Clinical trial results:
Therapeutic clinical trial of three types of “Phlogosol concentrate for gargle” products, comparing their efficacy in reducing different inflammations of the oral cavity.
(Changing the active ingredient of “Phlogosol concentrate for gargle” of oral cavity from hexachlorophene to chlorhexidine, the two products with different active ingredients in a non-inferiority clinical trial in comparison to the third control product.)

Summary

EudraCT number	2013-002190-22
Trial protocol	HU
Global end of trial date	21 October 2014

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	Phlogosol_2013/01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	PannonPharma Ltd.
Sponsor organisation address	PannonPharma ut 1., Pecsvarad, Hungary, 7720
Public contact	Head of Research and Development Department, PannonPharma Ltd., clinical.trials@pannonpharma.hu
Scientific contact	Head of Research and Development Department, PannonPharma Ltd., clinical.trials@pannonpharma.hu

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	16 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2014
Global end of trial reached?	Yes
Global end of trial date	21 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cure or healing improvement in inflammations of oral cavity mucosa

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, and ethical principles stated in the Declaration of Helsinki. All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 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	Hungary: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	62
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 1 investigational site located in Hungary, from 11 Aug 2014 to 21 Oct 2014.

Pre-assignment

Screening details:

Patients of both sexes aged 18 years or older suffering from local inflammatory changes of the oral cavity

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phlogosol Solution

Arm description:

Subject who received Phlogosol Solution with 30 mg/ml sodium samarium disulfosalicylate active substance and 1 mg/ml hexachlorophene antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Arm type	Active comparator
Investigational medicinal product name	Phlogosol Solution for external use only
Investigational medicinal product code	
Other name	Phlogosol külsőleges oldat
Pharmaceutical forms	Concentrate for gargle
Routes of administration	Oromucosal use, Oropharyngeal use

Dosage and administration details:

Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Arm title	Phlogosol Uno

Arm description:

Subject who received Phlogosol Uno with 30 mg/ml sodium samarium disulfosalicylate active substance without antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Arm type	Active comparator
Investigational medicinal product name	Phlogosol Uno 30 mg/ml concentrate for gargle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for gargle
Routes of administration	Oromucosal use, Oropharyngeal use

Dosage and administration details:

Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Arm title	Phlogosol Duo

Arm description:

Subject who received Phlogosol Duo with 30 mg/ml sodium samarium disulfosalicylate active substance and 2 mg/ml chlorhexidine gluconate antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Arm type	Experimental
Investigational medicinal product name	Phlogosol Duo 30 mg/2 mg/ml concentrate for gargle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for gargle
Routes of administration	Oromucosal use, Oropharyngeal use

Dosage and administration details:

Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Number of subjects in period 1	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo
Started	26	28	26
Completed	25	25	25
Not completed	1	3	1
Protocol deviation	1	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Phlogosol Solution
Reporting group description:	
Subject who received Phlogosol Solution with 30 mg/ml sodium samarium disulfosalicylate active substance and 1 mg/ml hexachlorophene antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	
Reporting group title	Phlogosol Uno
Reporting group description:	
Subject who received Phlogosol Uno with 30 mg/ml sodium samarium disulfosalicylate active substance without antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	
Reporting group title	Phlogosol Duo
Reporting group description:	
Subject who received Phlogosol Duo with 30 mg/ml sodium samarium disulfosalicylate active substance and 2 mg/ml chlorhexidine gluconate antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	

Reporting group values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo
Number of subjects	26	28	26
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)	21	23	18
From 65-84 years	5	5	8
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	46.12	46.54	49.35
standard deviation	± 21.087	± 21.049	± 19.978
Gender categorical Units: Subjects			
Female	19	15	16
Male	6	10	9
Not recorded	1	3	1

Reporting group values	Total		
Number of subjects	80		
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)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	62		
From 65-84 years	18		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	50		
Male	25		
Not recorded	5		

End points

End points reporting groups

Reporting group title	Phlogosol Solution

Reporting group description:

Subject who received Phlogosol Solution with 30 mg/ml sodium samarium disulfosalicylate active substance and 1 mg/ml hexachlorophene antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Reporting group title	Phlogosol Uno

Reporting group description:

Subject who received Phlogosol Uno with 30 mg/ml sodium samarium disulfosalicylate active substance without antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Reporting group title	Phlogosol Duo

Reporting group description:

Subject who received Phlogosol Duo with 30 mg/ml sodium samarium disulfosalicylate active substance and 2 mg/ml chlorhexidine gluconate antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.

Primary: Reduction in the size of inflamed area

End point title	Reduction in the size of inflamed area

End point description:

Area of inflammation in oral cavity was measured at Baseline (Visit 1) and after 7 days treatment (Visit 2). Changing in size of inflamed area from Visit 1 to Visit 2 was calculated. Negative values show decrease and positive values show increase in size of inflamed area, 0 represents no change.

End point type	Primary

End point timeframe:

From Baseline (Visit 1) to Day 7 (Visit 2)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	23	25	
Units: mm				
arithmetic mean (standard deviation)	-4.91 (± 9.113)	-5.67 (± 8.146)	-5.52 (± 7.886)	

Statistical analyses

Statistical analysis title	Non-inferiority analysis

Statistical analysis description:

Since data from different groups did not show normal distributions, in order to comparison of reduction in the size of inflamed area in group-pairs Mann-Whitney U-test (nonparametric counterpart of unpaired sample t-test) was used. Because of multiple comparisons Bonferroni correction was applied. Primary end point was to investigate non-inferiority of Phlogosol Duo and Phlogosol Solution. P-values for other group-pair comparisons see in Notes.

