1 SYNOPSIS

Name of Sponsor/Company: Schülke & Mayr GmbH Robert-Koch-Str. 2 22851 Norderstedt, Germany	**Individual Study Table Referring to Part of the Dossier** **Volume:** **Page:**	**(For National Authority Use only)**
Name of Finished Product: octenisept®		
Name of Active Ingredient: Octenidindihydrochlorid, Phenoxyethanol		

Title of Study:	Randomized, Double-blind, Single-center, Placebo-controlled Study to evaluate the Efficacy of octenisept® in Patients with Chronic Wounds
Investigators:	Prof. Dr. med. Matthias Augustin
Study center(s):	CTC North GmbH & Co. KG at the University Medical Center Hamburg-Eppendorf Martinistr. 52 20246 Hamburg, Germany
Publication (reference):	Not applicable
Protocol-No.	OCT-UKE-2011 (Sponsor), CTC09358 (CRO)
EudraCT-No.	2011-003402-25
Study Period	First subject screened: 12 November 2012 First subject dosed: 12 November 2012 Last subject dosed: 27 May 2013 Last subject last visit: 19 June 2013 Last subject last contact: 19 June 2013
Phase of development:	Phase IV
Objectives: **Primary Objective**	Efficacy of octenisept® compared to NaCl solution and antimicrobial effect in chronic wounds. Decrease of bacterial load after 14 days of treatment will be used as a parameter for efficacy. Bacterial count will be defined with a semi-quantitative bacterial swab.
Secondary Objective	• To assess subjective tolerance of octenisept® using the PBI and FLQA questionnaire • To evaluate the wound healing time and wound size • Development of bacterial load at the follow-up visit
Methodology:	This was a randomized, double-blind, placebo-controlled trial with octenisept® or placebo in patients with chronic leg ulcers. Patients received a daily application of study drug or placebo over a period up to 2 weeks. The study was to be conducted at a single center with a total of 70

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	patients. Patients were randomized to either the octenisept® group or to the placebo group. Patients were randomized to one group after eligibility is confirmed during the screening visit. Treatment started on Day 0 after the first swab. The Swab was standardized using the method “Essener Kreisel” (see appendix No. I) Daily application was performed over a period of 2 weeks. Patients returned to the study center on Day 3 and their eligibility was re-confirmed after having the results of the microbiology assessment. Patients without the evidence of at least one the species named in the inclusion criteria were excluded from the study. Additional ambulatory visits took place on Days 7, 14, and follow-up at Day 21. All study events are illustrated in the Schedule of Assessments below. The total study duration for each patient was 22 days including the follow-up visit.	
Number of patients (planned and analyzed):	70 male and female patients were planned to be included. Overall 9 patients were included and completed the study due to the premature termination of the study by the Sponsor.	

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Diagnosis and main criteria for inclusion:	Ulcus Cruris differential genesis Main inclusion criteria: 1. Male and female patients of at least 18 years at the time of consent 2. Females of non-childbearing potential (postmenopausal ≥ 50 years old and amenorrhea ≥ 12 month after break of exogenous hormones or ≤ 50 years old, documented FSH – and LH level equal to the postmenopausal range and amenorrhea ≥ 12 after break of all exogenous hormones) 3. Females of non-childbearing potential due to postoperative bilateral tubal ligation, bilateral salpingectomy, bilateral oophorectomile or hysterectomy 4. Patients with a venous leg ulcer (Ulcus cruris) 5. Patients with a chronic leg ulcer 6. Duration of the target venous ulcer ≥ 4 weeks 7. Surface area of the target venous ulcer (after debridement) ≥ 1 8. Patients with a chronic leg ulcer with bacterial load suspected in at least one of the following bacterial species: a. Staphylococcus aureus b. Streptococcus pyogenes c. Enterococcus spp. d. Escherichia coli e. Proteus mirabilis f. Pseudomonas aeruginosa 9. Satisfactory medical assessment with no clinically significant or relevant abnormalities as determined by medical history, physical examination, clinical [vital signs, 12-lead electrocardiogram (ECG)], and clinical laboratory evaluation (hematology, biochemistry, urinalysis) as assessed by the Investigator 10. Ability to provide written informed consent 11. Signed declaration of consent 12. Willingness to co-operate
Test product, dose and mode of administration, batch number:	octenisept® Batch number: KPS110815
Duration of Treatment:	Study duration: 8 months Duration per subject: 22 days Duration of treatment: 2 weeks
Reference therapy, dose and mode of administration, batch	NaCl Batch number: S12022801

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number:		
Criteria for evaluation: **Efficacy:**	Primary Endpoints: Reduction of the log sum of standardized bacterial densities of 6 bacteria species after 1 and 2 weeks in comparison to baseline (determined directly before start of treatment) Secondary Endpoints: ▪ Wound size after 2 weeks ▪ Patient benefit determined with the PBI and FLQA questionnaire after 2 weeks of treatment ▪ Descriptive analysis: occurrence of multi-resistant strains ▪ Safety: IMP related Adverse Events (AE)	
Safety:	AEs and Vital Signs throughout the study	
Statistical methods:	Analyses of variance (ANOVA) will be performed on all primary PK variables. The individual subject values for concentrations and pharmacokinetic parameters will be tabulated with descriptive statistics.	

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Efficacy Results	At baseline, relevant imbalances between treatment groups were observed, presumably due to the small sample size. While ANCOVA numerically adjusts for these imbalances, it cannot correct the loss of power resulting from the small sample size. Correspondingly, no significant treatment effects could be detected in this study regarding any of the primary endpoint variables, i.e., bacterial score changes over time. Significant treatment group differences could be detected for some secondary endpoint FLQA-variables, but these were usually already present at baseline and may thus represent poor randomization, rather than genuine treatment effects. In conclusion, patient number was too low to consider the results of this study representative.	
Safety Results	The doses of the study medication were well tolerated. There were no severe or serious adverse events. No adverse event led to a drop-out. Two adverse events were reported. One adverse event was of mild and one adverse event of moderate intensity. The two adverse events were suspected to be not related to the study medication. The adverse events resolved completely There were no relevant changes in physical findings when comparing pre-study and post-study results. There were no safety concerns after application of study drug or placebo. There were no relevant differences in safety profile between the two treatments compared. Frequency and intensity of systemic and local AE and serious AE were recorded in detail, based on the interviews at each visit - except for the first visit before randomization.	
Conclusion	The study analysis shows no indications for intolerance to the study product. Due to the premature termination of study, no further conclusions should be drawn.	
Date of Report:	31 January 2014	