



## Clinical trial results:

**Randomised, Double Dummy, Placebo Controlled, Multicentre, Parallel-Group, Single Dose Study to Compare the Analgesic Efficacy and Safety of IBALGIN Extra Fast /ibuprofen lysin/ to conventional Ibuprofen in the Treatment of Acute Pain**

### Summary

EudraCT number	2006-006942-33
Trial protocol	CZ
Global end of trial date	13 March 2008

### Results information

Result version number	v1 (current)
This version publication date	14 July 2016
First version publication date	14 July 2016

### Trial information

#### Trial identification

Sponsor protocol code	13/06/IBL/TP3
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Zentiva k.s
Sponsor organisation address	U kabelovny 130 , Praha 10 - Dolní Měcholupy, Czech Republic, 102 37
Public contact	MUDr. Tomas Hauser, Zentiva k.s, 00420 267243451, Tomas.Hauser@sanofi.com
Scientific contact	MUDr. Tomas Hauser, Zentiva k.s, 00420 267243451, Tomas.Hauser@sanofi.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	13 March 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 March 2008
Global end of trial reached?	Yes
Global end of trial date	13 March 2008
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that:

1. Ibalgin Extra Fast® is superior over placebo in overall analgesic efficacy.

This conclusion will be drawn if and only if the lower limit of the two-sided 95% confidence interval for the treatment difference (test-placebo) in TOTPAR is greater than zero.

2. Ibalgin Extra Fast® is non-inferior to Nurofen forte® (the active comparator) in overall analgesic efficacy.

This conclusion will be drawn if and only if 1. is concluded and two-sided 95% confidence interval for the treatment difference (test-active comparator) in TOTPAR lies entirely to the right of the non-inferiority margin.

3. Ibalgin Extra Fast® is superior over Nurofen forte® (the active comparator) in the onset of action.

This conclusion will be drawn if and only if 2. is concluded and the lower limit of the two-sided 95% confidence interval for the treatment difference (test-active comparator) in PAR45 is greater than zero.

Protection of trial subjects:

No specific measurements required

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	25 May 2007
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	Czech Republic: 351
Worldwide total number of subjects	351
EEA total number of subjects	351

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)	349
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

25 May 2007

Nine centres

### Pre-assignment

Screening details:

Subject indicated for outpatient surgical removal of one or more third molars, at least one of which is impacted in bone. inclusion/exclusion criteria check-list, medical history/ physical examination, laboratory examination: clinical chemistry, urinalysis, haematology, serology

### Period 1

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

Blinding implementation details:

A double-dummy technique was used due to the differences between IBALGIN Extra fast(R) and Nurofen forte(R). The medication was administered by study nurse.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	IBALGIN Extra Fast(R)

Arm description:

This arm includes subjects receiving the IBALGIN Extra Fast(R) medication

Arm type	Experimental
Investigational medicinal product name	IBALGIN Extra Fast
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg of ibuprofen as lysine salt, oral administration

<b>Arm title</b>	NUROFEN FORTE(R)
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Arm description:

This arm includes patient receiving NUROFEN FORTE(R) as a medication.

Arm type	Active comparator
Investigational medicinal product name	NUROFEN FORTE(R)
Investigational medicinal product code	NA
Other name	NA
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg of ibuprofen, oral administration

<b>Arm title</b>	Placebo
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Arm description:

This arm includes patients receiving placebo.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

0 mg of ibuprofen, oral administration

<b>Number of subjects in period 1</b>	IBALGIN Extra Fast(R)	NUROFEN FORTE(R)	Placebo
Started	141	139	71
Completed	141	139	71

## Baseline characteristics

### Reporting groups

Reporting group title	IBALGIN Extra Fast(R)
Reporting group description:	
This arm includes subjects receiving the IBALGIN Extra Fast(R) medication	
Reporting group title	NUROFEN FORTE(R)
Reporting group description:	
This arm includes patient receiving NUROFEN FORTE(R) as a medication.	
Reporting group title	Placebo
Reporting group description:	
This arm includes patients receiving placebo.	

Reporting group values	IBALGIN Extra Fast(R)	NUROFEN FORTE(R)	Placebo
Number of subjects	141	139	71
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	141	138	70
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	28.7	28.5	27.5
standard deviation	± 7.5	± 8.2	± 7.9
Gender categorical			
Units: Subjects			
Female	83	87	40
Male	58	52	31

Reporting group values	Total		
Number of subjects	351		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	349		

From 65-84 years	0		
85 years and over	0		

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	210		
Male	141		

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### Subject analysis sets

Subject analysis set title	Subject analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects used for analysis of data from both study periods.

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Reporting group values	Subject analysis set		
Number of subjects	351		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	349		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	28.2 ± 7.9		
Gender categorical Units: Subjects			
Female	210		
Male	141		

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## End points

### End points reporting groups

Reporting group title	IBALGIN Extra Fast(R)
Reporting group description: This arm includes subjects receiving the IBALGIN Extra Fast(R) medication	
Reporting group title	NUROFEN FORTE(R)
Reporting group description: This arm includes patient receiving NUROFEN FORTE(R) as a medication.	
Reporting group title	Placebo
Reporting group description: This arm includes patients receiving placebo.	
Subject analysis set title	Subject analysis set
Subject analysis set type	Full analysis
Subject analysis set description: Subjects used for analysis of data from both study periods.	

### Primary: TOTPAR6

End point title	TOTPAR6
End point description: Pain relief (PAR) was rated on a standard five-point scale (0-4) using following description: 0 = none 1 = a little 2 = some 3 = a lot 4 = complete Patients recorded their pain relief at regularly sheduled intervals (15, 30, 45, 60, 90 min and 2, 3, 4, 5 and 6 hours) after having taken the study medication. For the purposes of primary objectives, Total Pain Relief at 6 hours (TOTPAR6, calculated as the weighted sum of the pain relief scores at 6 hours) and time specific PAR at 45 min (PAR45) were evaluated based on PAR measurements.	
End point type	Primary
End point timeframe: comparison of data from whole period	

End point values	IBALGIN Extra Fast(R)	NUROFEN FORTE(R)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	141	139	71	
Units: TOTPAR				
arithmetic mean (standard error)	19.57 (± 1.08)	19.96 (± 1.14)	8.27 (± 1.36)	

### Statistical analyses

Statistical analysis title	TOTPAR6 - Ibalgin vs. Nurofen
Comparison groups	IBALGIN Extra Fast(R) v NUROFEN FORTE(R)



Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.74
upper limit	1.96
Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[1] - ANOVA

<b>Statistical analysis title</b>	TOTPAR6 - Ibalgin vs. Placebo
Comparison groups	IBALGIN Extra Fast(R) v Placebo
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority <sup>[2]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.45
upper limit	14.16
Variability estimate	Standard error of the mean
Dispersion value	1.45

Notes:

[2] - ANOVA

<b>Statistical analysis title</b>	TOTPAR6 - Nurofen vs. Placebo
Comparison groups	NUROFEN FORTE(R) v Placebo
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.83
upper limit	14.56
Variability estimate	Standard error of the mean
Dispersion value	1.46

Notes:

[3] - ANOVA

### Primary: PAR45

End point title	PAR45
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End point description:

End point type	Primary
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End point timeframe:

comparison of data from the whole study period

End point values	IBALGIN Extra Fast(R)	NUROFEN FORTE(R)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	141	139	71	
Units: PAR45				
arithmetic mean (standard error)	1.92 ( $\pm$ 0.13)	1.67 ( $\pm$ 0.13)	0.62 ( $\pm$ 0.16)	

### Statistical analyses

<b>Statistical analysis title</b>	PAR45 - Ibalgin vs. Nurofen
Comparison groups	IBALGIN Extra Fast(R) v NUROFEN FORTE(R)
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority <sup>[4]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[4] - ANOVA

<b>Statistical analysis title</b>	PAR45 - Ibalgin vs. Placebo
Comparison groups	IBALGIN Extra Fast(R) v Placebo

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority <sup>[5]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.63
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[5] - ANOVA

<b>Statistical analysis title</b>	PAR45 - Nurofen vs Placebo
Comparison groups	NUROFEN FORTE(R) v Placebo
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority <sup>[6]</sup>
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.38
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[6] - ANOVA

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For whole study period

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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### Reporting groups

Reporting group title	Adverse events
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Reporting group description: -

<b>Serious adverse events</b>	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 280 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

<b>Non-serious adverse events</b>	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 280 (4.64%)		
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Wound complication			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Wound dehiscence			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Seroma			

subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Post procedural oedema			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Procedural headache			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	4 / 280 (1.43%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Oral administration complication			
subjects affected / exposed	1 / 280 (0.36%)		
occurrences (all)	1		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	1 / 280 (0.36%) 1		
Dysphagia subjects affected / exposed occurrences (all)	1 / 280 (0.36%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 280 (0.36%) 1		
Skin and subcutaneous tissue disorders Swelling face subjects affected / exposed occurrences (all)	2 / 280 (0.71%) 2		
Infections and infestations Alveolar osteitis subjects affected / exposed occurrences (all)	1 / 280 (0.36%) 1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported