



## Clinical trial results:

**A double-blind, randomized, placebo-controlled, parallel-group study comparing safety and efficacy of Dorithricin® lozenges with placebo in the symptomatic treatment of patients with acute pharyngitis**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-003111-38 |
| Trial protocol           | DE             |
| Global end of trial date | 23 June 2016   |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 28 April 2022 |
| First version publication date | 28 April 2022 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | 6630-9050-03 |
|-----------------------|--------------|

#### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Medice Arzneimittel Pütter GmbH & Co. KG                                                        |
| Sponsor organisation address | Kuhloweg 37, Iserlohn, Germany, 58638                                                           |
| Public contact               | Medizinische Abteilung, Medice Arzneimittel Pütter GmbH & Co. KG, +49 023719370, dori@medice.de |
| Scientific contact           | Medizinische Abteilung, Medice Arzneimittel Pütter GmbH & Co. KG, +49 023719370, dori@medice.de |

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:

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**Results analysis stage**

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|                                                      |               |
|------------------------------------------------------|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 20 March 2017 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 23 June 2016  |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 23 June 2016  |
| Was the trial ended prematurely?                     | No            |

Notes:

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**General information about the trial**

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Main objective of the trial:

Safety and efficacy of Dorithricin® Halstabletten Classic (lozenges)

Protection of trial subjects:

Each study patient could be withdrawn from the study at any time. There was no detriment for the patient due to the discontinuation. The investigator should have tried to find out the reason for withdrawal, if possible. However, the patient was not obliged to disclose the reason for the withdrawal. The investigator could exclude patients from the study for one of the following reasons:

- Occurrence of unacceptable adverse events (definition: unacceptable according to patient's or investigator's assessment)
- Change in health conditions that put a patient at risk
- Investigator considered it medically necessary

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 11 January 2016 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 300 |
| Worldwide total number of subjects   | 300          |
| EEA total number of subjects         | 300          |

Notes:

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**Subjects enrolled per age group**

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|                                           |     |
|-------------------------------------------|-----|
| 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)                      | 286 |
| From 65 to 84 years                       | 14  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Overall, 311 adult male or female patients with acute pharyngitis were screened at 19 investigational study sites in Germany and gave their written informed consent for participation in this study. Eleven patients (3.5% of 311) were screening failures, and 300 patients were randomized to one of the two treatment groups

### 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, Carer, Assessor |

### Arms

|                                        |                           |
|----------------------------------------|---------------------------|
| Are arms mutually exclusive?           | Yes                       |
| <b>Arm title</b>                       | triple active combination |
| Arm description: -                     |                           |
| Arm type                               | Experimental              |
| Investigational medicinal product name | Dorithricin               |
| Investigational medicinal product code |                           |
| Other name                             |                           |
| Pharmaceutical forms                   | Lozenge                   |
| Routes of administration               | Oromucosal use            |

Dosage and administration details:

Patients of both treatment groups received up to 8 lozenges/day on Day 0, Day 1, Day 2, and Day 3. The number of lozenges taken on Day 0 and Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3). At Visit 1 (Day 0), the patients received the study medication and immediately administered an initial dose of 2 lozenges (to be taken all at once). Patients were instructed to administer subsequently 1 lozenge at intervals of 2 hrs ( $\pm$  15 minutes) up to a maximum of 8 lozenges per day.

The study medication was administered orally. A lozenge was to be sucked slowly until it fully dissolved in the mouth. This might have taken a couple of minutes.

Patients were instructed to administer study medication without interruption from Visit 1 to Visit 2 even if no symptoms of acute pharyngitis were present anymore

|                                        |                 |
|----------------------------------------|-----------------|
| <b>Arm title</b>                       | Placebo         |
| Arm description: -                     |                 |
| Arm type                               | Placebo         |
| Investigational medicinal product name | Placebo lozenge |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Lozenge         |
| Routes of administration               | Oromucosal use  |

Dosage and administration details:

Patients of both treatment groups received up to 8 lozenges/day on Day 0, Day 1, Day 2, and Day 3. The number of lozenges taken on Day 0 and Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3). At Visit 1 (Day 0), the patients received the study medication and immediately administered an initial dose of 2 lozenges (to be taken all at once). Patients were instructed to administer subsequently 1 lozenge at intervals of 2 hrs ( $\pm$  15 minutes) up to a maximum of 8 lozenges per day.

The study medication was administered orally. A lozenge was to be sucked slowly until it fully dissolved

in the mouth. This might have taken a couple of minutes. Patients were instructed to administer study medication without interruption from Visit 1 to Visit 2 even if no symptoms of acute pharyngitis were present anymore.

| <b>Number of subjects in period 1</b> | triple active combination | Placebo |
|---------------------------------------|---------------------------|---------|
| Started                               | 147                       | 153     |
| Completed                             | 141                       | 148     |
| Not completed                         | 6                         | 5       |
| Adverse event, non-fatal              | 4                         | 2       |
| Lost to follow-up                     | 1                         | -       |
| Protocol deviation                    | 1                         | 3       |

## Baseline characteristics

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | triple active combination |
|-----------------------|---------------------------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values                             | triple active combination | Placebo | Total |
|----------------------------------------------------|---------------------------|---------|-------|
| Number of subjects                                 | 147                       | 153     | 300   |
| Age categorical<br>Units: Subjects                 |                           |         |       |
| In utero                                           |                           |         | 0     |
| Preterm newborn infants (gestational age < 37 wks) |                           |         | 0     |
| Newborns (0-27 days)                               |                           |         | 0     |
| Infants and toddlers (28 days-23 months)           |                           |         | 0     |
| Children (2-11 years)                              |                           |         | 0     |
| Adolescents (12-17 years)                          |                           |         | 0     |
| Adults (18-64 years)                               |                           |         | 0     |
| From 65-84 years                                   |                           |         | 0     |
| 85 years and over                                  |                           |         | 0     |
| Age continuous<br>Units: years                     |                           |         |       |
| arithmetic mean                                    | 38.6                      | 39.5    |       |
| standard deviation                                 | ± 15.1                    | ± 14.9  | -     |
| Gender categorical<br>Units: Subjects              |                           |         |       |
| Female                                             | 88                        | 99      | 187   |
| Male                                               | 59                        | 54      | 113   |

## End points

### End points reporting groups

|                                |                           |
|--------------------------------|---------------------------|
| Reporting group title          | triple active combination |
| Reporting group description: - |                           |
| Reporting group title          | Placebo                   |
| Reporting group description: - |                           |
| Subject analysis set title     | FAS                       |
| Subject analysis set type      | Full analysis             |

Subject analysis set description:

The FAS for the efficacy analyses includes all randomized patients with at least one documented application of trial medication (Dorithricin® or placebo) and post-baseline efficacy data for the primary endpoint. Patients whose emergency envelopes were opened during the trial were excluded from the FAS.

### Primary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs and 78 hrs after first application

|                 |                                                                                                                                      |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title | percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs and 78 hrs after first application |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The primary endpoint variable was defined as the percentage of patients with complete resolution of throat pain and difficulty in swallowing 48 hrs and 72 hrs after first application of treatment. A complete resolution of throat pain and difficulty in swallowing was defined as complete disappearance of both pharyngitis symptoms with no subsequent reoccurrence of throat pain and difficulty in swallowing up to study end based on patient diary data.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

The primary endpoint variable was defined as the percentage of patients with complete resolution of throat pain and difficulty in swallowing 48 hrs and 72 hrs after first application of treatment.

| End point values            | triple active combination | Placebo         |  |  |
|-----------------------------|---------------------------|-----------------|--|--|
| Subject group type          | Reporting group           | Reporting group |  |  |
| Number of subjects analysed | 146                       | 153             |  |  |
| Units: patients             | 55                        | 58              |  |  |

### Statistical analyses

|                                         |                                                   |
|-----------------------------------------|---------------------------------------------------|
| Statistical analysis title              | complete resolution of throat pain and difficulty |
| Comparison groups                       | triple active combination v Placebo               |
| Number of subjects included in analysis | 299                                               |
| Analysis specification                  | Pre-specified                                     |
| Analysis type                           | superiority                                       |
| P-value                                 | = 0.9101                                          |
| Method                                  | repeated measurement model (GEE)                  |
| Parameter estimate                      | Difference between groups (%)                     |
| Point estimate                          | -0.6                                              |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -10.1   |
| upper limit         | 10      |

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**Secondary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs after first applikation**

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|                 |                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs after first applikation |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

48 hrs after first application of treatment

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| End point values            | triple active combination | Placebo         |  |  |
|-----------------------------|---------------------------|-----------------|--|--|
| Subject group type          | Reporting group           | Reporting group |  |  |
| Number of subjects analysed | 146                       | 153             |  |  |
| Units: patients             | 33                        | 39              |  |  |

**Statistical analyses**

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>       | free of symtoms after 48 hrs        |
| Comparison groups                       | triple active combination v Placebo |
| Number of subjects included in analysis | 299                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           | superiority                         |
| P-value                                 | = 0.5486                            |
| Method                                  | generalized estimation equation     |
| Parameter estimate                      | Difference between groups (%)       |
| Point estimate                          | -2.8                                |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -10.3                               |
| upper limit                             | 7.3                                 |

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**Secondary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 72hrs after first applikation**

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|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | percentage of patients with complete resolution of throat pain |
|-----------------|----------------------------------------------------------------|

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End point description:

End point type Secondary

End point timeframe:

72 hrs after first application of treatment

| End point values            | triple active combination | Placebo         |  |  |
|-----------------------------|---------------------------|-----------------|--|--|
| Subject group type          | Reporting group           | Reporting group |  |  |
| Number of subjects analysed | 146                       | 153             |  |  |
| Units: patients             | 86                        | 86              |  |  |

**Statistical analyses**

|                                         |                                     |
|-----------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>       | free of syptoms after 72 hrs        |
| Comparison groups                       | Placebo v triple active combination |
| Number of subjects included in analysis | 299                                 |
| Analysis specification                  | Pre-specified                       |
| Analysis type                           |                                     |
| P-value                                 | = 0.6383                            |
| Method                                  | generalized estimation equation     |
| Parameter estimate                      | Difference between groups (%)       |
| Point estimate                          | 2.8                                 |
| Confidence interval                     |                                     |
| level                                   | 95 %                                |
| sides                                   | 2-sided                             |
| lower limit                             | -9                                  |
| upper limit                             | 13.08                               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented by the investigator at each visit (Visit 1 and Visit 2). Additionally, patients were asked to document in the paper-based diary (before the administration of the last lozenge on Day 0, Day 1, Day 2, and Day 3).

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 18.1   |

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Dorithrcin |
|-----------------------|------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | Dorithrcin      | Placebo         |  |
|---------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 0 / 147 (0.00%) | 0 / 153 (0.00%) |  |
| number of deaths (all causes)                     | 0               | 0               |  |
| number of deaths resulting from adverse events    | 0               | 0               |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events                            | Dorithrcin        | Placebo           |  |
|-------------------------------------------------------|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 19 / 147 (12.93%) | 17 / 153 (11.11%) |  |
| Nervous system disorders                              |                   |                   |  |
| Headache                                              |                   |                   |  |
| subjects affected / exposed                           | 3 / 147 (2.04%)   | 7 / 153 (4.58%)   |  |
| occurrences (all)                                     | 3                 | 7                 |  |
| Gastrointestinal disorders                            |                   |                   |  |
| Diarrhoea                                             |                   |                   |  |
| subjects affected / exposed                           | 3 / 147 (2.04%)   | 2 / 153 (1.31%)   |  |
| occurrences (all)                                     | 3                 | 2                 |  |
| Nausea                                                |                   |                   |  |
| subjects affected / exposed                           | 2 / 147 (1.36%)   | 0 / 153 (0.00%)   |  |
| occurrences (all)                                     | 2                 | 0                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Cough                                           |                 |                 |  |
| subjects affected / exposed                     | 5 / 147 (3.40%) | 3 / 153 (1.96%) |  |
| occurrences (all)                               | 6               | 3               |  |
| Dysphonia                                       |                 |                 |  |
| subjects affected / exposed                     | 2 / 147 (1.36%) | 0 / 153 (0.00%) |  |
| occurrences (all)                               | 2               | 0               |  |
| Infections and infestations                     |                 |                 |  |
| Tonsillitis                                     |                 |                 |  |
| subjects affected / exposed                     | 2 / 147 (1.36%) | 3 / 153 (1.96%) |  |
| occurrences (all)                               | 2               | 3               |  |
| Rhinitis                                        |                 |                 |  |
| subjects affected / exposed                     | 2 / 147 (1.36%) | 3 / 153 (1.96%) |  |
| occurrences (all)                               | 2               | 3               |  |

## **More information**

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

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported