



## Clinical trial results:

**A monocentric, observer-blind, randomized clinical study using an abrasive wound model with an intra-individual comparison to investigate the wound healing properties of a topical wound healing product in comparison to untreated and a reference product in 36 healthy subjects.**

### Summary

EudraCT number	2014-001374-34
Trial protocol	DE
Global end of trial date	17 July 2014

### Results information

Result version number	v1 (current)
This version publication date	04 August 2016
First version publication date	04 August 2016
Summary attachment (see zip file)	Wound healing properties of a topical wound healing product (6630-0450-01 Synopsis.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	6630-0450-01
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#### 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	Medical Department OTC, MEDICE Arzneimittel Pütter GmbH & Co. KG, +49 023719370, info@medice.de
Scientific contact	Medical Department OTC, MEDICE Arzneimittel Pütter GmbH & Co. KG, +49 023719370, info@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:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 January 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 July 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was the comparison of the investigational product versus untreated on the size of the open wound area/crusts assessed by quantitative image analysis at the different assessment time points (Area Under the Curve (AUC) over time on relative differences to Baseline).

Protection of trial subjects:

At each visit at the test center from Day 1 on, the study nurse looked for signs of inflammation/infection (erythema, edema, pain, odor, non-healing, excessive exudates, hyperthermia) and/or allergic reactions (erythema, edema, itching). In case of signs for a strong allergic reaction or signs for strong inflammation/infection, the treatment of the respective test area had to be discontinued. The test area had to be follow-up for safety reasons as long as the allergic reaction or inflammation/infection was resolved or a stable condition was reached.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 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	Germany: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	36
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 42 healthy subjects were enrolled and screened. Excluded: not meeting inclusion/exclusion criteria (N=5) and Reserve (N=1). 36 subjects were randomised in this study.

### Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind <sup>[1]</sup>
Roles blinded	Monitor, Data analyst, Assessor, Investigator <sup>[2]</sup>

Blinding implementation details:

The trial was conducted under observer-blind conditions. Since there were untreated and treated areas and since the kind application and the dosage differed between the two test products, all persons (carer, subject) involved in the application were not blinded. Personnel responsible for the skin assessments and the visual & instrumental measurements including the investigator remained blinded.

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	Soventol Wund- und Heilgel

Arm description:

Soventol® Wund- und Heilgel is a certified medical device and is indicated for the treatment of acute and chronic wounds such as abrasions, cuts, scratches, laceration, blistering burns, and sunburns

Arm type	Experimental
Investigational medicinal product name	Soventol Wund- und Heilgel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

The investigational and reference products were applied twice daily (mornings and evenings) on the abrasive wounds on the left volar forearm. The test areas were then covered with a standard plaster. On study days with visits at the test center (Days 1, 3, 5, 8, 9, 10, and 12) the first daily application was done by a technician after instrumental measurements and visual assessments. The second daily application was done by the subjects at home (evening). On Days 2, 4, 6, 7, 11, 13, and 14 the test products were applied by the subjects themselves at home according to the instruction by a technician. Applications were always performed between 8 and 11 a.m. in the morning and 8 and 11 p.m. in the evening.

<b>Arm title</b>	Bepanthen Wund- und Heilsalbe
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Arm description:

Indications for Bepanthen® Wund- und Heilsalbe are promotion of healing in superficial minor skin and mucosa injuries

Arm type	Active comparator
Investigational medicinal product name	Bepanthen Wund- und Heilsalbe
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

The investigational and reference products were applied twice daily (mornings and evenings) on the abrasive wounds on the left volar forearm. The test areas were then covered with a standard plaster. On

study days with visits at the test center (Days 1, 3, 5, 8, 9, 10, and 12) the first daily application was done by a technician after instrumental measurements and visual assessments. The second daily application was done by the subjects at home (evening). On Days 2, 4, 6, 7, 11, 13, and 14 the test products were applied by the subjects themselves at home according to the instruction by a technician. Applications were always performed between 8 and 11 a.m. in the morning and 8 and 11 p.m. in the evening.

<b>Arm title</b>	untreated
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Arm description:

One abrasive wound on the left volar forearm of each subject was left untreated but covered with a standard bandage. On study days with visits at the test center (Days 1, 3, 5, 8, 9, 10, and 12) the first daily application was done by a technician after instrumental measurements and visual assessments. The second daily application was done by the subjects at home (evening). On Days 2, 4, 6, 7, 11, 13, and 14 the test products were applied by the subjects themselves at home according to the instruction by a technician. Applications were always performed between 8 and 11 a.m. in the morning and 8 and 11 p.m. in the evening.

Arm type	untreated control covered with standard bandage
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No investigational medicinal product assigned in this arm

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The trial was conducted under observer-blind conditions (see blinding implementation details)

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The trial was conducted under observer-blind conditions (see blinding implementation details).

<b>Number of subjects in period 1</b>	Soventol Wund- und Heilgel	Bepanthen Wund- und Heilsalbe	untreated
Started	36	36	36
Completed	36	36	36

## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	36	36	
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)	36	36	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	31	31	
Male	5	5	

### Subject analysis sets

Subject analysis set title	Full Analysis Set
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Subject analysis set type	Full analysis
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Subject analysis set description:

Full analysis set (FAS): includes all subjects who did not violate any in- or exclusion criteria at the beginning of the trial, who received at least one application of the test products and for whom at least one post-baseline assessment was performed.

Subject analysis set title	Safety Population
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Safety Population (SP): included all subjects who received at least one application of the test products, regardless of the number of assessments

Reporting group values	Full Analysis Set	Safety Population	
Number of subjects	33	36	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			

Adolescents (12-17 years)			
Adults (18-64 years)	33	36	
From 65-84 years			
85 years and over			
Gender categorical			
Units: Subjects			
Female	28	31	
Male	5	5	

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## End points

### End points reporting groups

Reporting group title	Soventol Wund- und Heilgel
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Reporting group description:

Soventol® Wund- und Heilgel is a certified medical device and is indicated for the treatment of acute and chronic wounds such as abrasions, cuts, scratches, laceration, blistering burns, and sunburns

Reporting group title	Bepanthen Wund- und Heilsalbe
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Reporting group description:

Indications for Bepanthen® Wund- und Heilsalbe are promotion of healing in superficial minor skin and mucosa injuries

Reporting group title	untreated
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Reporting group description:

One abrasive wound on the left volar forearm of each subject was left untreated but covered with a standard bandage. On study days with visits at the test center (Days 1, 3, 5, 8, 9, 10, and 12) the first daily application was done by a technician after instrumental measurements and visual assessments. The second daily application was done by the subjects at home (evening). On Days 2, 4, 6, 7, 11, 13, and 14 the test products were applied by the subjects themselves at home according to the instruction by a technician. Applications were always performed between 8 and 11 a.m. in the morning and 8 and 11 p.m. in the evening.

Subject analysis set title	Full Analysis Set
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Subject analysis set type	Full analysis
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Subject analysis set description:

Full analysis set (FAS): includes all subjects who did not violate any in- or exclusion criteria at the beginning of the trial, who received at least one application of the test products and for whom at least one post-baseline assessment was performed.

Subject analysis set title	Safety Population
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Safety Population (SP): included all subjects who received at least one application of the test products, regardless of the number of assessments

### Primary: Comparison of the investigational product versus untreated on the size of the open wound area/crusts

End point title	Comparison of the investigational product versus untreated on the size of the open wound area/crusts <sup>[1]</sup>
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End point description:

The primary objective was the comparison of the investigational product versus untreated on the size of the open wound area/crusts assessed by quantitative image analysis at the different assessment time points (AUC over time on relative differences to Baseline). The size of the open wound area (including area covered with crusts) was determined for defined time points by quantitative image analysis. The relative difference to Baseline was calculated. AUCs from Day 3 to Day 15 were calculated with the trapezoid formula for the three treatments on these relative differences to Baseline. The statistical analysis for the primary objective was done on the AUC values.

End point type	Primary
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End point timeframe:

AUC over time on relative differences to Baseline from Day 3 to Day 15

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: Due to intra-individual comparison all patients were included in each arm.

<b>End point values</b>	Soventol Wund- und Heilgel	untreated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: AUC				
geometric mean (standard deviation)	993.39 (± 79.36)	723.93 (± 142.52)		

## Statistical analyses

<b>Statistical analysis title</b>	open wound area/crusts - product versus untreated
Statistical analysis description:	
Paired t-test or Wilcoxon signed-ranks test (depending on Normality test) should be performed to analyze the difference between treatments regarding AUC over time on relative differences to Baseline from Day 3 to Day 15. Normality was rejected based on Shapiro-Wilk test. Therefore Wilcoxon signed-ranks test was used to compare areas treated with investigational product and untreated areas and found a significantly higher AUC ( $p < 0.0001$ ) for the areas treated with the investigational product.	
Comparison groups	Soventol Wund- und Heilgel v untreated
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon signed-rank test

## Secondary: Comparison of the investigational product versus reference on the size of the open wound area/crusts

End point title	Comparison of the investigational product versus reference on the size of the open wound area/crusts <sup>[2]</sup>
End point description:	
Comparisons of the reference product versus the investigational product and versus untreated on the size of open wound area/crusts assessed by quantitative image analysis at the different assessment time points (AUC over time on relative differences to Baseline).	
End point type	Secondary
End point timeframe:	
AUC over time on relative differences to Baseline from Day 3 to Day 15	

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: Due to intra-individual comparison all patients were included in each arm.

<b>End point values</b>	Soventol Wund- und Heilgel	Bepanthen Wund- und Heilsalbe		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: AUC				
geometric mean (standard deviation)	993.39 (± 79.36)	966.29 (± 106.91)		

### Statistical analyses

<b>Statistical analysis title</b>	open wound area/crust product versus reference
Comparison groups	Soventol Wund- und Heilgel v Bepanthen Wund- und Heilsalbe
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2553
Method	Wilcoxon signed-ranked test

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

At each visit at the test center from Day 1 on

Adverse event reporting additional description:

AEs and changes in concomitant medication were recorded at each visit at the test center from day 1 on. Assessment of possible signs of inflammation/infection and/or signs of allergic reactions.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	Soventol Wund- und Heilgel
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Reporting group description: -

Reporting group title	Bepanthen Wund- und Heilsalbe
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Reporting group description: -

Reporting group title	untreated control
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Reporting group description: -

<b>Serious adverse events</b>	Soventol Wund- und Heilgel	Bepanthen Wund- und Heilsalbe	untreated control
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 36 (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: 5 %

<b>Non-serious adverse events</b>	Soventol Wund- und Heilgel	Bepanthen Wund- und Heilsalbe	untreated control
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 36 (66.67%)	22 / 36 (61.11%)	28 / 36 (77.78%)
Injury, poisoning and procedural complications			
Inflammation of wound			
subjects affected / exposed	24 / 36 (66.67%)	20 / 36 (55.56%)	25 / 36 (69.44%)
occurrences (all)	28	22	29
Skin and subcutaneous tissue disorders			
Dermatitis allergic			

subjects affected / exposed	9 / 36 (25.00%)	3 / 36 (8.33%)	7 / 36 (19.44%)
occurrences (all)	10	3	7
<b>Erythema</b>			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	3	1	1
<b>Burning sensation</b>			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 36 (2.78%)
occurrences (all)	3	1	1

## **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