# Clinical trial results:
# Safety and intake effect of EPs®7630 (an extract from the roots of Pelargonium sidoides)

## Summary

| | |
|---|---|
| EudraCT number | 2013-004977-28 |
| Trial protocol | GB |
| Global end of trial date | 31 August 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 July 2018 |
| First version publication date | 01 July 2018 |
| Summary attachment (see zip file) | 701079.01.013 Summary of results 2016_09_07 (701079.01.013 Summary of Results_EudraCT_Version 1.0_mit Schwärzungen_20170907.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 701079.01.013 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | ISRCTN35425744 |
| ClinicalTrials.gov id (NCT number) | NCT02174653 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Dr. Willmar Schwabe GmbH & Co. KG |
| Sponsor organisation address | Willmar Schwabe Str. 4, Karlsruhe, Germany, 76227 |
| Public contact | Head Clinical Research, Dr. Willmar Schwabe GmbH & Co. KG, 0049 7214005573, |
| Scientific contact | Head Clinical Research, Dr. Willmar Schwabe GmbH & Co. KG, 0049 7214005573, |

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 | 29 January 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 July 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 August 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to investigate the occurrence of adverse drug reactions (ADRs) during the 4 months treatment, defined as the proportion of participants in each trial group with suspected adverse events.

Protection of trial subjects:

Possibility to withdraw consent. Monitoring of adverse Events and laboratory Parameters.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 27 March 2014 |
| 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 | United Kingdom: 798 |
| Worldwide total number of subjects | 798 |
| EEA total number of subjects | 798 |

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) | 797 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

n.a.

### Pre-assignment

Screening details:

Seventy eight participants were not randomized and did not receive the investigational product since they did not fulfill all in-/exclusion criteria.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 798 |
| Number of subjects completed | 683 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Screening Failures: 78 |
| Reason: Number of subjects | No Intake of Study Medication: 37 |

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | EPs® 7630 |

Arm description:

EPs® 7630 3x20 mg or 3x20/40 mg film-coated tablets

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | EPs® 7630 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

3x20 mg / 3x40 mg

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Placebo film-coated tablets

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

Dosage and administration details:

3x0 mg

| **Number of subjects in period 1[1]** | EPs® 7630 | Placebo |
|---|---|---|
| Started | 460 | 223 |
| Completed | 425 | 213 |
| Not completed | 35 | 10 |
| Adverse event, non-fatal | 2 | - |
| Other | 10 | 3 |
| Withdrawal of consent without giving the reason | 5 | - |
| Lost to follow-up | 18 | 7 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 78 Screening Failures and 37 subjects with no intake of study medication.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | EPs® 7630 |
| Reporting group description: | |
| EPs® 7630 3x20 mg or 3x20/40 mg film-coated tablets | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo film-coated tablets | |

| Reporting group values | EPs® 7630 | Placebo | Total |
|---|---|---|---|
| Number of subjects | 460 | 223 | 683 |
| Age categorical<br>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) | 459 | 223 | 682 |
| From 65-84 years | 1 | 0 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 21.7 | 21 | |
| standard deviation | ± 6.6 | ± 5 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 291 | 148 | 439 |
| Male | 169 | 75 | 244 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Safety Analysis set | |

| Reporting group values | Safety analysis set | | |
|---|---|---|---|
| Number of subjects | 683 | | |
| 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) | 682 | | |
| From 65-84 years | 1 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 21.5 | | |
| standard deviation | ± 6.1 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 439 | | |
| Male | 244 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | EPs® 7630 |
| Reporting group description: EPs® 7630 3x20 mg or 3x20/40 mg film-coated tablets | |
| Reporting group title | Placebo |
| Reporting group description: Placebo film-coated tablets | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Safety Analysis set | |

### Primary: Occurrence of adverse drug reactions (ADRs) during the 4 months treatment, defined as the proportion of participants in each trial group with suspected adverse events

| | |
|---|---|
| End point title | Occurrence of adverse drug reactions (ADRs) during the 4 months treatment, defined as the proportion of participants in each trial group with suspected adverse events |
| End point description: Note: Occurrence of adverse drug reactions is the primary pre-specified endpoint. See document for a complete description of the endpoints. | |
| End point type | Primary |
| End point timeframe: Baseline and End of Treatment (4 month Treatment Period) | |

| End point values | EPs® 7630 | Placebo | Safety analysis set | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 460 | 223 | 683 | |
| Units: Number of ADR | | | | |
| number (not applicable) | 89 | 43 | 132 | |

### Statistical analyses

| Statistical analysis title | Occurence of adverse drug reactions |
|---|---|
| Comparison groups | EPs® 7630 v Placebo |
| Number of subjects included in analysis | 683 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Risk difference (RD) % |
| Point estimate | 0.07 |

| Confidence interval | |
|---|---|
| level | Other: 97.5 % |
| sides | 1-sided |
| upper limit | 6.4 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: 4 Months | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18 |

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: Placebo | |
| Reporting group title | EPs®7630 |
| Reporting group description: EPs®7630 | |

| Serious adverse events | Placebo | EPs®7630 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 223 (0.00%) | 3 / 460 (0.65%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 223 (0.00%) | 1 / 460 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 223 (0.00%) | 1 / 460 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 0 / 223 (0.00%) | 1 / 460 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | Placebo | EPs®7630 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 65 / 223 (29.15%) | 135 / 460 (29.35%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 40 / 223 (17.94%) | 82 / 460 (17.83%) | |
| occurrences (all) | 95 | 198 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 14 / 223 (6.28%) | 36 / 460 (7.83%) | |
| occurrences (all) | 27 | 53 | |
| Nausea | | | |
| subjects affected / exposed | 13 / 223 (5.83%) | 18 / 460 (3.91%) | |
| occurrences (all) | 15 | 28 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 13 / 223 (5.83%) | 20 / 460 (4.35%) | |
| occurrences (all) | 20 | 30 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 31 / 223 (13.90%) | 33 / 460 (7.17%) | |
| occurrences (all) | 48 | 49 | |

## 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