APPLICATION OF TOPICAL AGENT FOR NON-EXCISIONAL ESCHAR REMOVAL

MARCH 2021

NexoBrid® Product Overview

NexoBrid is an Enzymatic Treatment for Eschar Removal in Hospitalized Burn Patients

- NexoBrid is a novel, non-surgical option for eschar removal. Eschar is the dead tissue and dried secretions following a burn, and removal is essential for wound healing
  - It is a botanical and biologic product for topical use and is comprised of 2 components: the NexoBrid Powder, containing a concentrate of proteolytic enzymes enriched in bromelain extracted from pineapple stems, and a Gel Vehicle
  - NexoBrid has been developed for patients with deep partial thickness (DPT) and/or full thickness (FT) thermal burns
- NexoBrid was approved by the European Medicines Agency (EMA) in 2012 and is currently commercially available in many ex-U.S. countries[1]. NexoBrid has an expected FDA approval date of June 29, 2021 and is seeking New Technology Add-On Payment for FY 2022.

NexoBrid is Associated with Reduced Incidence of Surgical Excision, Time to Complete Eschar Removal, and Actual Blood Loss vs. SOC

NexoBrid is Associated with Reduced Autografting vs. SOC

NexoBrid Demonstrates Substantial Clinical Improvement Over the Current Burn SOC Debridement and Excision Techniques

NexoBrid
Concentrate of proteolytic enzymes enriched in bromelain

Hirche et al, 2017
DETECT (data on file)Krieger et al, 2012; Giudice et al, 2017; Palao et al, 2017

Background on Burn Disease State and Eschar Removal®

Eschar removal is essential for wound healing

- In burn patients, timely and rapid eschar removal is essential to initiate the wound healing process and prevent further complications[1]
- The dead tissue, if not removed, often becomes heavily contaminated in 2 to 3 days and is the source of local and/or systemic infection or sepsis[2]
- The local inflammation and infection destroy healthy surrounding tissues and extends the original damage[3]. To prevent these complications, it is imperative to evaluate the burn and remove eschar at the earliest possible opportunity
- Only when the eschar is removed and the wound bed revealed, can the true damage be observed and assessed, and the appropriate wound closure modality prescribed

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SOC: Standard of Care

1. Edmondson et al, 2018; Gibran et al, 2013; Loo et al, 2018; Xiao-Wu et al, 2002
2. Atiyeh et al, 2005; Barret et al, 1999; Barret and Herndon, 2003; Ong et al, 2006; Xiao-Wu et al, 2002; Young, 2006
3. Singh et al, 2007

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NexoBrid® Clinical Value

NexoBrid is Associated with Non-Surgical, and Selective Eschar Removal

- Removal of eschar may be accomplished by surgical excision or non-surgical means. Choice of debridement method depends on many variables (e.g., burn depth/site, TBSA, patient's general condition, donor site availability, surgical facilities)[1]. Risks associated with surgical excision include the risks of severe trauma to already traumatized patient, sacrifice of healthy tissues, blood and heat loss, general anesthesia, and all other risks associated with surgical and postsurgical complication
  - NexoBrid is not dependent on operating room facilities since it can be applied at the patient's bedside, supporting faster time to eschar removal and eliminating need for general anesthesia / surgical personnel
  - NexoBrid is associated with selective debridement of eschar or denatured collagen while sparing healthy tissue. Greater levels of remaining healthy tissue can reduce need for autografting to close the wound
  - NexoBrid use in delicate, often difficult-to-debride, areas (e.g., hands, feet, face) offers particular value[2]
  - In accordance with bedside use, NexoBrid has been identified by the US Biomedical Advanced Research and Development Authority (BARDA) as a critical countermeasure for potential public health emergencies[3]

Current SOC Methods Can Damage Healthy Tissue:

The current standard of care (SOC) in the US relies primarily on surgical excision to remove eschar through use of sharp instruments such as scalpels and dermatomes.

NexoBrid Use Is Tissue Sparing:

NexoBrid is the first enzymatic eschar removal technology to achieve rapid, consistent eschar removal. NexoBrid's selectivity for eschar or denatured collagen is healthy tissue sparing

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1. Cancio et al, 2017; Gibran et al, 2013; Kwa et al, 2019
2. Hirche et al, 2017
3. 'BARDA Initiates the Procurement of NexoBrid for Emergency Response' (http://ir.mediwound.com/news-releases/news-release-details/barda-initiates-procurement-nexobrid-emergency-response)

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NexoBrid® Demonstrates Substantial Clinical Improvement Over the Current Burn SOC Debridement and Excision Techniques[1]

- NexoBrid can be used at the bedside and provides a novel non-surgical option for rapid eschar removal
- NexoBrid reduces need for surgical excision, reduces time to complete eschar removal, reduces the need for autograft, and reduces actual blood loss
  - NexoBrid reduces the surgical burden associated with surgical excision, and therefore reduces adverse events associated with surgery / requirement for general anesthesia
  - NexoBrid may reduce instances of surgical escharotomies
- NexoBrid can be used on delicate areas of the body (e.g., hands, feet, face); these patients are more likely to be poor candidates for current eschar removal approaches
- NexoBrid allows for depth-of-burn diagnoses of indeterminant depth and/or mixed depth wounds
- NexoBrid clinical evidence supports decreased scarring from the reduced need for autografting, and equal or improved scar cosmesis on NexoBrid-treated wounds

NexoBrid use is not dependent on operating room facilities since it can be applied at the patient's bedside

NexoBrid use eliminates the need for general anesthesia and the additional medical personnel required for surgical procedures

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1. DETECT (data on file); Rosenberg et al, 2014

SOC: Site of Care

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NexoBrid® Dosing and Storage

- NexoBrid is dispensed in grams, with 2g (+20g gel vehicle) covering ~1% of a patient's total body surface area (TBSA) and 5g (+50g vehicle) covering ~2.5% TBSA
  - Grams used depends on size of affected surface area
  - 15% TBSA max per application (consecutive applications performed, if necessary)
  - Must be refrigerated (2-8°C), shelf life is 3 years

NexoBrid powder and the Gel Vehicle are mixed to obtain NexoBrid Gel for topical use in a final concentration of 0.09 g/g concentrate of proteolytic enzymes enriched in Bromelain

Mixed NexoBrid Gel is applied for 4 hours to the burn wound at a dose of 2 g NexoBrid powder mixed with 20 g Gel Vehicle per 1% TBSA, or 5 g NexoBrid powder mixed with 50 g Gel Vehicle per 2.5% TBSA.

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NexoBrid® Preparation and Administration is Currently a Unique Procedure Used by Burn Clinics

Administration: NexoBrid is applied topically at the patient's bedside:

1. Apply sterile gauze soaked with antibacterial solution to the wound bed for 2 hours
2. Mix NexoBrid powder and gel and apply topically to wound within 15 minutes of mixing, maintaining a moist environment during application
    - Maintain appropriate pain control throughout the procedure, particularly during NexoBrid application and removal
3. Cover with an occlusive dressing and leave on for 4 hours
4. Remove NexoBrid with a blunt instrument, such as a sterile tongue depressor
5. Apply a dressing soaked with antibacterial solution for 2 hours to remove remnants of the dissolved eschar and cool the treatment area
6. NexoBrid can be applied to an area of up to 15% TBSA in one session

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Summary of NexoBrid®

- When compared to SOC, which included both surgical and non-surgical debridement methods, in the DETECT trial1, NexoBrid resulted in a statistically significant reduction in incidence of surgical eschar removal (tangential excision / minor / avulsion / Versajet and/or dermabrasion excision), time to complete eschar removal, and blood loss related to eschar removal ($p < 0.0001$)
- NexoBrid use dynamics (e.g., time to eschar removal) may reduce instances of surgical escharotomies2. An escharotomy is an emergency procedure used when circumferential eschar produces a tourniquet effect, compromising circulation and risking severe complications (e.g., loss of limb)
- A reduction in number of burns and burn area autografted translated into decrease need for donor site tissue and associated donor site morbidity

A unique code for the non-excisional topical administration of NexoBrid will:

- Aid in the tracking and monitoring of treating patients with partial or full thickness burns;

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1. DETECT (data on file)
2. Krieger et al, 2012; Giudice et al, 2017; Palao et al, 2017

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