This educational material is mandatory as a condition of the marketing authorisation in order to further minimise important selected risks

EDUCATIONAL MATERIALS

All Healthcare Professionals in specialised burn centres who are expected to use and/or prescribe this medicinal product should receive specific training and be provided with these Educational Materials.

The main purpose of these educational materials is to provide the medical personnel at burn centres with the following information about NexoBrid:

1. Posology and method of administration in in all age groups (adults and paediatric patients).
2. Instructions on preparation of the medicinal product before application, method of preparation of the patient and the wound area and method of application of the medicinal product.
3. The required risk minimisation activities for NexoBrid:
    a) For the product's important identified risks of pain, pyrexia/hyperthermia, wound complications (including wound infections) and allergic reaction (including anaphylactic reaction), which were identified and managed by preventive and corrective measures during the NexoBrid clinical developmental programme.
    b) For the product's important potential risks of severe irritation and increased tendency to bleeding.
4. Monitoring during and post NexoBrid application.

Version 01, date 04-June-2026

This educational material fulfils the conditions of the marketing authorisation and has been approved by the competent authority.

Please read and understand the Summary of Product Characteristics (SmPC) which is available on www.hpra.ie before prescribing NexoBrid.

Up-to-date versions of these educational materials (EdM) and SmPC are also available electronically on www.hpra.ie (enter 'NexoBrid under 'Find a Medicine' and click 'SPC and 'EdM' under the 'Documents' column). Additional hard copies of the educational materials may also be requested by contacting MediWound Germany GmbH, infoeurope@mediwound.com.

1 THERAPEUTIC INDICATIONS

NexoBrid is indicated in all age groups for removal of eschar in patients with deep partial- and full-thickness thermal burns.

2 CHEMICAL CLASS AND MODE OF ACTION

NexoBrid consists of a mixture of proteolytic enzymes from the stem of *Ananas comosus* (pineapple plant). The major constituent is stem bromelain.

The mixture of enzymes in NexoBrid dissolves burn wound eschar. The specific components of the mixture responsible for this effect have not been identified.

3 NEXOBRID® GENERAL BACKGROUND

3.1 PRODUCT DESCRIPTION:

NexoBrid is an enzymatic eschar removal medicinal product for topical application.

It is a lyophilised sterile mixture of proteolytic enzymes (concentrate of proteolytic enzymes enriched in bromelain) from pineapple plant stem.

3.2 PRODUCT PRESENTATION:

Vial of sterile lyophilized powder (5 g).

Bottle of sterile gel vehicle (50 g).

3.3 PRODUCT INDICATION:

NexoBrid is indicated in all age groups for removal of eschar in patients with deep partial- and full-thickness thermal burns.

4 BEFORE PRESCRIBING NEXOBRID

Healthcare professional and treating physician (burn specialist) should be aware of the followings before prescribing NexoBrid.

4.1 POSOLOGY AND METHOD OF ADMINISTRATION:

NexoBrid should only be applied by trained healthcare professionals in burn centres.

- In Adults burn patients:

  NexoBrid should not be applied to more than 15% Total Body Surface Area (TBSA).

  5 g powder in 50 g gel is applied to 2.5 % TBSA that corresponds to approximately 450 cm2 of an adult, with a gel layer thickness of 1.5 to 3 mm.

- In children and adolescents (from birth to 18 years of age) burn patients:

  For paediatric patients aged 4-18 years old NexoBrid should not be applied to more than 15% TBSA.

  For paediatric patients aged 0-3 years old this medicine should not be applied to more than 10% TBSA.

4.1.1 Anaphylactic reaction and cross reactivity

The use of NexoBrid is contraindicated in patients allergic to the active substance concentrate of proteolytic enzymes enriched in bromelain, to pineapples or papayas/papain, or to any of the excipients.

Healthcare professionals need to be aware of the risk of allergic reaction in subsequent use of NexoBrid in burn injuries and patients that are re-exposed to bromelain-containing products at a later point in time.

4.1.2 Coagulation disorders

The treatment should not be used in patients with uncontrolled disorders of coagulation. It should be used with caution in patients under anticoagulant therapy or other medicinal products affecting coagulation, and in patients with low platelet counts and increased risk of bleeding from other causes, e.g. peptic ulcers and sepsis.

4.1.3 Patients with cardiopulmonary disease

Healthcare professionals need to be aware of the increased risk of mortality in patients with cardiopulmonary diseases. Therefore, NexoBrid should be used with caution in patients with cardiopulmonary and pulmonary disease, including pulmonary burn trauma and suspected pulmonary burn trauma.

Precautions should be taken in case the patient's lung has been or may have been damaged by inhalation of smoke.

4.2 BEFORE APPLICATION OF NEXOBRID:

The treating physician needs to be aware of the following prior to applying NexoBrid.

4.2.1 Pain

Enzymatic debridement is a painful procedure and requires adequate analgesia and/or anaesthesia. Pain management must be used as commonly practiced for an extensive dressing change; it should be initiated at least 15 minutes prior to this medicinal product application.

4.2.2 Initial Wound Cleansing

- The wound must be cleaned thoroughly, and the superficial keratin layer or blisters removed from the wound area, as the keratin will isolate the eschar from direct contact with the gel and prevent eschar removal by it.
- Dressing soaked with an antibacterial solution must be applied for 2 hours
- All topically applied antibacterial medicinal products must be removed before applying NexoBrid. Remaining antibacterial medicinal products may reduce NexoBrid's activity and efficacy.

4.2.3 Adhesive Barrier

- The area from which you wish to remove the eschar must be surrounded with a sterile paraffin ointment adhesive barrier by applying it a few centimetres outside of the treatment area (using a dispenser). The paraffin layer must not come into contact with the area to be treated to avoid covering the eschar, thus isolating the eschar from direct contact with the gel.
- To prevent possible irritation of abraded skin by inadvertent contact with the gel and possible bleeding from the wound bed, acute wound areas such as lacerations or escharotomy incisions should be protected by a layer of a sterile fatty ointment or fatty dressing (e.g. petrolatum gauze).

4.2.4 Moisture

Sterile isotonic sodium chloride 9 mg/ml (0.9%) solution must be sprinkled on the burn wound. The wound must be kept moist during the application procedure.

4.3 PREPARATION FOR NEXOBRID APPLICATION:

4.3.1 Preparation of the Wound

a. Use pain management as commonly practiced for an extensive dressing change; it should be initiated at least 15 minutes prior to NexoBrid application as described in Section 4.2.1.

b. Clean the wound thoroughly and remove all of the superficial keratin layer or blisters from the wound area see Section 4.2.2 as the keratin will isolate the eschar from direct contact with NexoBrid and prevent eschar removal by NexoBrid.

c. Remove all topically applied antibacterial medicinal products before applying NexoBrid. Remaining antibacterial medicinal products may interfere with the activity of NexoBrid by decreasing its efficacy.

d. Surround the area from which you wish to remove the eschar with a sterile paraffin ointment adhesive barrier by applying it a few centimetres outside of the treatment area see Figure 1. The paraffin layer must not come into contact with the area to be treated to avoid covering the eschar, thus isolating the eschar from direct contact with NexoBrid.

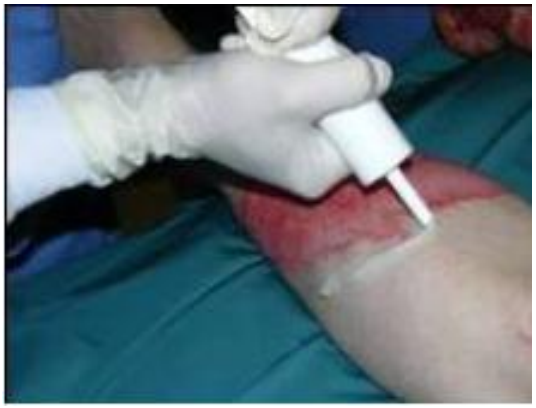


Figure 1: Application of Adhesive Barrier around the Treatment Area

e. Protect areas of abraded/injured skin, lacerations or escharotomy incisions from possible inadvertent contact with NexoBrid that may cause irritation and bleeding of the raw tissue, by applying a layer of a sterile fatty ointment or fatty dressing (e.g. petrolatum gauze) into the wound.

f. Sprinkle the burn wound with sterile isotonic sodium chloride 9 mg/ml (0.9%) solution. The wound must be kept moist during the application procedure Figure 2.

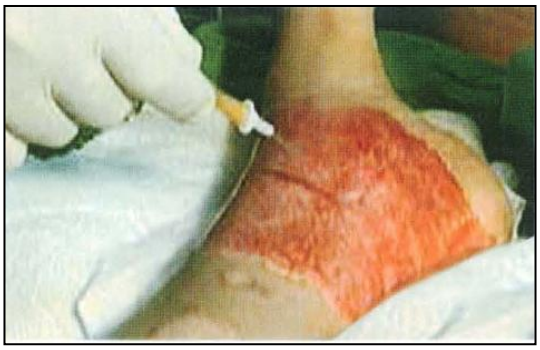


Figure 2: Application of Sterile Isotonic Sodium Chloride Solution

4.3.2 NexoBrid Preparation

a. Assess the patient's target wound area to determine the amount of NexoBrid to be used during treatment. NexoBrid powder and gel are supplied in one presentation:

- 5g NexoBrid powder plus 50g gel to cover ~2.5 %TBSA of an adult in a layer 1.5 -3 mm thick (see Section 4.1).

b. Mix 5g of NexoBrid sterile powder with or 50g respectively of sterile Gel (ratio of 1:10). Aseptic technique must be used when mixing the powder with the gel. The NexoBrid powder and gel are mixed using a sterile tongue depressor at the patient's bedside until a homogenous, light brown mixture is achieved (see Figure 3). This usually requires mixing the powder and the gel for 1 to 2 minutes.

Figure 3: NexoBrid Powder and Gel Homogenous Mixture

4.4 PATIENT MONITORING DURING NEXOBRID TREATMENT (DEBRIDEMENT):

Patients should be monitored for the following during NexoBrid treatment:

4.4.1 Inflammation and infection

- Rise in body temperature
- Signs of local and systemic inflammatory and infectious process (for example low blood pressure, fast heart rate).

4.4.2 Conditions precipitated by analgesia

- Conditions that could be precipitated or worsened by analgesic premedication (e.g., hypersensitivity reactions, breathing difficulties, low blood pressure, acute gastric dilatation, nausea and risk of sudden vomiting, constipation) or antibiotic prophylaxis (e.g., diarrhoea, hypersensitivity reactions).

4.4.3 Bleeding

- Signs of bleeding (including from exposed large vessels in very deep burns or in escharotomy incisions) and potential effects on haemostasis.

4.4.4 Allergic reactions

- Signs of local or systemic allergic reactions, such as breathing difficulties, low blood pressure, fast heart rate, hives, other rash or redness of the skin, or a combination of such effects.
- Allergic reactions, systemic inflammatory reactions, and symptoms such as hypotension.

4.5 STEP BY STEP DESCRIPTION OF THE DEBRIDEMENT PHASE OF THE TREATMENT:

a. Apply NexoBrid topically to the moistened burn wound within 15 minutes of mixing, at a thickness of 1.5 to 3 millimetres (Figure 4) in a dosing of 5 gr. NexoBrid/50 gr. Gel Vehicle to 2.5 % TBSA of an adult. NexoBrid should not be applied to more than 15% TBSA in adults. For paediatric patients aged 4-18 years old NexoBrid should not be applied to more than 15% TBSA. For paediatric patients aged 0-3 years old this medicine should not be applied to more than 10% TBSA. The NexoBrid gel is applied so that it covers the entire wound area, filling the entire area confined by the sterile paraffin ointment adhesive barrier (Figure 5).

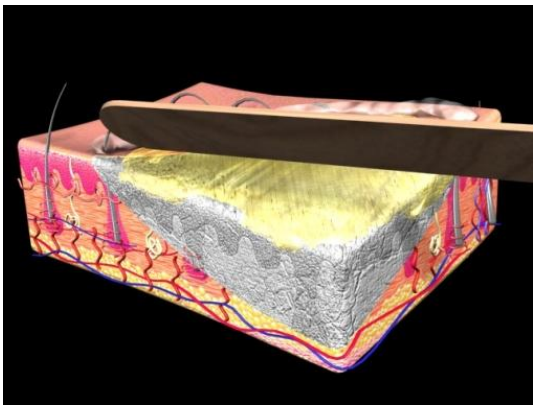


Figure 4: Application of NexoBrid to Treatment Area

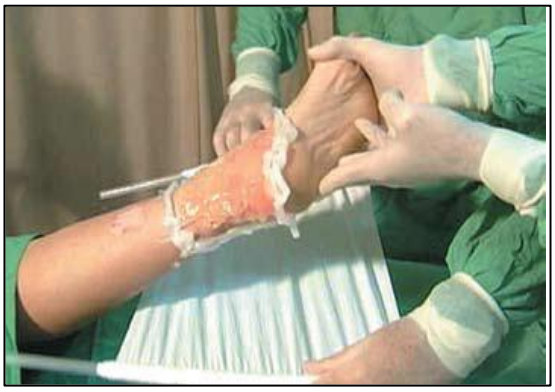


Figure 5: NexoBrid Coverage

b. Cover the wound (Figure 6) with a sterile occlusive film dressing that adheres to the applied sterile adhesive barrier material (Figure 7). The NexoBrid gel must fill the entire occlusive dressing, and special care should be taken not to leave air under this occlusive dressing. Gentle pressing of the occlusive dressing at the area of contact with the adhesive barrier will ensure adherence between the occlusive film and the sterile adhesive barrier and achieve complete containment of NexoBrid on the treatment area.

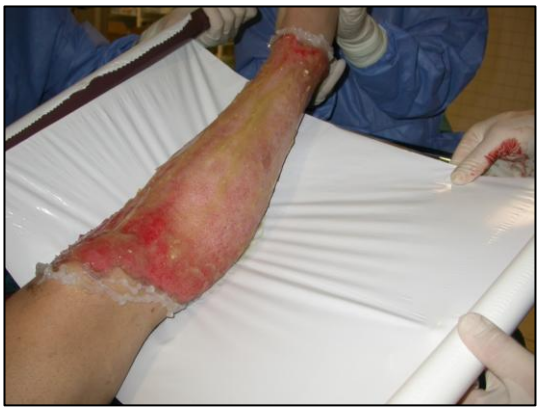


Figure 6: Treatment Area

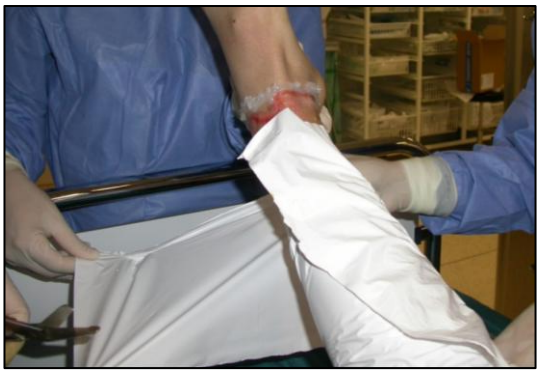


Figure 7: Application of Sterile Occlusive Film Dressing

c. Cover the dressed wound with a loose, thick fluffy dressing, held in place with a bandage (Figure 8).

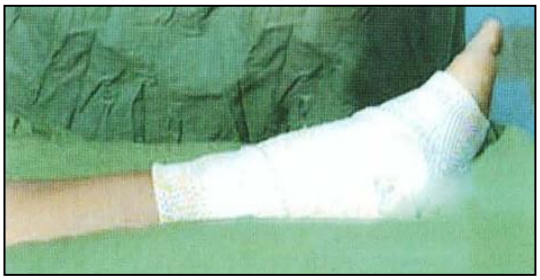


Figure 8: External, Stabilizing Dressing

d. Keep the dressing in place for 4 hours.

e. Discard all unused NexoBrid gel.

4.6 POST DEBRIDEMENT:

4.6.1 Removal of NexoBrid dressing

a. Administer appropriate preventive analgesia/sedation (see Section 4.2.1) as practiced in a dressing change.

b. After 4 hours of NexoBrid treatment, remove the occlusive film dressing using aseptic techniques.

c. Remove the adhesive barrier using a sterile blunt-edged instrument (e.g., tongue depressor). (Figure 9a).

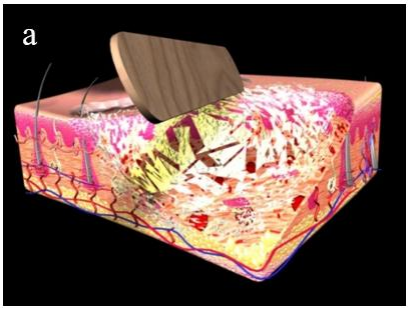


Figure 9a- Wiping - removal of the Adhesive Barrier

d. The dissolved eschar must be removed from the wound. Wipe it away with a sterile blunt-edged instrument as shown in Figure 9b.

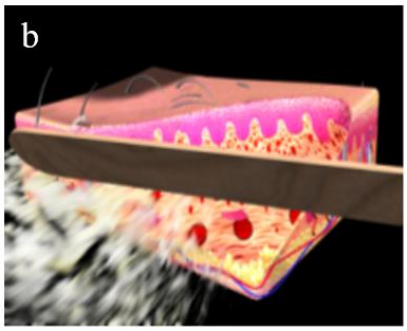


Figure 9b- Removal of Dissolved Eschar

e. Wipe the wound thoroughly, first with a large sterile dry gauze or napkin, followed by a sterile gauze or napkin that has been soaked with sterile isotonic sodium chloride 9 mg/ml (0.9%) solution. Rub the treated area until the appearance of a pinkish surface with bleeding points or a whitish tissue. Rubbing will not remove adhering undissolved eschar in areas where the eschar still remains.

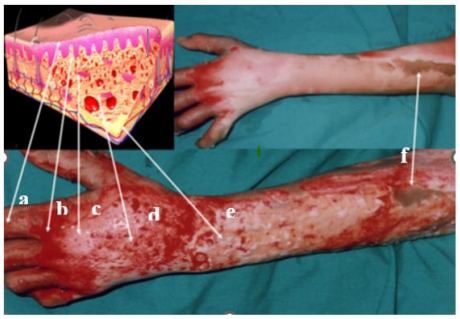
f. Apply a dressing soaked with an antibacterial solution (e.g. 3-5% Sulfamylon or 0.05-0.5% Chlorhexidine) to the treatment area for an additional 2 hours.

4.6.2 Wound Assessment

After soaking the wound with antibacterial solution for 2 hours (see Section 4.2.2), remove the soaking dressing and assess the wound for the following, as presented in Figure 10.

- Completeness of Debridement

% TBSA and burn depth in order to determine further wound management.



a. Non burned skin, uninjured by NexoBrid.
b. Superficial dermal burn with bleeding.
c. Mid depth dermal burn with well-preserved dermal collagen matrix.
d. Deep dermal burn with larger and wider spaced bleeding capillaries and a very thin dermal matrix.
e. Full Thickness burn.
f. Non dissolved eschar protected by charred blister that was not removed prior to NexoBrid application

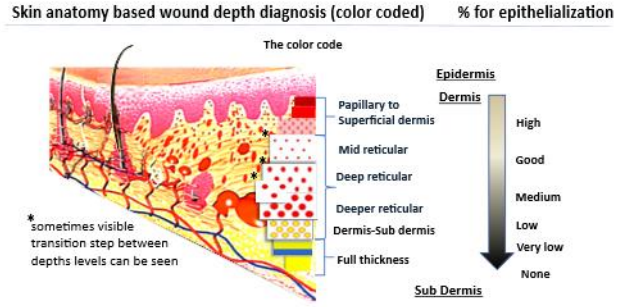


Figure 10: Wound Bed Assessment
©Prof. Lior Rosenberg

4.7 REPEAT DEBRIDEMENT:

NexoBrid should be left in contact with the burn for duration of 4 hours. A second and subsequent application is not recommended. There is limited information on the use of NexoBrid on area where eschar remained after the first application.

4.8 WOUND CARE AFTER DEBRIDEMENT:

- Cover the debrided area immediately post debridement by temporary or permanent skin substitutes or dressings to prevent desiccation and/or formation of pseudoeschar and/or infection.
- Before a permanent or temporary skin cover/substitute is applied to a freshly enzymatically debrided area, use a soaking wet-to-dry dressing to remove remaining dissolved eschar and NexoBrid gel.
- Refresh the debrided bed before application of the grafts or primary adhering dressing, by, e.g., brushing or scraping to promote dressing adherence.

Wounds with areas of full-thickness and deep burns that could not epithelialize should be autografted as soon as possible after NexoBrid debridement. Careful consideration should also be given to the option of placing permanent skin covers (e.g. autografts) on deep partial thickness wounds soon after NexoBrid debridement.

Debrided dermal bed can be treated toward epithelialization-over-dermis by using dressings that will provide the adequate conditions for epithelialization, will keep the bed moist, preventing desiccation and tissue death. Granulation tissue should be promptly controlled by short (2-3 days) courses of corticosteroid ointment, or if epithelialization and wound closure do not progress: by autografting of the not healed areas.

In NexoBrid studies, wounds with visible and rich dermal remnants were allowed to heal by spontaneous epithelialization under proper dressing. In several cases healing was delayed, and autografting was required at a later stage, leading to delays in wound closure. Delayed wound closure may be associated with increased risk of wound-related complications (e.g. graft failure, infection). Therefore, wounds with areas of full-thickness and deep burn without reasonable likelihood of spontaneous epithelialization should be autografted before the development of granulation tissue, as soon as possible after NexoBrid debridement.

As in the case of surgically debrided bed, in order to prevent desiccation and/or formation of pseudoeschar and/or infection, the debrided area should be covered immediately by temporary or permanent skin substitutes or dressings. When applying a permanent skin cover (e.g., autograft) or temporary skin substitute (e.g., allograft) to a freshly enzymatically debrided area, care should be taken to clean and refresh the debrided bed by, e.g., brushing or scraping to allow dressing adherence.

Pseudoeschar, a white layer of fibrin deposits may appear immediately after post debridement soaking on dermal burns. Topical medications such as SSD may promote this pseudoeschar that with time may acquire grayish tint due to oxidation of the silver (Ag). This pseudoeschar will not impede the epithelialization-over-dermis that will continue to progress over the surviving dermis and slowly will dislodge the pseudoeschar. The epithelialized surface will be seen with the progression of the pseudoeschar maceration. Thus, do not remove or excise pseudoeschar as it will delay healing. In healing, epithelializing dermal wounds be careful not to harm and remove (scrape) epithelial edges and islands.

4.8.1 Patient Monitoring Post NexoBrid Administration

In addition to routine monitoring for burn patients (e.g., vital signs, volume/water/electrolyte status, complete blood count, serum albumin and hepatic enzyme levels), monitor patients treated with NexoBrid for the following:

- Rise in body temperature (fever, pyrexia) was seen in adults and children.
- Signs of local and systemic inflammatory processes (including for example low blood pressure, fast heart rate) and infectious processes.

- Conditions that could be precipitated or worsened by analgesic premedication (e.g., dizziness, acute gastric dilatation, nausea and risk of sudden vomiting, constipation, low blood pressure) or antibiotic prophylaxis (e.g., allergy, diarrhoea).
- Signs of local or systemic allergic reactions such as breathing difficulties, low blood pressure, hives, rash or redness of the skin, or a combination of such effects.
- Signs of bleeding and potential effects on haemostasis.

Treatment or prophylactic measures (e.g., IV-line, insertion of a nasogastric tube, pulse oximetry, diagnosis of Burn Induced Compartment Syndrome (BICS) should be initiated as indicated following standard medical guidelines and post debridement soaking that mitigates the post debridement pyrexia.