Comparison groups	Phlogosol Solution v Phlogosol Uno v Phlogosol Duo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.45 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - P-value for Phlogosol solution and Phlogosol Uno comparison p=0.500
P-value for Phlogosol Duo and Phlogosol Uno comparison p=0.702
Significance threshold is p<0.017 with Bonferroni correction

Secondary: Extent, painfulness and degree of inflammation

End point title	Extent, painfulness and degree of inflammation

End point description:

Extent, painfulness and degree of inflammation were assessed at Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point type	Secondary

End point timeframe:

At Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	25	25	
Units: number of subjects				
significantly decreased	10	11	15	
decreased	8	10	8	
unchanged	5	3	2	
worsened	2	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Status of oral hygiene

End point title	Status of oral hygiene

End point description:

Status of oral hygiene was assessed at Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point type	Secondary

End point timeframe:

At Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	25	25	
Units: number of subjects				
good (Visit 1)	13	12	14	
moderate (Visit 1)	12	12	11	
inadequate (Visit 1)	0	1	0	
good (Visit 2)	15	16	18	
moderate (Visit 2)	10	8	7	
inadequate (Visit 2)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of pain

End point title	Degree of pain

End point description:

Degree of pain was assessed at Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point type	Secondary

End point timeframe:

At Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	25	24[2]	
Units: number of subjects				
No pain (Visit 1)	7	10	10	
Mild (Visit 1)	11	9	9	
Moderate (Visit 1)	6	5	5	
Severe (Visit 1)	1	1	1	
No pain (Visit 2)	20	19	16	
Mild (Visit 2)	3	5	7	
Moderate (Visit 2)	1	1	1	
Severe (Visit 2)	1	0	0	

Notes:

[2] - Visit 1 (N=25), Visit 2 (N=24)

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of pain on VAS (Visual analog scale)

End point title	Degree of pain on VAS (Visual analog scale)

End point description:

On the VAS scale: 0 cm = no pain and 10 cm = extreme pain

End point type	Secondary

End point timeframe:

At Baseline and during the 7 day period of treatment (Day 1-7)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[3]	25[4]	25	
Units: cm				
arithmetic mean (standard deviation)				
Baseline (N=25,25,25)	3.46 (± 2.304)	3.56 (± 2.805)	3.63 (± 2.428)	
Day 1 (N=25,25,25)	3.46 (± 2.304)	3.58 (± 2.841)	3.52 (± 2.21)	
Day 2 (N=25,25,25)	3.31 (± 2.452)	3.54 (± 2.71)	3.32 (± 2.191)	
Day 3 (N=24,25,25)	2.84 (± 2.098)	2.98 (± 2.593)	3.02 (± 2.187)	
Day 4 (N=24,25,25)	2.51 (± 1.973)	2.68 (± 2.364)	2.52 (± 2.03)	
Day 5 (N=23,25,25)	1.91 (± 1.305)	2.24 (± 1.837)	2.27 (± 1.726)	
Day 6 (N=23,24,25)	1.89 (± 1.333)	2 (± 1.841)	1.93 (± 1.633)	
Day 7 (N=23,24,25)	1.7 (± 1.358)	1.78 (± 1.903)	1.88 (± 1.655)	

Notes:

[3] - At the end of treatment N=23

[4] - At the end of treatment N=24

Statistical analyses

No statistical analyses for this end point

Secondary: Hyperaemia, Swelling, Erosio, Ulceratio

End point title	Hyperaemia, Swelling, Erosio, Ulceratio

End point description:

Incidence of Hyperaemia, Swelling, Erosio and Ulceration were assessed at Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point type	Secondary

End point timeframe:

At Baseline (Visit 1) and after 7 days treatment (Visit 2)

End point values	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	25	25	
Units: Incidence				
Hyperaemia (Visit 1)	25	25	25	
Swelling (Visit 1)	14	13	13	
Erosio (Visit 1)	3	6	5	
Ulceratio (Visit 1)	2	1	2	
Hyperaemia (Visit 2)	14	13	10	

Swelling (Visit 2)	9	6	7	
Erosio (Visit 2)	2	3	4	
Ulceratio (Visit 2)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the entire study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	Phlogosol Solution
Reporting group description:	
Subject who received Phlogosol Solution with 30 mg/ml sodium samarium disulfosalicylate active substance and 1 mg/ml hexachlorophene antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	
Reporting group title	Phlogosol Uno
Reporting group description:	
Subject who received Phlogosol Uno with 30 mg/ml sodium samarium disulfosalicylate active substance without antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	
Reporting group title	Phlogosol Duo
Reporting group description:	
Subject who received Phlogosol Duo with 30 mg/ml sodium samarium disulfosalicylate active substance and 2 mg/ml chlorhexidine gluconate antiseptic agent. Add 10 ml of investigational medicinal product to 1 dl water, rinsing for 1 minute three times daily after toothbrushing, for a period of 7 days.	

Serious adverse events	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 3.5 %

Non-serious adverse events	Phlogosol Solution	Phlogosol Uno	Phlogosol Duo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	1 / 28 (3.57%)	0 / 26 (0.00%)
General disorders and administration site conditions			
Application site dryness			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Application site redness			

subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Application site burn			
subjects affected / exposed	1 / 26 (3.85%)	1 / 28 (3.57%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Application site anaesthesia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	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