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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

NEXOBRID (concentrate of proteolytic enzymes enriched in bromelain), enzymes

Insufficient actual benefit in the treatment of eschars associated with deep partial- and full-thickness thermal burns

Main points

- NEXOBRID has a Marketing Authorisation for removal of eschar in adults with deep partial- and full-thickness thermal burns.
- Given the absence of demonstrated clinical benefit and the increase in adverse effects by comparison with the standard treatment, the actual benefit of NEXOBRID is insufficient to justify its reimbursement.

Therapeutic use

- The objective of burn treatment is to limit the extent of the lesions and ensure the maintenance of vital organ functions during the crisis period and then to achieve re-epithelialisation of injured or destroyed skin either by promoting spontaneous healing or by removal (debridement) of necrotic tissue followed where necessary by skin grafts, depending on the severity of the damage.
- Debridement may achieved by surgical (tangential excision, dermabrasion, hydrosurgery) or non-surgical (autolytic debridement through topical treatments and mechanical scraping) methods according to the individual situation.

Role of the medicinal product in the therapeutic strategy

The data currently available do not allow to define a position for NEXOBRID in the treatment strategy for eschars secondary to deep partial- and full-thickness thermal burns in adults.

Clinical data

- In a phase II single-blind study (evaluator blinded) that evaluated NEXOBRID versus its excipient and versus standard of care (surgical or non-surgical) in 140 patients, no difference between treatment groups was observed in the time to complete wound closure (primary efficacy endpoint).
- In a phase III open study that evaluated NEXOBRID versus standard of care in 156 patients, the percentage of deep partial thickness wounds requiring excision or dermabrasion and the percentage of deep partial thickness wounds autografted (co-primary efficacy endpoints) in patients with at least one wound consisting entirely of a deep partial-thickness burn was lower in the NEXOBRID group, with 15% (16/106) of wounds requiring excision or dermabrasion versus 63% (55/88) in the “standard of care” group ($p < 0.0001$), and 18% (19/106) of wounds requiring an autograft versus 34% (30/88) in the “standard of care” group ($p = 0.0099$). The time to successful eschar removal (secondary endpoint) was longer in the NEXOBRID group (36.2 days versus 28.8 days, $p = 0.0185$).
- The methodological shortcomings of these studies make their results difficult to interpret.
- Safety data are very limited. The frequency of adverse events was higher in patients treated with NEXOBRID than in patients who received the standard of care (surgical or non-surgical debridement). The main adverse events requiring special attention are local pain, fever, hyperthermia and local complications and infections.

Special prescribing conditions

- Medicinal product reserved for hospital use
- Medicine requiring special monitoring during treatment

Benefit of the medicinal product

- The actual benefit* of NEXOBRID is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend inclusion on the list of medicines approved for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 23 September 2015 (CT-14127) and is available at **www.has-sante.fr**

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[i] * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.