t1/2) of S-(+) Ibuprofen

End point description:

The elimination half-life (t1/2) is the time measured for the plasma concentration to decrease by 1 half to its original concentration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z).

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: hours (h)				
arithmetic mean (standard deviation)	2.47 (± 0.51)	2.44 (± 0.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half Life (t1/2) of R-(-) Ibuprofen and Total Ibuprofen

End point title	Terminal Half Life (t1/2) of R-(-) Ibuprofen and Total Ibuprofen

End point description:

The elimination half-life (t1/2) is the time measured for the plasma concentration to decrease by 1 half to its original concentration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z).

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: hours (h)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	1.61 (± 0.38)	1.6 (± 0.39)		
Total ibuprofen	2.22 (± 0.43)	2.12 (± 0.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Residence Time (MRT) for S-(+) Ibuprofen

End point title	Mean Residence Time (MRT) for S-(+) Ibuprofen

End point description:

The Mean Residence Time (MRT) is the average time at which the number of absorbed molecules reside in the body, after single-dose administration, and calculated as area under the first moment curve AUMC (0-infinity)/Area Under the Plasma Concentration-Time Curve AUC (0-infinity), where AUMC (0-infinity) is area under the plasma concentration-time first moment curve from time zero to infinite time and AUC (0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: hours (h)				
arithmetic mean (standard deviation)	5.23 (± 0.98)	4.58 (± 0.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Residence Time (MRT) for R-(-) Ibuprofen and Total Ibuprofen

End point title	Mean Residence Time (MRT) for R-(-) Ibuprofen and Total Ibuprofen

End point description:

The Mean Residence Time (MRT) is the average time at which the number of absorbed molecules reside in the body, after single-dose administration, and calculated as area under the first moment curve AUMC (0-infinity)/Area Under the Plasma Concentration-Time Curve AUC (0-infinity), where AUMC (0-infinity) is area under the plasma concentration-time first moment curve from time zero to infinite time and AUC (0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: hours (h)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	3.66 (± 0.66)	3.26 (± 0.72)		
Total ibuprofen	4.57 (± 0.84)	4.01 (± 0.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Rate Constant for S-(+) Ibuprofen

End point title	Terminal Elimination Rate Constant for S-(+) Ibuprofen

End point description:

Lambda(z) is first-order elimination rate constant associated with the terminal portion of the curve, determined as the negative slope of the terminal log-linear phase of the drug concentration-time curve.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	29		
Units: 1/hour (1/h)				
arithmetic mean (standard deviation)	0.29 (± 0.07)	0.29 (± 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Rate Constant for R-(-) Ibuprofen and Total Ibuprofen

End point title	Terminal Elimination Rate Constant for R-(-) Ibuprofen and Total Ibuprofen

End point description:

Lambda(z) is first-order elimination rate constant associated with the terminal portion of the curve, determined as the negative slope of the terminal log-linear phase of the drug concentration-time curve.

End point type	Secondary

End point timeframe:

Pre-dose, 0.25, 0.5, 0.66, 0.83, 1, 1.16, 1.33, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 7, 9 and 12 hours post-dose.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: 1/hour (1/h)				
arithmetic mean (standard deviation)				
R-(-) ibuprofen	0.46 (± 0.13)	0.46 (± 0.1)		
Total ibuprofen	0.32 (± 0.07)	0.34 (± 0.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Occurence of Adverse Events

End point title	Occurence of Adverse Events

End point description:

Serious adverse events required immediate notification within 24 hours to the sponsor or its designated representative beginning from the time that the subject provides informed consent, which was obtained prior to the subject's participation in the clinical study (i.e. prior to undergoing any study-related procedure and/or receiving investigational product), through and
including 30 calendar days after the last administration of the investigational product. Any serious adverse event occurring any time after the reporting period was to be promptly reported if a causal relationship to investigational product was suspected.
Adverse events (serious and non-serious) were recorded on the CRF from the time the subjects had taken at least one dose of study treatment through last subject visit.

End point type	Secondary

End point timeframe:

Serious adverse events require notification within 24 hours to the sponsor or its designated representative beginning from the time that the subject provides informed consent, through and including 30 calendar days after the last administration.

End point values	Ipren	Brufen		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	30		
Units: Number of Adverse Events				
Serious adverse events	0	0		
Non serious adverse events	6	11		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events required notification within 24 hours to the sponsor or its designated representative beginning from the time that the subject provides informed consent, through and including 30 calendar days after the last administration.

Adverse event reporting additional description:

The investigator obtained and recorded on the eCRF/CRF all observed or volunteered adverse events. For all adverse events, the investigator pursued and obtained information adequate to determine both the outcome of the adverse event and whether it met the criteria for classification as a serious adverse event.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Brufen

Reporting group description:

Ibuprofen (Brufen) Film Coated Tablet 200 mg

Reporting group title	Ipren

Reporting group description:

Ibuprofen (Ipren) Film Coated Tablet 200 mg

Serious adverse events	Brufen	Ipren	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Brufen	Ipren	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 30 (30.00%)	6 / 29 (20.69%)	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 30 (23.33%)	6 / 29 (20.69%)	
occurrences (all)	7	6	
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 29 (0.00%) 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