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

Summary

EudraCT number	2019-001038-32
Trial protocol	DE
Global end of trial date	19 March 2020

Results information

Result version number	v1 (current)
This version publication date	04 April 2021
First version publication date	04 April 2021

Trial information

Trial identification

Sponsor protocol code	48-03LXPU

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Lead Chemical Co. Ltd.
Sponsor organisation address	77-3 Himata, Toyama, Japan, 930-0912
Public contact	Dr. Regenold GmbH, Dr. Regenold GmbH, +49 763282260, info@regenold.com
Scientific contact	Dr. Regenold GmbH, Dr. Regenold GmbH, +49 763282260, info@regenold.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	28 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of a loxoprofen sodium 60 mg tape medicated plaster, applied once a day, compared with placebo for up to 7 days, in male and female subjects with acute blunt, soft tissue injuries of the limbs (i.e. sports injuries). The study had a double-blind, randomized, multi-center, placebo-controlled, parallel group design.

Patients were randomized soon after the injury (from injury to initial treatment not >6 h). After the randomization Visit (V) 1 = Baseline, Day (D) 1, patients returned to the study center for post-baseline visits. Patients applied the plaster approximately every 24 hours for the following 7 days witnessed by clinical trial staff at the trial center for the first 5 days, then alone at home.

Patients assessed pain-on-movement (POM) and spontaneous pain-at-rest (PAR), as well as efficacy and safety of the treatment at each study visit i.e. V1 (D1), V2 (D1 or D2), V3 (D2), V4 (D3), V5 (D4), V6 (D5), and Final visit V7 (D7 ± 1D).

Protection of trial subjects:

The clinical trial protocol and amendments were approved by local ethics committees/Institutional Review Boards and Competent Authorities. The clinical trial was conducted in accordance with good clinical practice (GCP) and the Declaration of Helsinki. Informed consent was obtained in writing prior to any trial-related activities.
Patients were monitored for adverse events throughout participation in the study.

Background therapy:

Standard care by rest, ice, compression (non-occlusive bandage), or elevation (RICE) at the discretion of the Investigator.
Rescue medication (paracetamol) except for the 6 hours immediately preceding Visit 5 (72 h).

Evidence for comparator:

None.

Abbreviations used in this study entry
AE=Adverse event
ANCOVA=Analysis of covariance
AUC=Area under the curve
CI=Confidence interval
D=Day
GCP=Good Clinical Practice
h=hour
LSMeans = Least Square Means
PAR=Pain-at-rest
POM=Pain-on-movement
V=Visit
VAS=Visual Analogue Scale

Actual start date of recruitment	15 November 2019
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: 127
Worldwide total number of subjects	127
EEA total number of subjects	127

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	127
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall 127 adult male and female patients were recruited. All patients had acute blunt, soft-tissue injury or contusion (such as sports injuries) of the upper or lower limb. The trial was performed in 3 study centers in Germany.

Pre-assignment

Screening details:

Patients were eligible for enrollment according to the trial inclusion and exclusion criteria. The size of injury was measured by the Investigator at randomisation (V1). The size had to be at least 25 cm2 and at most 120 cm2, based on the largest perpendicular diameters.

Period 1

Period 1 title	Overall treatment (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:

The identity of the treatments was concealed by the use of study drugs that were all identical in packaging, labeling, schedule of administration, appearance, and odor.

Arms

Are arms mutually exclusive?	Yes
Arm title	Loxoprofen sodium

Arm description:

Patients received Loxoprofen sodium 60 mg tape medicated plaster applied once a day for up to 7 days.

Arm type	Experimental
Investigational medicinal product name	Loxoprofen sodium
Investigational medicinal product code	
Other name	Loxoprofen sodium hydrate
Pharmaceutical forms	Medicated plaster
Routes of administration	Transdermal use

Dosage and administration details:

Loxoprofen sodium 60 mg tape medicated plaster was applied once a day, for up to 7 days.

Active ingredient: Loxoprofen sodium hydrate 68 mg (60 mg as anhydrate).

Arm title	Placebo

Arm description:

Patients received placebo plasters that were applied once a day for up to 7 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated plaster
Routes of administration	Transdermal use

Dosage and administration details:

Placebo plaster applied once a day, for up to 7 days.

Placebo plaster did not contain the active ingredient but was otherwise indistinguishable from the investigational drug tape medicated plaster.

Number of subjects in period 1	Loxoprofen sodium	Placebo
Started	65	62
Completed	65	61
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Loxoprofen sodium
Reporting group description:	
Patients received Loxoprofen sodium 60 mg tape medicated plaster applied once a day for up to 7 days.	
Reporting group title	Placebo
Reporting group description:	
Patients received placebo plasters that were applied once a day for up to 7 days.	

Reporting group values	Loxoprofen sodium	Placebo	Total
Number of subjects	65	62	127
Age categorical Units: Subjects			
Adults (18-64 years)	65	62	127
Age continuous Units: years arithmetic mean standard deviation	 31.1 ± 10.1	 35.6 ± 10.6	 -
Gender categorical Units: Subjects			
Female Male	30 35	26 36	56 71
Race Units: Subjects			
Asian Caucasian Other	1 64 0	0 61 1	1 125 1
Height Units: cm arithmetic mean standard deviation	 176.0 ± 10.2	 177.0 ± 10.3	 -
Weight Units: kg arithmetic mean standard deviation	 80.7 ± 14.4	 83.5 ± 19.2	 -
Pain-on-movement at baseline			
Pain-on-movement at baseline.			
Units: mm arithmetic mean standard deviation	 75.8 ± 8.2	 75.7 ± 8.6	 -
Pain-at-rest at baseline			
Pain-at-rest at baseline			
Units: mm arithmetic mean standard deviation	 27.9 ± 21.2	 28.9 ± 22.4	 -
Size of injury at baseline			
Size of injury at baseline.			
Units: cm2			

arithmetic mean	42.3	44.3	
standard deviation	± 12.3	± 11.8	-

End points

End points reporting groups

Reporting group title	Loxoprofen sodium
Reporting group description:	
Patients received Loxoprofen sodium 60 mg tape medicated plaster applied once a day for up to 7 days.	
Reporting group title	Placebo
Reporting group description:	
Patients received placebo plasters that were applied once a day for up to 7 days.	

Primary: 1_Pain-on-movement (POM) -- post treatment at 72 h

End point title	1_Pain-on-movement (POM) -- post treatment at 72 h
End point description:	
Pain-on-movement (POM) at injured site in mm, measured using a 100 mm Visual Analogue Scale (VAS) at Visit 5 (Day 4, 72 h after start of the treatment). POM was assessed in mm on a 100 mm VAS, where 0 mm = 'no pain', and 100 mm = 'extreme pain'. Results are expressed as absolute change from baseline (baseline values minus post-baseline values).	
End point type	Primary
End point timeframe:	
Baseline (pre treatment Day 1), post treatment at 72 h (Day 4).	

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[1]	62[2]		
Units: mm				
arithmetic mean (standard deviation)	59.5 (± 16.7)	36.5 (± 19.7)		

Notes:

[1] - Full Analysis Set

[2] - Full Analysis Set

Statistical analyses

Statistical analysis title	POM Visit 5 (72 h post treatment)
Statistical analysis description:	
Pain-on-movement at Visit 5 (72 h post treatment). ANCOVA – Analysis-of-covariance with the factors treatment group, center, and baseline VAS pain-on-movement, as covariate. LS Means treatment effect at V5 (72h post treatment), [Placebo minus Loxoprofen] in (mm). LSMeans = Least Square Means	
Comparison groups	Loxoprofen sodium v Placebo

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	23.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	18
upper limit	28.2
Variability estimate	Standard error of the mean
Dispersion value	2.6

Notes:

[3] - ANCOVA= Analysis-of-covariance with the factors treatment group, center, and baseline.

Secondary: 2_AUC for pain-on-movement (POM) -- post treatment at 24, 48, 72, 96, and 168 h

End point title	2_AUC for pain-on-movement (POM) -- post treatment at 24, 48, 72, 96, and 168 h

End point description:

Area under the curve (AUC) over time between baseline and the first 24, 48, 72, 96, and 168 h of treatment, for POM, as measured by visual analogue scale (VAS).

POM was assessed in mm on a 100 mm VAS, where 0 mm = 'no pain', and 100 mm = 'extreme pain'.

AUC was presented as ordinate = POM score in mm, abscissa = time after treatment.

End point type	Secondary

End point timeframe:

Baseline (pre treatment, Day 1), post treatment at 24, 48, 72, 96, and 168 h.

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[4]	62[5]		
Units: mm*h				
arithmetic mean (standard deviation)				
AUC (0-24 h)	1433.2 (± 206.1)	1587.2 (± 198.3)		
AUC (0-48 h)	2291.5 (± 489.2)	2868.5 (± 461.2)		
AUC (0-72 h)	2850.3 (± 776.8)	3958.0 (± 761.4)		
AUC (0-96 h)	3147.9 (± 1008.2)	4770.2 (± 1063.2)		
AUC (0-168 h)	3578.1 (± 1509.6)	6272.0 (± 1879.2)		

Notes:

[4] - Full Analysis Set

[5] - Full Analysis Set

Statistical analyses

Statistical analysis title	1_AUC (0-24 h) for POM

Statistical analysis description:

Results shown represent the LS Mean difference for [Placebo minus Loxoprofen sodium], in mm*h.

AUC=Area-under-the-curve; ANCOVA=Analysis-of-covariance with the factors treatment group, center, and baseline as covariate.

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	156.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	99.4
upper limit	213.4
Variability estimate	Standard error of the mean
Dispersion value	28.8

Statistical analysis title	2_AUC (0-48 h) for POM

Statistical analysis description:

Results shown represent the LS Mean difference for [Placebo minus Loxoprofen sodium], in mm*h.

AUC=Area-under-the-curve; ANCOVA=Analysis-of-covariance with the factors treatment group, center, and baseline as covariate.

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	582.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	427.8
upper limit	736.9
Variability estimate	Standard error of the mean
Dispersion value	78.1

Statistical analysis title	3_AUC (0-72 h) for POM

Statistical analysis description:

Results shown represent the LS Mean difference for [Placebo minus Loxoprofen sodium], in mm*h.

AUC=Area-under-the-curve; ANCOVA=Analysis-of-covariance with the factors treatment group, center, and baseline as covariate.

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	1115.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	852.6
upper limit	1377.8
Variability estimate	Standard error of the mean
Dispersion value	132.7

Statistical analysis title	4_AUC (0-96 h) for POM

Statistical analysis description:

Results shown represent the LS Mean difference for [Placebo minus Loxoprofen sodium], in mm*h.

AUC=Area-under-the-curve; ANCOVA=Analysis-of-covariance with the factors treatment group, center, and baseline as covariate.

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	1632.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1274.6
upper limit	1990.6
Variability estimate	Standard error of the mean
Dispersion value	180.8

Statistical analysis title	5_AUC (0-168 h) for POM

Statistical analysis description:

Results shown represent the LS Mean difference for [Placebo minus Loxoprofen sodium], in mm*h.

AUC=Area-under-the-curve; ANCOVA=Analysis-of-covariance with the factors treatment group, center, and baseline as covariate.

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	2711.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2136.8
upper limit	3285.7
Variability estimate	Standard error of the mean
Dispersion value	290.2

Secondary: 3_Pain-on-movement (POM) -- post treatment at 24, 48, 96, and 168 h

End point title	3_Pain-on-movement (POM) -- post treatment at 24, 48, 96, and 168 h

End point description:

Pain-on-movement (POM) at injured site in mm, measured using a 100 mm Visual Analogue Scale (VAS).

POM was assessed in mm on a 100 mm VAS, where 0 mm = 'no pain', and 100 mm = 'extreme pain'.

Results are expressed as absolute change from baseline (baseline values minus post-baseline values).

End point type	Secondary

End point timeframe:

Baseline (pre treatment Day 1), post treatment at 24, 48, 96, and 168 h.

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[6]	62[7]		
Units: mm				
arithmetic mean (standard deviation)				
POM (0-24 h)	31.6 (± 14.5)	15.6 (± 12.8)		
POM (0-48 h)	45.5 (± 15.8)	24.2 (± 16.5)		
POM (0-96 h)	67.2 (± 14.1)	47.3 (± 21.7)		
POM (0-168 h)	72.4 (± 12.8)	62.8 (± 19.9)		

Notes:

[6] - Full Analysis Set

[7] - Full Analysis Set

Statistical analyses

Statistical analysis title	1_POM (0-24 h)

Statistical analysis description:

ANCOVA – Analysis-of-covariance with the factors treatment group, center, and baseline VAS pain-on-

movement, as covariate.

LS Means treatment effect at respective visit, [Placebo minus Loxoprofen] in (mm).

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.4
upper limit	20.4
Variability estimate	Standard error of the mean
Dispersion value	2.3

Statistical analysis title	2_POM (0-48 h)

Statistical analysis description:

ANCOVA – Analysis-of-covariance with the factors treatment group, center, and baseline VAS pain-on-movement, as covariate.

LS Means treatment effect at respective visit, [Placebo minus Loxoprofen] in (mm).

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	21.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.2
upper limit	26.3
Variability estimate	Standard error of the mean
Dispersion value	2.6

Statistical analysis title	3_POM (0-96 h)

Statistical analysis description:

ANCOVA – Analysis-of-covariance with the factors treatment group, center, and baseline VAS pain-on-movement, as covariate.

LS Means treatment effect at respective visit, [Placebo minus Loxoprofen] in (mm).

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.5
upper limit	24.4
Variability estimate	Standard error of the mean
Dispersion value	2.2

Statistical analysis title	4_POM (0-168 h)

Statistical analysis description:

ANCOVA – Analysis-of-covariance with the factors treatment group, center, and baseline VAS pain-on-movement, as covariate.

LS Means treatment effect at respective visit, [Placebo minus Loxoprofen] in (mm).

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	12.9
Variability estimate	Standard error of the mean
Dispersion value	1.6

Secondary: 4_Pain-at-rest (PAR)

End point title	4_Pain-at-rest (PAR)

End point description:

Pain-at-rest (PAR) at injured site at 24, 48, and 72 h post treatment.

PAR was assessed in mm on a 100 mm visual analogue scale (VAS), where 0 mm = 'no pain', and 100 mm = 'extreme pain'.

Results are expressed as absolute change from baseline (baseline values minus post-baseline values).

End point type	Secondary

End point timeframe:

Baseline (pre treatment, Day 1), post treatment at 24, 48, 72 h.

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[8]	62[9]		
Units: mm				
arithmetic mean (standard deviation)				
PAR (0-24 h)	10.1 (± 13.9)	5.1 (± 7.8)		
PAR (0-48 h)	16.3 (± 16.1)	9.5 (± 11.8)		
PAR (0-72 h)	21.4 (± 18.4)	14.5 (± 15.6)		

Notes:

[8] - Full Analysis Set

[9] - Full Analysis Set

Statistical analyses

Statistical analysis title	1_PAR (0-24 h)

Statistical analysis description:

LSMeans and p-values from ANCOVA with treatment and site as fixed effects and baseline PAR assessment as a covariate.

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	8.7
Variability estimate	Standard error of the mean
Dispersion value	1.5

Statistical analysis title	2_PAR (0-48 h)

Statistical analysis description:

LSMeans and p-values from ANCOVA with treatment and site as fixed effects and baseline PAR

assessment as a covariate.

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	7.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	10.5
Variability estimate	Standard error of the mean
Dispersion value	1.4

Statistical analysis title	3_PAR (0-72 h)

Statistical analysis description:

LSMeans and p-values from ANCOVA with treatment and site as fixed effects and baseline PAR assessment as a covariate.

LSMeans = Least Square Means

Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.6
upper limit	10.4
Variability estimate	Standard error of the mean
Dispersion value	1.2

Secondary: 5_Time to meaningful reduction (30%) of pain-on-movement (POM)

End point title	5_Time to meaningful reduction (30%) of pain-on-movement (POM)

End point description:

Time to meaningful (30%) reduction of POM.

A meaningful reduction of pain was defined as a reduction of 30% from baseline, measured on a visual analogue scale (VAS) for POM.

POM was assessed in mm on a 100 mm VAS, where 0 mm = 'no pain', and 100 mm = 'extreme pain'.

Results are expressed as the number of patients reaching a meaningful (30%) reduction of POM during the respective time interval.

Time to meaningful (30%) reduction of pain in hours (h):
Loxoprofen sodium, Median: 23.5 h, 95% CI: (23.1, 24.0)
Placebo, Median: 69.1 h, 95% CI: (48.5, 71.7)

End point type	Secondary

End point timeframe:

Baseline (pre treatment, Day 1), post treatment at 12, 24, 48, 72, 96, and 192 h.

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[10]	62[11]		
Units: subjects				
Not achieved	0	1		
< 12 h	2	0		
12 to < 24 h	44	10		
24 to < 48 h	12	13		
48 to < 72 h	4	18		
72 to < 96 h	3	14		
96 to < 192 h	0	6		

Notes:

[10] - Full Analysis Set

[11] - Full Analysis Set

Statistical analyses

Statistical analysis title	Time to meaningful reduction (30%) of POM
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

Secondary: 6_Time to optimal reduction (50%) of pain-on-movement (POM)

End point title	6_Time to optimal reduction (50%) of pain-on-movement (POM)

End point description:

Time to optimal (50%) reduction of POM.

An optimal reduction of pain was defined as a reduction of 50% from baseline, measured on a visual analogue scale (VAS) for POM.

POM was assessed in mm on a 100 mm VAS, where 0 mm = 'no pain', and 100 mm = 'extreme pain'.

Results are expressed as the number of patients reaching an optimal (50%) reduction of POM during the

respective time interval.

Time to optimal (50%) reduction of pain in hours (h):
Loxoprofen sodium, Median: 47.3 h, 95% CI: (44.8, 47.8)
Placebo, Median: 95.6 h, 95% CI: (71.9, 166.6)

End point type	Secondary

End point timeframe:

Baseline (pre treatment, Day 1), post treatment at 12, 24, 48, 72, 96, and 192 h.

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[12]	62[13]		
Units: subjects				
Not achieved	1	4		
< 12 h	1	0		
12 to < 24 h	16	3		
24 to < 48 h	27	8		
48 to < 72 h	15	13		
72 to < 96 h	4	10		
96 to < 192 h	1	24		

Notes:

[12] - Full Analysis Set

[13] - Full Analysis Set

Statistical analyses

Statistical analysis title	Time to optimal reduction (50%) of POM
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

Secondary: 7_Responder rate -- at least 50% reduction of POM at 72 h

End point title	7_Responder rate -- at least 50% reduction of POM at 72 h

End point description:

Responder rate.

The responder rate is defined as the proportion of patients achieving at least 50% reduction of POM on Day 4 (72 h), compared with baseline.

Results are expressed as the number of responders reaching that level of POM reduction.

End point type	Secondary

End point timeframe:

Baseline (pre treatment, Day 1), post treatment at 72 h (Day 4).

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[14]	62[15]		
Units: subjects	34	22		

Notes:

[14] - Full Analysis Set

[15] - Full Analysis Set

Statistical analyses

Statistical analysis title	Responder rate on Day 4 (72 h)
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0444
Method	Cochran-Mantel-Haenszel

Secondary: 8_Clinical global assessment of efficacy -- 48 h -- (Investigator)

End point title	8_Clinical global assessment of efficacy -- 48 h -- (Investigator)

End point description:

Clinical global assessment of efficacy at V4 (48 h post treatment), assessed by the Investigator

The investigator's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the investigator had to answer was:
Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?
The response options were: ‘very good’, ‘good’, ‘fair’, ‘poor’, or 'very poor’.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 4 (48 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[16]	62[17]		
Units: subjects				
Very good	16	5		
Good	39	13		
Fair	8	32		

Poor	2	12		
Very poor	0	0		

Notes:

[16] - Full Analysis Set

[17] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 4 (48 h) -- Investigator
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 9_Clinical global assessment of efficacy -- 72 h -- (Investigator)

End point title	9_Clinical global assessment of efficacy -- 72 h -- (Investigator)

End point description:

Clinical global assessment of efficacy at V5 (72 h post treatment), assessed by the Investigator.

The investigator's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the investigator had to answer was:
Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?
The response options were: 'very good', 'good', 'fair', 'poor', or 'very poor'.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 5 (72 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[18]	62[19]		
Units: subjects				
Very good	30	5		
Good	26	15		
Fair	6	27		
Poor	3	15		
Very poor	0	0		

Notes:

[18] - Full Analysis Set

[19] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 5 (72 h) -- Investigator
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 10_Clinical global assessment of efficacy -- 168 h -- (Investigator)

End point title	10_Clinical global assessment of efficacy -- 168 h -- (Investigator)

End point description:

Clinical global assessment of efficacy at V7 (168 h post treatment), assessed by the Investigator.

The investigator's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the investigator had to answer was:
Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?
The response options were: ‘very good’, ‘good’, ‘fair’, ‘poor’, or 'very poor’.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 7 (168 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[20]	62[21]		
Units: subjects				
Very good	34	9		
Good	23	16		
Fair	6	21		
Poor	2	16		
Very poor	0	0		

Notes:

[20] - Full Analysis Set

[21] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 7 (168 h) -- Investigator
Comparison groups	Loxoprofen sodium v Placebo

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 11_Clinical global assessment of efficacy -- 48 h -- (Patient)

End point title	11_Clinical global assessment of efficacy -- 48 h -- (Patient)

End point description:

Clinical global assessment of efficacy at V4 (48 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
Considering all the ways this treatment has affected you since you started in the clinical trial, how well are you doing?
The response options were: 'very good', 'good', 'fair', 'poor', or 'very poor'.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 4 (48 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[22]	62[23]		
Units: subjects				
Very good	14	3		
Good	39	15		
Fair	11	38		
Poor	1	6		
Very poor	0	0		

Notes:

[22] - Full Analysis Set

[23] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 4 (48 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 12_Clinical global assessment of efficacy -- 72 h -- (Patient)

End point title	12_Clinical global assessment of efficacy -- 72 h -- (Patient)

End point description:

Clinical global assessment of efficacy at V5 (72 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
Considering all the ways this treatment has affected you since you started in the clinical trial, how well are you doing?
The response options were: 'very good', 'good', 'fair', 'poor', or 'very poor'.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 5 (72 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[24]	62[25]		
Units: subjects				
Very good	31	5		
Good	26	23		
Fair	6	21		
Poor	2	13		
Very poor	0	0		

Notes:

[24] - Full Analysis Set

[25] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 5 (72 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 13_Clinical global assessment of efficacy -- 168 h -- (Patient)

End point title	13_Clinical global assessment of efficacy -- 168 h -- (Patient)

End point description:

Clinical global assessment of efficacy at V7 (168 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
Considering all the ways this treatment has affected you since you started in the clinical trial, how well are you doing?
The response options were: ‘very good’, ‘good’, ‘fair’, ‘poor’, or 'very poor’.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 7 (168 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64[26]	62[27]		
Units: subjects				
Very good	32	10		
Good	23	18		
Fair	8	25		
Poor	1	9		
Very poor	0	0		

Notes:

[26] - Full Analysis Set

[27] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 7 (168 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 14_Treatment assessment -- 48 h -- (Patient)

End point title	14_Treatment assessment -- 48 h -- (Patient)

End point description:

Treatment assessment at V4 (48 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
How do you rate this medication as a treatment for the pain of your soft tissue injury/contusion?
The response options were: ‘excellent’, ‘very good’, ‘good’, ‘fair’, or ‘poor’.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 4 (48 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[28]	62[29]		
Units: subjects				
Excellent	5	1		
Very good	22	8		
Good	30	13		
Fair	7	32		
Poor	1	8		

Notes:

[28] - Full Analysis Set

[29] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 4 (48 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 15_Treatment assessment -- 72 h -- (Patient)

End point title	15_Treatment assessment -- 72 h -- (Patient)

End point description:

Treatment assessment at V5 (72 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
How do you rate this medication as a treatment for the pain of your soft tissue injury/contusion?”
The response options were: ‘excellent’, ‘very good’, ‘good’, ‘fair’, or ‘poor’.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 5 (72 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65[30]	62[31]		
Units: subjects				
Excellent	10	2		
Very good	32	10		
Good	13	14		
Fair	8	26		
Poor	2	10		

Notes:

[30] - Full Analysis Set

[31] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 5 (72 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: 16_Treatment assessment -- 168 h -- (Patient)

End point title	16_Treatment assessment -- 168 h -- (Patient)

End point description:

Treatment assessment at V7 (168 h post treatment), assessed by the patient.

The patient's opinion on the global efficacy assessment of the IMP on the following 5-point Likert scale was documented.

The question that the patient had to answer was:
How do you rate this medication as a treatment for the pain of your soft tissue injury/contusion?"
The response options were: 'excellent', 'very good', 'good', 'fair', or 'poor'.

The results are shown as the number of patients per response category.

End point type	Secondary

End point timeframe:

Visit 7 (168 h post treatment)

End point values	Loxoprofen sodium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64[32]	62[33]		
Units: subjects				
Excellent	8	5		
Very good	32	8		
Good	16	15		
Fair	7	26		

Poor	1	8		

Notes:

[32] - Full Analysis Set

[33] - Full Analysis Set

Statistical analyses

Statistical analysis title	Visit 7 (168 h) -- Patient
Comparison groups	Loxoprofen sodium v Placebo
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of signing the informed consent form and to trial completion or discontinuation.

Adverse event reporting additional description:

Safety analysis set was used to evaluate the adverse events.

Safety analysis set = Full analysis set, defined as all randomized patients who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Loxoprofen sodium

Reporting group description:

Patients received Loxoprofen sodium 60 mg tape medicated plaster applied once a day for up to 7 days.

Reporting group title	Placebo

Reporting group description:

Patients received placebo plasters that were applied once a day for up to 7 days.

Serious adverse events	Loxoprofen sodium	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 65 (0.00%)	0 / 62 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Loxoprofen sodium	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 65 (1.54%)	2 / 62 (3.23%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 65 (1.54%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Application site irritation			
subjects affected / exposed	0 / 65 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Application site pain			
subjects affected / exposed	0 / 65 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	
Application site swelling			
subjects affected / exposed	0 / 65 (0.00%)	1 / 62 (1.61%)	
occurrences (all)	0	1	

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

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

None.

Notes: