



## Clinical trial results:

**Double-blind, randomised clinical study comparing efficacy and safety of Gentamicin 0.1%\_Betamethasone 0.05% Cream (Test) vs. Diprogenta (R) Cream (Reference) vs. Vehicle in patients with bacterial infected eczema**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-005518-44  |
| Trial protocol           | DE              |
| Global end of trial date | 11 January 2017 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 11 January 2022 |
| First version publication date | 11 January 2022 |

### Trial information

#### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | 15-01/GentaBet-C |
|-----------------------|------------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Dermapharm AG  |
| Sponsor organisation address | Lil-Dagover-Ring 7, Grünwald, Germany, 82031   |
| Public contact               | Clinical Research Department, Dermapharm AG, +49 089641860, Clinicaltrials.Dermapharm@dermapharm.com |
| Scientific contact           | Clinical Research Department, Dermapharm AG, +49 089641860, Clinicaltrials.Dermapharm@dermapharm.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                       | 09 November 2017 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 January 2017  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 11 January 2017  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Assessment of efficacy and safety of a new cream with gentamicin 0.1% and betamethasone dipropionate 0.05% in comparison with the approved preparation Diprogenta(R) Cream and the underlying vehicle in patients with bacterial infected eczema.

Protection of trial subjects:

There were no specific measures necessary.

Background therapy:

There was no background therapy.

Evidence for comparator:

The trial aimed to show comparable efficacy and safety to the comparator in order to obtain a generic marketing authorization for the test product.

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 04 November 2015 |
| 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: 401 |
| Worldwide total number of subjects   | 401          |
| EEA total number of subjects         | 401          |

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)                      | 343 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 51 |
| 85 years and over   | 7  |

## Subject disposition

### Recruitment

Recruitment details:

12 study centers in Germany; first patient first visit: 17 November 2015; last patient last visit: 11 January 2017

### Pre-assignment

Screening details:

Main criteria for inclusion:

Women and men  $\geq 18$  years of age; Diagnosis of "bacterial super-infected eczema" based on clinical symptoms in a treatment area between 5 and 25 cm<sup>2</sup>; at least moderately severe clinical picture with presence of the clinical parameter "exudate/ pus"

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Treatment Period               |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator, Monitor |

Blinding implementation details:

All study preparations were indistinguishable in terms of appearance and were filled in white tubes of identical appearance.

### Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| <b>Arm title</b>             | GentaBet Cream |

Arm description:

Test product

|  |   |
|--|---|
| Arm type                               | Experimental                              |
| Investigational medicinal product name | Gentamicin 0.1%_Betamethasone 0.05% Cream |
| Investigational medicinal product code | D07CC01                                   |
| Other name                             |   |
| Pharmaceutical forms                   | Cream                                     |
| Routes of administration               | Cutaneous use                             |

Dosage and administration details:

twice daily (in the morning and in the evening) at the affected area of the skin

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Diprogenta |
|------------------|------------|

Arm description:

Reference Product

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Diprogenta Cream  |
| Investigational medicinal product code | D07CC01           |
| Other name                             |                   |
| Pharmaceutical forms                   | Cream             |
| Routes of administration               | Cutaneous use     |

Dosage and administration details:

twice daily (in the morning and the evening) on the affected area of the skin

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Vehicle |
|------------------|---------|

Arm description: -

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|  |               |
|--|---------------|
| Investigational medicinal product name | Placebo       |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Cream         |
| Routes of administration               | Cutaneous use |

Dosage and administration details:

twice daily (in the morning and the evening) on the affected area of the skin

| Number of subjects in period 1 | GentaBet Cream | Diprogenta | Vehicle |
|--------------------------------|----------------|------------|---------|
| Started                        | 159            | 159        | 83      |
| Completed                      | 148            | 149        | 76      |
| Not completed                  | 11             | 10         | 7       |
| Consent withdrawn by subject   | 3              | 3          | -       |
| Adverse event, non-fatal       | 1              | 3          | -       |
| Lost to follow-up              | 4              | 2          | 3       |
| Lack of efficacy               | 2              | 1          | 2       |
| Protocol deviation             | 1              | 1          | 2       |

## Period 2

|                              |                                |
|------------------------------|--------------------------------|
| Period 2 title               | Follow-up Period               |
| Is this the baseline period? | No                             |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator, Monitor |

Blinding implementation details:

No treatment in the follow-up period.

## Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| Arm title                    | GentaBet Cream |

Arm description:

Test product

|  |   |
|--|---|
| Arm type                               | Experimental                              |
| Investigational medicinal product name | Gentamicin 0.1%_Betamethasone 0.05% Cream |
| Investigational medicinal product code | D07CC01                                   |
| Other name                             |   |
| Pharmaceutical forms                   | Cream                                     |
| Routes of administration               | Cutaneous use                             |

Dosage and administration details:

twice daily (in the morning and in the evening) at the affected area of the skin

|           |            |
|-----------|------------|
| Arm title | Diprogenta |
|-----------|------------|

|  |                   |
|--|-------------------|
| Arm description:                       |                   |
| Reference Product                      |                   |
| Arm type                               | Active comparator |
| Investigational medicinal product name | Diprogenta Cream  |
| Investigational medicinal product code | D07CC01           |
| Other name                             |                   |
| Pharmaceutical forms                   | Cream             |
| Routes of administration               | Cutaneous use     |

Dosage and administration details:

twice daily (in the morning and the evening) on the affected area of the skin

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Vehicle |
|------------------|---------|

Arm description: -

|  |               |
|--|---------------|
| Arm type                               | Placebo       |
| Investigational medicinal product name | Placebo       |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Cream         |
| Routes of administration               | Cutaneous use |

Dosage and administration details:

twice daily (in the morning and the evening) on the affected area of the skin

| <b>Number of subjects in period 2</b> | GentaBet Cream | Diprogenta | Vehicle |
|---------------------------------------|----------------|------------|---------|
| Started                               | 148            | 149        | 76      |
| Completed                             | 142            | 142        | 74      |
| Not completed                         | 6              | 7          | 2       |
| Consent withdrawn by subject          | 2              | 2          | -       |
| Complete healing at day 7             | 2              | 2          | -       |
| Lost to follow-up                     | 2              | 1          | -       |
| Lack of efficacy                      | -              | 2          | 2       |

## Baseline characteristics

### Reporting groups

|                                |                  |
|--------------------------------|------------------|
| Reporting group title          | Treatment Period |
| Reporting group description: - |                  |

| Reporting group values                             | Treatment Period | Total |  |
|--|------------------|-------|--|
| Number of subjects                                 | 401              | 401   |  |
| 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)                               | 334              | 334   |  |
| From 65-84 years                                   | 47               | 47    |  |
| 85 years and over                                  | 6                | 6     |  |
| Not recorded                                       | 14               | 14    |  |
| Gender categorical                                 |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| Female   | 198              | 198   |  |
| Male   | 203              | 203   |  |

### Subject analysis sets

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | ITT                |
| Subject analysis set type  | Intention-to-treat |

Subject analysis set description:

Includes all patients of the safety data set who provide the baseline value and at least one post-baseline value of the symptom score.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Safety data set |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

comprises all patients who had administered the study medication at least once

|                            |              |
|----------------------------|--------------|
| Subject analysis set title | PP           |
| Subject analysis set type  | Per protocol |

Subject analysis set description:

includes all patients of the ITT data set who do not exhibit any major protocol violation

| Reporting group values                             | ITT | Safety data set | PP  |
|--|-----|-----------------|-----|
| Number of subjects                                 | 387 | 387             | 357 |
| 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)                     | 334 | 334 | 309 |
| From 65-84 years                         | 47  | 47  | 43  |
| 85 years and over                        | 6   | 6   | 5   |
| Not recorded                             | 0   | 0   | 0   |
| Gender categorical                       |     |     |     |
| Units: Subjects                          |     |     |     |
| Female                                   | 192 | 192 | 184 |
| Male                                     | 195 | 195 | 173 |



## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | GentaBet Cream     |
| Reporting group description:   |                    |
| Test product   |                    |
| Reporting group title  | Diprogenta         |
| Reporting group description:   |                    |
| Reference Product  |                    |
| Reporting group title  | Vehicle            |
| Reporting group description: -   |                    |
| Reporting group title  | GentaBet Cream     |
| Reporting group description:   |                    |
| Test product   |                    |
| Reporting group title  | Diprogenta         |
| Reporting group description:   |                    |
| Reference Product  |                    |
| Reporting group title  | Vehicle            |
| Reporting group description: -   |                    |
| Subject analysis set title   | ITT                |
| Subject analysis set type  | Intention-to-treat |
| Subject analysis set description:  |                    |
| Includes all patients of the safety data set who provide the baseline value and at least one post-baseline value of the symptom score. |                    |
| Subject analysis set title   | Safety data set    |
| Subject analysis set type  | Safety analysis    |
| Subject analysis set description:  |                    |
| comprises all patients who had administered the study medication at least once   |                    |
| Subject analysis set title   | PP                 |
| Subject analysis set type  | Per protocol       |
| Subject analysis set description:  |                    |
| includes all patients of the ITT data set who do not exhibit any major protocol violation  |                    |

### Primary: Treatment effect

|  |                  |
|--|------------------|
| End point title  | Treatment effect |
| End point description:   |                  |
| Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment |                  |
| End point type   | Primary          |
| End point timeframe:   |                  |
| start of treatment (visit 1) to end of treatment (visit 3)   |                  |

| End point values            | GentaBet Cream  | Diprogenta      | Vehicle         | ITT                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 140             | 142             | 78              | 309                  |
| Units: Number               | 127             | 124             | 46              | 268                  |

| End point values            | PP                   |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 282                  |  |  |  |
| Units: Number               | 251                  |  |  |  |

## Statistical analyses

| Statistical analysis title   | Analysis of efficacy           |
|--|--------------------------------|
| Statistical analysis description:  |                                |
| Non-Inferiority test (one-sided) with alpha = 0.025 and beta = 0.20, based on the PP data set. The Non-Inferiority margin was set to 0.1 (= 10%) |                                |
| Comparison groups  | Diprogenta v GentaBet Cream    |
| Number of subjects included in analysis  | 282                            |
| Analysis specification   | Pre-specified                  |
| Analysis type  | non-inferiority                |
| Parameter estimate   | Mean difference (final values) |
| Point estimate   | 0.0339                         |
| Confidence interval  |                                |
| level  | 95 %                           |
| sides  | 1-sided                        |
| lower limit  | -0.046                         |

## Other pre-specified: Superiority of Test over Vehicle

|  |   |
|--|---|
| End point title  | Superiority of Test over Vehicle <sup>[1]</sup> |
| End point description:   |   |
| Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment |   |
| End point type   | Other pre-specified                             |
| End point timeframe:   |   |
| start of treatment (visit 1) to end of treatment (visit 3)   |   |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis for this end point served as verification of the assay sensitivity and had to be done individually for each active preparation in accordance with CPMP/EWP/908/99.

| End point values            | GentaBet Cream  | Vehicle         | ITT                  |  |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type          | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed | 154             | 78              | 232                  |  |
| Units: Number               | 135             | 46              | 181                  |  |

## Statistical analyses

| Statistical analysis title  | Sensitivity analysis     |
|---|--------------------------|
| Statistical analysis description:   |                          |
| Superiority of the efficacy of Test over Vehicle for the primary variable |                          |
| Comparison groups   | GentaBet Cream v Vehicle |
| Number of subjects included in analysis                                   | 232                      |
| Analysis specification  | Pre-specified            |
| Analysis type   | superiority              |
| P-value   | < 0.0001                 |
| Method  | Fisher exact             |

## Other pre-specified: Superiority of Reference over Vehicle

|  |  |
|--|--|
| End point title  | Superiority of Reference over Vehicle <sup>[2]</sup> |
| End point description:   |  |
| Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment |  |
| End point type   | Other pre-specified                                  |
| End point timeframe:   |  |
| start of treatment (visit 1) to end of treatment (visit 3)   |  |

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis for this end point served as verification of the assay sensitivity and had to be done individually for each active preparation in accordance with CPMP/EWP/908/99.

| End point values            | Diprogenta      | Vehicle         | ITT                  |  |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type          | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed | 155             | 78              | 233                  |  |
| Units: Number               | 133             | 46              | 179                  |  |

## Statistical analyses

| Statistical analysis title   | Sensitivity analysis |
|--|----------------------|
| Statistical analysis description:  |                      |
| Superiority of the efficacy of Reference over Vehicle for the primary variable |                      |
| Comparison groups  | Vehicle v Diprogenta |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 233           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | Fisher exact  |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from the inclusion visit (visit 1) to the final visit (visit 4)

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | GentaBet Cream |
|-----------------------|----------------|

Reporting group description:

Test product

|                       |            |
|-----------------------|------------|
| Reporting group title | Diprogenta |
|-----------------------|------------|

Reporting group description:

Reference Product

|                       |         |
|-----------------------|---------|
| Reporting group title | Vehicle |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | GentaBet Cream  | Diprogenta      | Vehicle        |
|---|-----------------|-----------------|----------------|
| Total subjects affected by serious adverse events |                 |                 |                |
| subjects affected / exposed                       | 0 / 154 (0.00%) | 2 / 155 (1.29%) | 0 / 78 (0.00%) |
| number of deaths (all causes)                     | 0               | 0               | 0              |
| number of deaths resulting from adverse events    | 0               | 0               | 0              |
| Injury, poisoning and procedural complications    |                 |                 |                |
| Fall  |                 |                 |                |
| subjects affected / exposed                       | 0 / 154 (0.00%) | 1 / 155 (0.65%) | 0 / 78 (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          |
| Surgical and medical procedures                   |                 |                 |                |
| Hospitalisation                                   |                 |                 |                |
| subjects affected / exposed                       | 0 / 154 (0.00%) | 1 / 155 (0.65%) | 0 / 78 (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                          |                 |                 |                |
| Syncope   |                 |                 |                |
| subjects affected / exposed                       | 0 / 154 (0.00%) | 1 / 155 (0.65%) | 0 / 78 (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          |

Frequency threshold for reporting non-serious adverse events: 0.05 %

| <b>Non-serious adverse events</b>                                   | GentaBet Cream   | Diprogenta       | Vehicle        |
|---|------------------|------------------|----------------|
| Total subjects affected by non-serious adverse events               |                  |                  |                |
| subjects affected / exposed   | 11 / 154 (7.14%) | 11 / 155 (7.10%) | 3 / 78 (3.85%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |                |
| Seborrhoeic keratosis   |                  |                  |                |
| subjects affected / exposed   | 1 / 154 (0.65%)  | 0 / 155 (0.00%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 1                | 0                | 0              |
| Squamous cell carcinoma   |                  |                  |                |
| subjects affected / exposed   | 1 / 154 (0.65%)  | 0 / 155 (0.00%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 1                | 0                | 0              |
| Injury, poisoning and procedural complications                      |                  |                  |                |
| Contusion   |                  |                  |                |
| subjects affected / exposed   | 0 / 154 (0.00%)  | 1 / 155 (0.65%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 0                | 1                | 0              |
| Skin abrasion   |                  |                  |                |
| subjects affected / exposed   | 1 / 154 (0.65%)  | 0 / 155 (0.00%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 1                | 0                | 0              |
| Wound   |                  |                  |                |
| subjects affected / exposed   | 0 / 154 (0.00%)  | 1 / 155 (0.65%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 0                | 1                | 0              |
| Surgical and medical procedures                                     |                  |                  |                |
| Varicose vein operation   |                  |                  |                |
| subjects affected / exposed   | 0 / 154 (0.00%)  | 1 / 155 (0.65%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 0                | 1                | 0              |
| Nervous system disorders  |                  |                  |                |
| Headache  |                  |                  |                |
| subjects affected / exposed   | 1 / 154 (0.65%)  | 0 / 155 (0.00%)  | 0 / 78 (0.00%) |
| occurrences (all)   | 1                | 0                | 0              |
| Sciatica  |                  |                  |                |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 154 (0.00%)<br>0 | 1 / 155 (0.65%)<br>1 | 0 / 78 (0.00%)<br>0 |
| General disorders and administration<br>site conditions<br>Application site pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 154 (0.00%)<br>0 | 2 / 155 (1.29%)<br>2 | 0 / 78 (0.00%)<br>0 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 154 (0.65%)<br>1 | 0 / 155 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Eye disorders<br>Visual impairment<br>subjects affected / exposed<br>occurrences (all)   | 1 / 154 (0.65%)<br>1 | 0 / 155 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Toothache<br>subjects affected / exposed<br>occurrences (all)  | 1 / 154 (0.65%)<br>1 | 0 / 155 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Reproductive system and breast<br>disorders<br>Prostatitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 154 (0.00%)<br>0 | 1 / 155 (0.65%)<br>1 | 0 / 78 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal<br>disorders<br>Dysphonia<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 154 (0.65%)<br>1 | 0 / 155 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Eczema<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 154 (0.65%)<br>1 | 0 / 155 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Nail bed inflammation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 154 (0.00%)<br>0 | 1 / 155 (0.65%)<br>1 | 0 / 78 (0.00%)<br>0 |
| Seborrhoeic dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 154 (0.00%)<br>0 | 1 / 155 (0.65%)<br>1 | 0 / 78 (0.00%)<br>0 |
| Skin ulcer   |                      |                      |                     |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 154 (0.00%)<br>0 | 1 / 155 (0.65%)<br>1 | 0 / 78 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders  |                      |                      |                     |
| Back pain  |                      |                      |                     |
| subjects affected / exposed                      | 1 / 154 (0.65%)      | 0 / 155 (0.00%)      | 0 / 78 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Pain in extremity                                |                      |                      |                     |
| subjects affected / exposed                      | 0 / 154 (0.00%)      | 0 / 155 (0.00%)      | 1 / 78 (1.28%)      |
| occurrences (all)                                | 0                    | 0                    | 1                   |
| Infections and infestations                      |                      |                      |                     |
| Cellulitis                                       |                      |                      |                     |
| subjects affected / exposed                      | 1 / 154 (0.65%)      | 0 / 155 (0.00%)      | 0 / 78 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Impetigo   |                      |                      |                     |
| subjects affected / exposed                      | 1 / 154 (0.65%)      | 0 / 155 (0.00%)      | 0 / 78 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Oral herpes                                      |                      |                      |                     |
| subjects affected / exposed                      | 1 / 154 (0.65%)      | 0 / 155 (0.00%)      | 0 / 78 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Respiratory tract infection                      |                      |                      |                     |
| subjects affected / exposed                      | 0 / 154 (0.00%)      | 1 / 155 (0.65%)      | 2 / 78 (2.56%)      |
| occurrences (all)                                | 0                    | 1                    | 2                   |
| Tinea pedis                                      |                      |                      |                     |
| subjects affected / exposed                      | 1 / 154 (0.65%)      | 0 / 155 (0.00%)      | 0 / 78 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

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| None reported |
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Notes: