

Title: A prospective, non-interventional multicenter study, performed in patients with burns, to evaluate efficacy and safety aspects of NexoBrid in clinical practice.

Protocol: IIT C - 01

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OS-BURN2014- STUDY Protocol

Protocol Number:	OS-BURN2014
Name of Medicinal Product (IMP):	NexoBrid
Name of Active Ingredient:	Partially purified Bromelain
Study Title:	A prospective, non-interventional multicenter study, performed in patients with burns, to evaluate efficacy and safety aspects of NexoBrid in clinical practice.
Clinical Phase:	Postmarketing
Study Duration:	The total duration of the study period of each participating patient is the time (days) from admission to hospital until delivery.
Study Population:	Any patient treated with NexoBrid
Study Objective(s):	<p>The European Commission granted a marketing authorisation valid throughout the European Union for NexoBrid on 18 December 2012. Efficacy and safety of NexoBrid for removal of eschar from burn wounds have been evaluated in a confirmatory Phase 3 study (MW 2004-11-02) as well as in several supportive studies.</p> <p>Study objectives are to gather data about the application of NexoBrid in real clinical practice and to evaluate if application is performed in accordance to approval. Additionally the study should prove the efficacy of MediWounds' comprehensive training program at implementation of NexoBrid. Another objective of this study is to gather data regarding outcomes of treatment and therapeutic experiences of NexoBrid in clinical practice, which are important for the acceptance of new medical product therapy aimed at removing eschar in patients with deep thermal burns (grade IIb - III: „deep partial“ and „full thickness“).</p> <p>Specific objectives regarding outcomes of treatment and therapeutic experiences are:</p> <ul style="list-style-type: none"> - Is there any evidence for an increased risk of infections related to the use of NexoBrid? - Are there any changes in haematological parameters related to the use of NexoBrid? - How is efficacy of NexoBrid judged by physicians in clinical practice? - Which adverse events are reported in the use of NexoBrid?

<p>Study Design Overview:</p>	<p>This study will be a prospective, non-interventional study, performed in patients with burns, to evaluate safety and efficacy aspects of NexoBrid in clinical practice.</p> <p>Documentation of the treatment outcomes will be performed by using the case report form as well as photographing the burns before and after application of NexoBrid.</p> <p>As per approval, application of NexoBrid should be performed as following:</p> <p>Prior to eschar removal treatment with NexoBrid, subjects should be medicated with appropriate analgesia and undergo wound cleansing and dressing of all wounds with antibacterial solutions.</p> <p>Eschar Removal with NexoBrid should be performed as following: Cleansing and soaking, NXB application and wound assessment should be performed. If medically judged, NXB may be applied for a second time to the same burn area however, not more than twice to the same burn wound area. Additional surgical and/or non-surgical procedures might be performed, if medically warranted.</p> <p>Subsequent to eschar removal, all wounds should be assessed and treated in the same manner, in accordance with post-eschar removal wound care strategy.</p>
<p>Dosage and route of administration:</p>	<p>NexoBrid</p> <p>As per approval NexoBrid should only be applied by trained healthcare professionals in specialist burn centres.</p> <p>NexoBrid is presented as partially purified Bromelain powder and gel vehicle for preparation of a gel for cutaneous use. Two grams or five grams of NexoBrid sterile powder are mixed in 20 grams or 50 grams of sterile Gel Vehicle (ratio of 1:10) to obtain sterile NexoBrid Gel .NexoBrid Gel should be applied to the burn wound at a dose of 2 g NexoBrid sterile powder mixed with 20g sterile Gel Vehicle per 1% of TBSA (~ surface of an adult palm) for four hours. The NexoBrid powder and the Gel Vehicle should be mixed at the patient bedside ≤ 15 min prior to use.</p> <p>In most cases, NexoBrid is effective after a single application; however it may be applied for a second time to the same burn area, if medically warranted. NexoBrid should only be applied twice to the same burn wound area.</p>

<p>Inclusion/ Exclusion Criteria:</p>	<p>Inclusion criteria of the study: Any patient who is treated with NexoBrid in order to treat burn wounds.</p> <p>The criteria for the use of NexoBrid as per marketing authorization of NexoBrid are:</p> <ol style="list-style-type: none">1. Males and females; 18 years of age,2. Deep partial- and full-thickness thermal burns3. A total wound area of not more than 15% TBSA <p>Contraindications or Warnings</p> <ol style="list-style-type: none">1. Hypersensitivity to the active substance, to pineapples or papain or to any of the excipients2. Penetrating burn wounds where foreign materials (e.g. implants, pacemakers, and shunts) and/or vital structures (e.g. larger vessels, eyes) are or could become exposed during debridement3. Chemical burn wounds4. Wounds contaminated with radioactive and other hazardous substances to avoid unforeseeable reactions with the product and an increased risk of spreading the noxious substance5. NexoBrid should not be applied to more than 15% Total Body Surface Area (TBSA)6. Special populations:<ul style="list-style-type: none">- NexoBrid is not indicated for use in patients younger than 18 years.- There is no information on the use of NexoBrid in patients with renal impairment.- There is no information on the use of NexoBrid in patients with hepatic impairment.- Experience with NexoBrid in elderly patients (>65 years) is limited.7. NexoBrid should be used with caution in patients with cardiopulmonary and pulmonary disease, including pulmonary burn trauma and suspected pulmonary burn trauma.
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	<p>8. NexoBrid should be used with caution in patients with perineal and genital burns, electrical burns or facial burns.</p> <p>9. NexoBrid should be used with caution in patients with disorders of coagulation, low platelet counts and increased risk of bleeding from other causes e.g. peptic ulcers and sepsis. Patients should be monitored for possible signs of coagulation abnormalities.</p> <p>10. NexoBrid is not recommended during pregnancy. Breast-feeding should be discontinued for at least 4 days after NexoBrid application.</p>
<p>Data collection</p>	<p>The following data will be collected in this study:</p> <ol style="list-style-type: none"> 1. Institution and demographics: <ul style="list-style-type: none"> • Date, name of institution, name of treating physician and Nexobrid-Batch Number • Patients date of birth, gender, relevant comorbidities, date and person who signed informed consent 2. Burn injuries: <ul style="list-style-type: none"> • Indication of anatomical location of burn injuries and size of affected area in TBSA 3. Etiology: <ul style="list-style-type: none"> • Indication of burn etiology: <ul style="list-style-type: none"> - Scalding - Electricity - Thermal burn - Chemicals - Other • Estimated time of injury and time of arrival in ER • Visual indication of affected areas according to burn depth 4. Application: <ul style="list-style-type: none"> • Localization, begin and end of NexoBrid application • Type and duration of pre- and post-use soaking • Time of additional NexoBrid application

- Type of Analgo-/Sedation during NexoBrid application and NexoBrid removal phase
- Resources of personnel and space
- Time of photo-documentation before and after application of Nexobrid
- Type of primary dressing pre- and post-NexoBrid, time of primary dressing change, type of secondary dressings
- Time of complete wound closure
- Area of skin grafted on %TBSA, time of skin graft transplantation, area of skin treated with NexoBrid and transplated

5. Additional information

- Wound infection
- Other infections
- Sepsis
- Organ failure
- Ventilation
- IV antibiotics use
- Surgical intervention due to infection in area of NexoBrid treated wound and description of procedure
- Begin and end of ICU stay
- Begin and end of hospitalization
- Indication and date of death
- Haematological findings before and up to 48 hours post NexoBrid:
 - Hb (g/dl)
 - Hkt (%)
 - Platelets
 - INR
 - aPTT
 - pRBC Units

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	<ul style="list-style-type: none">- FFP- Systemic Coagulation factors.• Judgement by Physician, ranging from 1 (insufficient) to 10 (excellent):- Efficacy of debridement- Help on the initial diagnosis of depth of burn- Less traumatic than surgical debridement- Easier to use than SOC.• Indication and description of adverse events.• Name and signature of physician
Sample size:	Up to 200 patients