Clinical trial results:
Randomized, controlled, multi-center trial to evaluate the efficacy and safety of a Loxoprofen sodium 60 mg medicated plaster vs. placebo and vs. a marketed comparator in the local symptomatic and short term treatment of pain in acute strains, sprains or bruises of the muscles or joints following blunt trauma, e.g. sports injuries.

Summary

EudraCT number	2020-003543-29
Trial protocol	DE
Global end of trial date	30 June 2023

Results information

Result version number	v1 (current)
This version publication date	16 October 2024
First version publication date	16 October 2024

Trial information

Trial identification

Sponsor protocol code	48-04LXPU

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Lead Chemical Company
Sponsor organisation address	77-3 Himata, Toyama, Japan, 930-0912
Public contact	Ilias Zontiros, regenold GmbH, +49 76328226270, ilias.zontiros@regenold.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002626-PIP01-19
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	06 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of a Loxoprofen sodium 60 mg medicated plaster applied once a day compared with placebo and a marketed active comparator in patients with acute blunt, soft tissue injuries of the muscles or joints.

Protection of trial subjects:

This clinical study was designed and was implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice E6 (R2) [European Medicines Agency 2016], with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki. Eligible patients were only to be included in the study after providing written (witnessed, where required by law or regulation), IRB/IEC/REB-approved informed consent, or, if incapable of doing so, after such consent had been provided by a legally acceptable representative of the patient. In cases where the patient's representative had given consent, the patient had to be informed about the study to the extent possible given his/her understanding. Patients less than 18 years of age were also required to provide the consent of both legal guardians. If the patient was capable of doing so, he/she was to indicate assent by personally signing and dating the written informed consent document or a separate assent form. Informed consent was obtained before conducting any study-specific procedures (i.e., all of the procedures described in the protocol). The process of obtaining informed consent was documented in the patient source documents. Women of child bearing potential were informed that taking the study medication could have involved unknown risks to the fetus if pregnancy occurred during the study and agreed that in order to participate in the study, they adhered to the contraception requirement for the duration of the study. If there was any question that the patient would not reliably comply, they have not been entered in the study.

Background therapy:

Concomitant therapies allowed during the study:
- Rescue medication (paracetamol, 500 mg tablets) except for the 6 hours prior to visit 5 (72h).
- Standard care by rest, ice, compression (non-occlusive bandage), or elevation (RICE) could have been considered at the discretion of the Investigator.
Concomitant therapies prohibited during the study:
- Use of systemic or topical NSAIDs (other than study treatment), analgesics (other than paracetamol), opioids, corticosteroids (except for topical treatment of bronchial asthma), heparin, or psychotropic agents.

The Investigator instructed the patient to notify the study center about any new medications and significant non-drug therapies (i.e., RICE) he/she took after the start of the study drug. All medications and significant non-drug therapies taken during the 30 days prior to Visit 1 (0h, Day 1) (including physical therapy and blood transfusions) or administered after the patient started treatment with study drug were listed on the Concomitant medications/Significant non-drug therapies CRF page. An AE CRF page was also completed, if appropriate.

Evidence for comparator:

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Actual start date of recruitment	15 June 2021
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	Germany: 257
Worldwide total number of subjects	257
EEA total number of subjects	257

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)	5
Adults (18-64 years)	250
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 257 patients (123 female and 134 male) suffering from acute sports-related soft-tissue injury/contusion of the upper or lower limb were randomised. In total 256 out of 257 study participants (99.61 %) were Caucasian.
The trial was performed in 5 centers in Germany.

Pre-assignment

Screening details:

Subjects were eligible for enrollment according to the trial inclusion and exclusion criteria.

Period 1

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

Blinding implementation details:

Double-blind study with respect to the loxoprofen sodium + placebo plaster. Patients, investigator staff, assessors, monitors and data analysts remained blinded to the identity of these treatments from the time of randomization until database lock. With respect to the active comparator, patients and investigators could not have been fully blinded due to a difference in appearance of the active comparator. Measures were put in place to avoid awareness of treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Loxoprofen sodium 60 mg medicated plaster

Arm description:

Loxoprofen sodium 60 mg medicated plaster was applied to the injured site once a day for up to 7 days (maximum of 7 plasters).

Arm type	Experimental
Investigational medicinal product name	Loxoprofen sodium 60 mg medicated plaster
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Cutaneous use, Local use , Transdermal use

Dosage and administration details:

In the Loxoprofen treatment group, patients applied 1 medicated plaster (Loxoprofen, 60 mg loxoprofen sodium) every 24 hours for a total of 7 days, resulting in 7 applications of 60 mg loxoprofen sodium each. This adds up to an exposure of 7 x 60 mg, resulting in 420 mg loxoprofen sodium over 7 days.

Arm title	Placebo

Arm description:

Placebo plaster that did not contain the active ingredient as well as the excipient phosphoric acid, but was otherwise indistinguishable from the investigational drug Loxoprofen sodium 60 mg medicated plaster.

Arm type	Placebo
Investigational medicinal product name	Placebo plaster
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Cutaneous use, Local use , Transdermal use

Dosage and administration details:

Placebo plaster was applied to the injury site once a day for up to 7 days (maximum of 7 plasters).

Arm title	Active comparator

Arm description:

Nurofen 24-Stunden Schmerzpflaster containing 200 mg Ibuprofen each was used as marketed active comparator and was applied to the injured site once a day for up to 7 days.

Arm type	Active comparator
Investigational medicinal product name	Nurofen 24-Stunden Schmerzpflaster
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Cutaneous use, Local use , Transdermal use

Dosage and administration details:

In the Nurofen 24-Stunden Schmerzpflaster group, patients applied 1 medicated plaster (200 mg ibuprofen) every 24 hours for a total of 7 days, resulting in 7 applications of 200 mg ibuprofen each. This adds up to an exposure of 7 x 200 mg, resulting in 1400 mg ibuprofen over 7 days.

Number of subjects in period 1	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator
Started	128	65	64
Completed	128	65	64

Baseline characteristics

Reporting groups	
Reporting group title	Loxoprofen sodium 60 mg medicated plaster
Reporting group description:	
Loxoprofen sodium 60 mg medicated plaster was applied to the injured site once a day for up to 7 days (maximum of 7 plasters).	
Reporting group title	Placebo
Reporting group description:	
Placebo plaster that did not contain the active ingredient as well as the excipient phosphoric acid, but was otherwise indistinguishable from the investigational drug Loxoprofen sodium 60 mg medicated plaster.	
Reporting group title	Active comparator
Reporting group description:	
Nurofen 24-Stunden Schmerzpflaster containing 200 mg Ibuprofen each was used as marketed active comparator and was applied to the injured site once a day for up to 7 days.	

Reporting group values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator
Number of subjects	128	65	64
Age categorical Units: Subjects			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
Age continuous Units: years			
arithmetic mean	35.1	34.9	35.5
standard deviation	± 12.1	± 12.0	± 12.7
Gender categorical Units: Subjects			
Female	63	31	29
Male	65	34	35

Reporting group values	Total		
Number of subjects	257		
Age categorical Units: Subjects			
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	123		
Male	134		

End points

End points reporting groups

Reporting group title	Loxoprofen sodium 60 mg medicated plaster

Reporting group description:

Loxoprofen sodium 60 mg medicated plaster was applied to the injured site once a day for up to 7 days (maximum of 7 plasters).

Reporting group title	Placebo

Reporting group description:

Placebo plaster that did not contain the active ingredient as well as the excipient phosphoric acid, but was otherwise indistinguishable from the investigational drug Loxoprofen sodium 60 mg medicated plaster.

Reporting group title	Active comparator

Reporting group description:

Nurofen 24-Stunden Schmerzpflaster containing 200 mg Ibuprofen each was used as marketed active comparator and was applied to the injured site once a day for up to 7 days.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) was all randomized patients who received at least one dose of study drug. The FAS population was primary population for the analysis of efficacy. Any exclusions from the FAS population were made and documented before unblinding (e.g. never used study medication, randomized twice). Additional secondary populations could have been defined before unblinding.

Primary: Pain-on-movement (POM) change from baseline (pain intensity difference = PID) to Visit 5

End point title	Pain-on-movement (POM) change from baseline (pain intensity difference = PID) to Visit 5

End point description:

Pain-on-movement (POM) served as primary efficacy outcome and was assessed by Visual Analogue Scale (VAS). At each study visit POM was induced by the same standardised movement, and/or investigator-derived passive manipulation of the nearest joint. The primary efficacy variable was the change from baseline in pain-on-movement (POM) assessed at Visit 5 (72 h after initiating treatment); i.e., pain intensity difference (PID). From POM values the PID was calculated by subtracting POM VAS from baseline, so that greater negative PID values indicate greater pain reduction.

End point type	Primary

End point timeframe:

Pain-on-movement (POM) was assessed at Visit 5 (72 hours after initiating treatment). From POM values the PID was calculated by subtracting POM VAS from baseline, so that greater negative PID values indicate greater pain reduction.

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-50.6 (± 18.7)	-37.6 (± 16.8)	-50.5 (± 16.9)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.5235
upper limit	-7.3333

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.4436
upper limit	-7.8361

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Active comparator v Loxoprofen sodium 60 mg medicated plaster
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6074
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4266
upper limit	5.8494

Secondary: POM VAS PID – Visit 2

End point title	POM VAS PID – Visit 2

End point description:

End point type	Secondary

End point timeframe:

VAS-based PID values for POM was assessed at Visits 2 (12 h).

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-11.6 (± 10.0)	-10.5 (± 9.2)	-12.7 (± 10.1)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4079
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1933
upper limit	1.3013

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0806
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9044
upper limit	0.2833

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2372
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9037
upper limit	3.6328

Secondary: POM VAS PID – Visit 3

End point title	POM VAS PID – Visit 3

End point description:

End point type	Secondary

End point timeframe:

VAS-based PID values for POM was assessed at Visits 3 (24 h).

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-21.9 (± 16.1)	-17.5 (± 13.7)	-22.5 (± 15.5)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo

Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0256
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7979
upper limit	-0.5122

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4922
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3927
upper limit	4.9611

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0114
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6439
upper limit	-1.2346

Secondary: POM VAS PID – Visit 4

End point title	POM VAS PID – Visit 4

End point description:

End point type	Secondary

End point timeframe:

VAS-based PID values for POM was assessed at Visits 4 (48 h).

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-37.3 (± 17.5)	-26.9 (± 16.0)	-38.9 (± 15.8)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Placebo v Loxoprofen sodium 60 mg medicated plaster
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.0281
upper limit	-5.3139

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2375
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7539
upper limit	7.0417

Statistical analysis title	Active comparator vs. placebo

Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.344
upper limit	-7.2858

Secondary: POM VAS PID – Visit 6

End point title	POM VAS PID – Visit 6
End point description:	

End point type	Secondary
End point timeframe:	
VAS-based PID values for POM was assessed at Visits 6 (96 h).	

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-59.0 (± 17.0)	-48.0 (± 17.1)	-58.4 (± 16.4)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6119
upper limit	-5.6948

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6294
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.0153
upper limit	4.9758

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Active comparator v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2026
upper limit	-6.0645

Secondary: POM VAS PID – Visit 7	
End point title	POM VAS PID – Visit 7
End point description:	

End point type	Secondary
End point timeframe:	
VAS-based PID values for POM was assessed at Visits 7 (168 h).	

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: millimetre(s)				
arithmetic mean (standard deviation)	-65.5 (± 13.5)	-61.7 (± 15.8)	-64.7 (± 14.4)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0909
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4806
upper limit	0.4068

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6155
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2127
upper limit	3.7297

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator

Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0572
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6931
upper limit	0.1023

Secondary: POM Sum of Pain Intensity Differences (SPID) - visit 3

End point title	POM Sum of Pain Intensity Differences (SPID) - visit 3

End point description:

End point type	Secondary

End point timeframe:

POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values at visit 3 (24h)

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: mm*h				
arithmetic mean (standard deviation)	-279.90332030 (± 194.79110723)	-248.75833330 (± 181.59943331)	-303.81250000 (± 186.85579855)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2312
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.2734
upper limit	17.7833

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1787
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4923
upper limit	77.4148

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0274
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-111.76
upper limit	-6.6567

Secondary: POM SPID - visit 4	
End point title	POM SPID - visit 4

End point description:

End point type	Secondary

End point timeframe:

POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values at visit 4 (48h)

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: mm*h				
arithmetic mean (standard deviation)	-1031.785482 (± 536.319692)	-821.88589740 (± 494.071467)	-1076.3294270 0 (±	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0041
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-320.56
upper limit	-60.9891

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2653
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.7383
upper limit	205.25

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator

Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-414.83
upper limit	-115.23

Secondary: POM SPID - visit 5

End point title	POM SPID - visit 5

End point description:

End point type	Secondary

End point timeframe:

POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values at visit 5 (72h)

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: mm*h				
arithmetic mean (standard deviation)	-2086.087240 (± 910.976682)	-1589.825000 (± 858.575055)	-2146.391927 (± 840.636362)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-679.7
upper limit	-230.71

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3057
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-108.51
upper limit	344.67

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-832.4
upper limit	-314.17

Secondary: POM SPID - visit 6	
End point title	POM SPID - visit 6
End point description:	

End point type	Secondary
End point timeframe:	
POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values at visit 6 (96h)	

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: mm*h				
arithmetic mean (standard deviation)	-3404.158854 (± 1269.484755)	-2614.990385 (± 1209.780291)	-3454.000651 (± 1188.243277)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1030.28
upper limit	-404.73

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.374
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-172.93
upper limit	458.46

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator

Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1221.29
upper limit	-499.26

Secondary: POM SPID - visit 7

End point title	POM SPID - visit 7

End point description:

End point type	Secondary

End point timeframe:

POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values at visit 7 (168h)

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	65	64	
Units: mm*h				
arithmetic mean (standard deviation)	-7886.418294 (± 2197.77886)	-6557.007051 (± 2146.971309)	-7881.054687 (± 2170.171946)	

Statistical analyses

Statistical analysis title	Treatment vs. placebo
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1678.41
upper limit	-646.11

Statistical analysis title	Treatment vs. active comparator
Comparison groups	Loxoprofen sodium 60 mg medicated plaster v Active comparator
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4514
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-321.46
upper limit	720.48

Statistical analysis title	Active comparator vs. placebo
Comparison groups	Placebo v Active comparator
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1957.52
upper limit	-766.02

Secondary: POM - Time to meaningful (30 %) reduction	
End point title	POM - Time to meaningful (30 %) reduction

End point description:

End point type	Secondary

End point timeframe:

Time to meaningful reduction of pain was calculated as 30 % of baseline POM, respectively, based on the VAS values measured for POM at each of the study visits.

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	63	62	
Units: hour				
arithmetic mean (standard deviation)	42.74 (± 32.74)	47.85 (± 29.25)	35.86 (± 25.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: POM - Time to optimal (50 %) reduction

End point title	POM - Time to optimal (50 %) reduction

End point description:

End point type	Secondary

End point timeframe:

Time to optimal reduction of pain was calculated as 50 % reduction of baseline POM, respectively, based on the VAS values measured for POM at each of the study visits.

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	120	62	61	
Units: hour				
arithmetic mean (standard deviation)	59.38 (± 33.48)	86.39 (± 45.18)	52.54 (± 28.79)	

Statistical analyses

No statistical analyses for this end point

Secondary: POM - Time to complete resolution of pain by treatment

End point title	POM - Time to complete resolution of pain by treatment

End point description:

End point type	Secondary

End point timeframe:

Time to complete resolution of pain was calculated as 100 % reduction of baseline POM (i.e., the timepoint where a VAS value of 0 mm was reached), based on the VAS values measured for POM at each of the study visits.

End point values	Loxoprofen sodium 60 mg medicated plaster	Placebo	Active comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	35	42	
Units: hour				
arithmetic mean (standard deviation)	126.66 (± 45.43)	150.86 (± 38.15)	127.89 (± 44.85)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The occurrence of AEs was sought by non-directive questioning of the patient at each visit during the study.

Adverse event reporting additional description:

AEs could have been detected when they were volunteered by the patient during/between visits or through physical examination or other assessments.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Treatment
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Active comparator
Reporting group description: -	

Serious adverse events	Treatment	Placebo	Active comparator
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 128 (0.00%)	0 / 65 (0.00%)	0 / 64 (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	Treatment	Placebo	Active comparator
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 128 (0.78%)	4 / 65 (6.15%)	2 / 64 (3.13%)
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 128 (0.78%)	0 / 65 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Condition aggravated			
subjects affected / exposed	0 / 128 (0.00%)	2 / 65 (3.08%)	1 / 64 (1.56%)
occurrences (all)	0	2	1

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 128 (0.00%)	1 / 65 (1.54%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 65 (1.54%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 128 (0.00%)	0 / 65 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2022	Substantial amendment to move investigator site 04 to new premises.
19 August 2022	Addition of a new investigator at site 05.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported