Clinical trial results:
A phase III, multicentre, randomised, double-blind, parallel-group trial to evaluate the efficacy and safety of a generic gel (calcipotriol + betamethasone 50 microg/g + 0.5 mg/g gel) compared to originator gel (Daivobet® gel) and vehicle in the treatment of mild to moderate plaque-type psoriasis

Summary

EudraCT number	2018-002532-24
Trial protocol	DE
Global end of trial date	04 November 2019

Results information

Result version number	v1 (current)
This version publication date	23 December 2020
First version publication date	23 December 2020

Trial information

Trial identification

Sponsor protocol code	0155/2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Helm AG
Sponsor organisation address	Nordkanalstr. 28, Hamburg, Germany, 20097
Public contact	Senior Manager Clinical Development, Helm AG, 0049 402375 1446, tertia.dejager@helmag.com
Scientific contact	Senior Manager Clinical Development, Helm AG, 0049 402375 1446, tertia.dejager@helmag.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	19 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2019
Global end of trial reached?	Yes
Global end of trial date	04 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

a) To demonstrate that topical treatment with the generic calcipotriol- betamethasone gel is therapeutically equivalent to the originator Daivobet® gel in the treatment of chronic stable, mild to moderate plaque-type psoriasis as determined by the percentage reduction in psoriasis area and severity index (PASI).
b) To demonstrate the superiority of the generic gel to its vehicle

Protection of trial subjects:

Prior to recruitment of patients, all relevant documents of the clinical study were submitted and approved by the Independent Ethics Committees (IECs) responsible for the participating investigators. Written consent documents embodied the elements of informed consent as described in the Declaration of Helsinki, the ICH Guidelines for Good Clinical Practice (GCO) and were in accordance with all applicable laws and regulations. The informed consent form and patient information sheet described the planned and permitted uses, transfers and disclosures of the patient's personal data and personal health information for purposes of conducting the study. The informed consent form and the patient information sheet further explained the nature of the study, its objectives and potential risks and benefits as well as the date informed consent was given. Before being enrolled in the clinical study, every patient was informed that participation in this study was voluntary and that s/he could withdraw from the study at any time without giving a reason and without having to fear any loss in his/her medical care. The patient's consent was obtained in writing before the start of the study. By signing the informed consent the patient declared that s/he was participating voluntarily and intended to follow the study protocol instructions and the instructions of the investigator and to answer the questions asked during the course of the study.

Background therapy:

Any pre-existing long-term medication for treatment of existing disorders, which was not considered to interfere with absorption, efficacy, or safety of the IMP or is not listed in the restrictions, was permitted.

Evidence for comparator:

Comparators were the following products:
- Originator (marketed product): Daivobet gel (LEO Pharma, Ireland)
- Placebo for test product: Vehicle gel

Actual start date of recruitment	28 February 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	Poland: 237
Country: Number of subjects enrolled	Germany: 49
Worldwide total number of subjects	286
EEA total number of subjects	286

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)	238
From 65 to 84 years	47
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Date trial initiated (first subject first screening): 28FEB2019
Date trial completed (last subject last visit): 04NOV2019
Countries: Germany and Poland
The subjects were either known patients at a site, referred to the site by other physicians or recruited via advertisements.

Pre-assignment

Screening details:

Male and female subjects with mild to moderate Psoriasis (IGA 2-4), BSA up to 20%,
no clinically relevant disease or condition, no active skin disease, no finding during physical examination, wash-out phases for indication related treatment and prohibited medication, no alcohol and drug abuse

Period 1

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

Blinding implementation details:

In order to avoid bias the study was realised with a double-blind approach for assessment of efficacy and safety, i.e. subjects and investigators as well as the laboratory have not been aware of the treatment administered.
Test and reference treatments were supplied in identical form and similar in color, and general appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	Generic calcipotriol-betamethasone gel

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Generic calcipotriol-betamethasone gel
Investigational medicinal product code	IMP 1
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Once daily application of a thin layer of IMP to all psoriatic lesions (except face, and genitoanal and intertriginous regions) for up to 8 weeks (56 consecutive days).
Based on application guidance and maximum affected BSA of ≤ 20% (4000 cm2) it is calculated that each application will require approximately 5 g gel.
During the course of trial, all new lesions have also to be treated.

Arm title	Daivobet gel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Daivobet gel
Investigational medicinal product code	IMP 2
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Once daily application of a thin layer of IMP to all psoriatic lesions (except face, and genitoanal and intertriginous regions) for up to 8 weeks (56 consecutive days).
Based on application guidance and maximum affected BSA of ≤ 20% (4000 cm2) it is calculated that each application will require approximately 5 g gel.
During the course of trial, all new lesions have also to be treated.

Arm title	Generic vehicle
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Generic vehicle
Investigational medicinal product code	IMP 3
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Once daily application of a thin layer of IMP to all psoriatic lesions (except face, and genitoanal and intertriginous regions) for up to 8 weeks (56 consecutive days).
Based on application guidance and maximum affected BSA of ≤ 20% (4000 cm2) it is calculated that each application will require approximately 5 g gel.
During the course of trial, all new lesions have also to be treated.

Number of subjects in period 1	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle
Started	124	123	39
Completed	122	121	30
Not completed	2	2	9
Consent withdrawn by subject	-	1	3
Physician decision	-	-	1
Adverse event, non-fatal	-	1	2
Pregnancy	1	-	-
start of prohibited medication	1	-	-
Lack of efficacy	-	-	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	286	286	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	238	238	
From 65-84 years	47	47	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	46.7		
standard deviation	± 15.4	-	
Gender categorical Units: Subjects			
Female	137	137	
Male	149	149	
Psoriasis Affected BSA [%] Units: 20			
arithmetic mean	8.1		
standard deviation	± 4.6	-	
Baseline IGA Units: 4.0			
arithmetic mean	2.7		
standard deviation	± 0.7	-	
Baseline PASI Units: 15			
arithmetic mean	8.32		
standard deviation	± 2.69	-	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) will include all randomised subjects who receive at least one IMP application. Subjects may, however, be excluded from the FAS on individual justification in case of serious violations of inclusion or exclusion criteria which are likely to invalidate the assessment of treatment efficacy,

notably those which occurred already before randomisation but were not appropriately considered at the time of randomisation. Subjects will be analyzed for efficacy according to the investigational treatment that they were randomised to.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol analysis set (PPS) will include all FAS eligible subjects who complete the 4-week treatment phase with at least 75% of the scheduled applications, attend the efficacy assessments at the Week 4/Day 29 visit within a window of +/- 2 days, and have no major protocol deviations interfering with the assessment of the primary efficacy outcome measure. The administration of an IMP other than the randomised treatment will be considered a serious protocol deviation and will thus also lead to exclusion from the PPS. Subjects terminating their trial participation prior to the efficacy assessments at the Week 4/Day 29 visit due to efficacy or tolerability issues will also be retained in the PPS unless other reasons for exclusion also apply.

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomised subjects who receive at least one dose of the study medication will be included in the safety evaluation set (SES). Subjects will be analyzed for safety according to the investigational treatment that they have actually received.

Reporting group values	FAS	Per Protocol	Safety analysis
Number of subjects	283	244	286
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	0	0
Adults (18-64 years)	236	206	238
From 65-84 years	46	37	47
85 years and over	1	1	1
Age continuous Units: years			
arithmetic mean	46.6	46.0	46.7
standard deviation	± 15.4	± 15.3	± 15.4
Gender categorical Units: Subjects			
Female	135	117	137
Male	148	127	149
Psoriasis Affected BSA [%] Units: 20			
arithmetic mean	8.1	7.9	8.1
standard deviation	± 4.6	± 4.5	± 4.6
Baseline IGA Units: 4.0			
arithmetic mean	2.7	2.7	2.7
standard deviation	± 0.7	± 0.7	± 0.7
Baseline PASI Units: 15			
arithmetic mean	8.34	8.17	8.32

standard deviation	± 2.68	± 2.55	± 2.69

End points

End points reporting groups

Reporting group title	Generic calcipotriol-betamethasone gel
Reporting group description: -	
Reporting group title	Daivobet gel
Reporting group description: -	
Reporting group title	Generic vehicle
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) will include all randomised subjects who receive at least one IMP application. Subjects may, however, be excluded from the FAS on individual justification in case of serious violations of inclusion or exclusion criteria which are likely to invalidate the assessment of treatment efficacy, notably those which occurred already before randomisation but were not appropriately considered at the time of randomisation. Subjects will be analyzed for efficacy according to the investigational treatment that they were randomised to.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol analysis set (PPS) will include all FAS eligible subjects who complete the 4-week treatment phase with at least 75% of the scheduled applications, attend the efficacy assessments at the Week 4/Day 29 visit within a window of +/- 2 days, and have no major protocol deviations interfering with the assessment of the primary efficacy outcome measure. The administration of an IMP other than the randomised treatment will be considered a serious protocol deviation and will thus also lead to exclusion from the PPS. Subjects terminating their trial participation prior to the efficacy assessments at the Week 4/Day 29 visit due to efficacy or tolerability issues will also be retained in the PPS unless other reasons for exclusion also apply.

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomised subjects who receive at least one dose of the study medication will be included in the safety evaluation set (SES). Subjects will be analyzed for safety according to the investigational treatment that they have actually received.

Primary: FAS - Mean % change from baseline in PASI

End point title	FAS - Mean % change from baseline in PASI

End point description:

End point type	Primary

End point timeframe:

From study day 1 to study day 29

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	121	39	
Units: -100				
least squares mean (confidence interval	-58.1 (-62.5 to	-59.8 (-64.2 to	-21.8 (-30.0 to	

95%)	-53.7)	-55.3)	-13.5)

Statistical analyses

Statistical analysis title	MMRM - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	7.9
Variability estimate	Standard error of the mean
Dispersion value	3.2

Statistical analysis title	MMRM - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-36.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.7
upper limit	-27
Variability estimate	Standard error of the mean
Dispersion value	4.7

Primary: PPS -Mean % change from baseline in PASI

End point title	PPS -Mean % change from baseline in PASI

End point description:

End point type	Primary

End point timeframe:

From study day 1 to study day 29

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	103	32	
Units: -100				
least squares mean (confidence interval 95%)	-57.7 (-62.5 to -53.0)	-59.6 (-64.4 to -54.7)	-23.2 (-32.2 to -14.2)	

Statistical analyses

Statistical analysis title	MMRM - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	8.6
Variability estimate	Standard error of the mean
Dispersion value	3.4

Statistical analysis title	MMRM - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-34.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.7
upper limit	-24.3
Variability estimate	Standard error of the mean
Dispersion value	5.2

Secondary: FAS - Improvement in IGA

End point title	FAS - Improvement in IGA

End point description:

End point type	Secondary

End point timeframe:

From study day 1 to study day 29

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	120	33	
Units: subjects				
Responder	95	93	10	
Non-Responder	28	27	23	

Statistical analyses

Statistical analysis title	MI - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Odds ratio (OR)
Point estimate	0.959
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.517
upper limit	1.778

Statistical analysis title	MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	8.667

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.496
upper limit	21.487

Secondary: PPS - Improvement in IGA

End point title	PPS - Improvement in IGA

End point description:

End point type	Secondary

End point timeframe:

From study day 1 to study day 29

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	103	32	
Units: subjects				
Responder	84	81	9	
Non-Responder	25	22	19	

Statistical analyses

Statistical analysis title	MI - Eqilvalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Odds ratio (OR)
Point estimate	0.896
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.463
upper limit	1.732

Statistical analysis title	MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	8.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.162
upper limit	25.223

Secondary: FAS mPASI Subgroup - Mean % change from baseline in mPASI Week 4

End point title	FAS mPASI Subgroup - Mean % change from baseline in mPASI Week 4

End point description:

End point type	Secondary

End point timeframe:

From study day 1 to study day 29

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	107	39	
Units: -100				
least squares mean (confidence interval 95%)	-55.59 (-60.51 to -50.68)	-58.69 (-63.67 to -53.71)	-19.81 (-28.51 to -11.12)	

Statistical analyses

Statistical analysis title	ANCOVA MI - Eqivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.89
upper limit	10.08

Variability estimate	Standard error of the mean
Dispersion value	3.55

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-35.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.76
upper limit	-25.8
Variability estimate	Standard error of the mean
Dispersion value	5.07

Secondary: PPS mPASI Sungroup - Mean % change from baseline in mPASI Week 4

End point title	PPS mPASI Sungroup - Mean % change from baseline in mPASI Week 4
End point description:	
End point type	Secondary
End point timeframe:	
From study day 1 to study day 29	

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	90	32	
Units: -100				
least squares mean (confidence interval 95%)	-55.07 (-60.38 to -49.76)	-58.32 (-63.83 to -52.81)	-21.14 (-30.70 to -11.59)	

Statistical analyses

Statistical analysis title	ANCOVA MI - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	3.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.41
upper limit	10.91
Variability estimate	Standard error of the mean
Dispersion value	3.89

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-33.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.84
upper limit	-23.01
Variability estimate	Standard error of the mean
Dispersion value	5.53

Secondary: FAS mPASI Subgroup - Mean % change from baseline in mPASI Week 8

End point title	FAS mPASI Subgroup - Mean % change from baseline in mPASI Week 8

End point description:

End point type	Secondary

End point timeframe:

From study day 1 to study day 56

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	107	39	
Units: -100				
least squares mean (confidence interval	-63.18 (-68.68	-67.01 (-72.58	-22.00 (-32.41	

95%)	to -57.69)	to -61.44)	to -11.58)

Statistical analyses

Statistical analysis title	ANCOVA MI - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	3.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.98
upper limit	11.64
Variability estimate	Standard error of the mean
Dispersion value	3.97

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic vehicle v Generic calcipotriol-betamethasone gel
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-41.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.95
upper limit	-29.43
Variability estimate	Standard error of the mean
Dispersion value	5.96

Secondary: PPS mPASI Subgroup - Mean % change from baseline in mPASI Week 8

End point title	PPS mPASI Subgroup - Mean % change from baseline in mPASI Week 8

End point description:

End point type	Secondary

End point timeframe:

From study day 1 to study day 56

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	90	32	
Units: -100				
least squares mean (confidence interval 95%)	-63.86 (-69.76 to -57.95)	-67.14 (-73.26 to -61.02)	-22.08 (-33.36 to -10.8)	

Statistical analyses

Statistical analysis title	ANCOVA MI - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	3.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.23
upper limit	11.8
Variability estimate	Standard error of the mean
Dispersion value	4.32

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-41.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.47
upper limit	-29.07
Variability estimate	Standard error of the mean
Dispersion value	6.44

Secondary: PSSI Subgroup in FAS - Mean % change from baseline in PSSI	
End point title	PSSI Subgroup in FAS - Mean % change from baseline in PSSI
End point description:	

End point type	Secondary
End point timeframe:	
From study day 1 to study day 29	

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	70	22	
Units: -100				
least squares mean (confidence interval 95%)	-66.4 (-75.5 to -57.4)	-65.8 (-75.2 to -56.3)	-33.3 (-50.7 to -15.9)	

Statistical analyses

Statistical analysis title	ANCOVA MI - Equivalence
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	12.3
Variability estimate	Standard error of the mean
Dispersion value	6.6

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-33.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.6
upper limit	-13.6
Variability estimate	Standard error of the mean
Dispersion value	9.9

Secondary: PSSI Subgroup in PPS - Mean % change from baseline in PSSI

End point title	PSSI Subgroup in PPS - Mean % change from baseline in PSSI
End point description:	
End point type	Secondary
End point timeframe:	
From study day 1 to study day 29	

End point values	Generic calcipotriol-betamethasone gel	Daivobet gel	Generic vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	59	19	
Units: -100				
least squares mean (confidence interval 95%)	-66.3 (-76.0 to -56.5)	-65.5 (-76.0 to -55.0)	-27.8 (-47.2 to -8.3)	

Statistical analyses

Statistical analysis title	ANCOVA MI - Equivalnce
Comparison groups	Generic calcipotriol-betamethasone gel v Daivobet gel
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.1
upper limit	13.6
Variability estimate	Standard error of the mean
Dispersion value	7.2

Statistical analysis title	ANCOVA MI - Superiority
Comparison groups	Generic calcipotriol-betamethasone gel v Generic vehicle
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-38.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.2
upper limit	-16.8
Variability estimate	Standard error of the mean
Dispersion value	11

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From study day 1 to study day 56	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Generic Cal/Bet gel
Reporting group description: -	
Reporting group title	Daivobet gel
Reporting group description: -	
Reporting group title	Generic vehicle gel
Reporting group description: -	

Serious adverse events	Generic Cal/Bet gel	Daivobet gel	Generic vehicle gel
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 124 (0.81%)	4 / 123 (3.25%)	0 / 39 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive breast carcinoma			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sensitisation			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cholecystitis infective			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Generic Cal/Bet gel	Daivobet gel	Generic vehicle gel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 124 (16.94%)	22 / 123 (17.89%)	10 / 39 (25.64%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Renal neoplasm			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 124 (1.61%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Application site pruritus			

subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
General physical health deterioration			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 124 (0.00%)	2 / 123 (1.63%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 124 (3.23%)	2 / 123 (1.63%)	1 / 39 (2.56%)
occurrences (all)	5	2	1
Sciatica			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Eye irritation			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Occular hyperaemia			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			

subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 124 (0.81%)	1 / 123 (0.81%)	2 / 39 (5.13%)
occurrences (all)	1	1	2
Psoriasis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	4 / 39 (10.26%)
occurrences (all)	0	1	4
Pruritus generalised			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Skin burning sensation			
subjects affected / exposed	2 / 124 (1.61%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Skin irritation			
subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	5	0
Back pain			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 124 (0.00%)	2 / 123 (1.63%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Osteoarthritis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	3	0
Psoriatic arthropathy			

subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 124 (1.61%)	3 / 123 (2.44%)	1 / 39 (2.56%)
occurrences (all)	2	4	1
Oral herpes			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	2	0	0
Pulpitis dental			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 124 (0.00%)	0 / 123 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 124 (0.81%)	2 / 123 (1.63%)	1 / 39 (2.56%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	1 / 124 (0.81%)	1 / 123 (0.81%)	0 / 39 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 124 (0.81%)	0 / 123 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			

subjects affected / exposed occurrences (all)	1 / 124 (0.81%) 1	1 / 123 (0.81%) 1	0 / 39 (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