Clinical trial results:
Safety and tolerability of Pelargonium sidoides extract EPs® 7630 in children (1 to 5 years old) suffering from acute bronchitis

Summary

EudraCT number	2011-002652-14
Trial protocol	DE
Global end of trial date	15 July 2013

Results information

Result version number	v1 (current)
This version publication date	30 September 2018
First version publication date	30 September 2018
Summary attachment (see zip file)	701003.01.010 Summary of results of postin in eudra Ct database V1.0 2018_09_14 (701003.01.010_SummaryOfResults_EUDRA_CT_Version 1.0_mit Schwärzungen_20180914.pdf)

Trial information

Trial identification

Sponsor protocol code	701003.01.010

Additional study identifiers

ISRCTN number	ISRCTN77419032
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. Willmar Schwabe GmbH & Co. KG
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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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 April 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 April 2012
Global end of trial reached?	Yes
Global end of trial date	15 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of a treatment with EPs® 7630 syrup in comparison to EPs® 7630 solution in patients between 1 and 5 years old suffering from acute bronchitis.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2011
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: 602
Worldwide total number of subjects	602
EEA total number of subjects	602

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)	110
Children (2-11 years)	492
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were recruited in 35 investigational sites. All 602 subjects were randomized.

Pre-assignment period milestones

Number of subjects started	602
Number of subjects completed	602

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	EPs® 7630 syrup

Arm description:

100 g (= 93.985 ml) syrup contain: Herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10), dried.

Eight randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

Arm type	Active comparator
Investigational medicinal product name	EPs® 7630 syrup
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

2.5 ml syrup three times daily for 7 consecutive days (SMC 7651, batch no. 0201101)

Arm title	EPs® 7630 solution

Arm description:

10 g (= 9.75 mL) of oral solution contain 8.0 g herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10) (EPs® 7630)

Three randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

Arm type	Active comparator
Investigational medicinal product name	EPs® 7630 solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:
10 drops three times daily for 7 consecutive days (SMC 7521, batch no. 0201102)

Number of subjects in period 1	EPs® 7630 syrup	EPs® 7630 solution
Started	411	191
Completed	387	178
Not completed	24	13
Consent withdrawn by subject	1	3
Adverse event, non-fatal	4	-
Other specifications	19	10

Baseline characteristics

Reporting groups

Reporting group title	EPs® 7630 syrup

Reporting group description:

100 g (= 93.985 ml) syrup contain: Herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10), dried.

Eight randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

Reporting group title	EPs® 7630 solution

Reporting group description:

10 g (= 9.75 mL) of oral solution contain 8.0 g herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10) (EPs® 7630)

Three randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

Reporting group values	EPs® 7630 syrup	EPs® 7630 solution	Total
Number of subjects	411	191	602
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)	73	37	110
Children (2-11 years)	338	154	492
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	3.03	2.97	
standard deviation	± 1.34	± 1.39	-
Gender categorical Units: Subjects			
Female	192	86	278
Male	219	105	324

Subject analysis sets

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

Subject analysis set description:

The safety analysis set (SAF) included all subjects having taken their randomised EPs® 7630 medication at least once. The safety analysis set corresponded with the full analysis set (FAS).

Reporting group values	Safety analysis set		
Number of subjects	591		
Age categorical			
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)	108		
Children (2-11 years)	483		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	3.01		
standard deviation	± 1.35		
Gender categorical			
Units: Subjects			
Female	275		
Male	316		

End points

End points reporting groups

Reporting group title	EPs® 7630 syrup

Reporting group description:

100 g (= 93.985 ml) syrup contain: Herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10), dried.

Eight randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

Reporting group title	EPs® 7630 solution

Reporting group description:

10 g (= 9.75 mL) of oral solution contain 8.0 g herbal drug preparation from the roots of Pelargonium sidoides (1 : 8 - 10) (EPs® 7630)

Three randomized children were drop-outs without any intake of the investigational product. These subjects were excluded from the safety analysis set. The full analysis set corresponded with the safety analysis set.

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

Subject analysis set description:

The safety analysis set (SAF) included all subjects having taken their randomised EPs® 7630 medication at least once. The safety analysis set corresponded with the full analysis set (FAS).

This document in its section "End points" specifies commercially confidential information of Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe referred to in Article 81 Section (4) b) Regulation (EU) 536/2014 that is a trade secret and released by the holder for purposes of Regulation (EU) 536/2014 only under the condition of confidence. Trade secrets may not - even in part - be published or released to third parties other than to competent authorities without express permission of the trade secret holder.

Primary: Number of subjects with adverse events related to gastrointestinal complaints

End point title	Number of subjects with adverse events related to gastrointestinal complaints

End point description:

Note: Number of subjects with adverse events related to gastrointestinal complaints is one of several pre-specified endpoints. See document for a complete description of the endpoints.

Codes related to gastrointestinal complaints according to MedDRA Version 14:
(10000059), (10000081), (10000084), (10000087), (10000133), (10010774), (10012735), (10013781), (10013911), (10013946), (10013950), (10014866), (10015137), (10016101), (10016766), (10017367), (10017888), (10017944), (10028813), (10030973), (10042101), (10043951), (10047700), (10048714), (10052402), (10053155), (10056819), (10060961)

End point type	Primary

End point timeframe:

Baseline and End of Treatment (Day 7)

End point values	EPs® 7630 syrup	EPs® 7630 solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	188		
Units: Subjects				
Subjects affected	13	6		

Statistical analyses

Statistical analysis title	Chi-squared test for risk difference

Statistical analysis description:

For each of the treatment arms the relative frequencies of patients with AEs and adverse drug reactions of the mentioned system group are estimated.

In addition a 95% confidence interval is calculated for the risk difference according to Newcombe.

Comparison groups	EPs® 7630 syrup v EPs® 7630 solution
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.982 [2]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.0003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.038
upper limit	0.0284

Notes:

[1] - Difference between treatment arms

[2] - two-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 14 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14

Reporting groups	
Reporting group title	EPs(R) 7630 Syrup
Reporting group description: Pelargonium extract	
Reporting group title	EPs(R) 7630 Solution
Reporting group description: Pelargonium extract	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The were no preferred Terms affected by more than than frequeny threshold of 5%.

Serious adverse events	EPs(R) 7630 Syrup	EPs(R) 7630 Solution	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 403 (0.00%)	1 / 188 (0.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 403 (0.00%)	1 / 188 (0.53%)	
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	EPs(R) 7630 Syrup	EPs(R) 7630 Solution	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 403 (0.00%)	0 / 188 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None reported

Notes: