Consensus statement on the use of Xelma in diabetic foot ulcers

Roundtable Group

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Diabetic foot ulcers are a common and costly complication of diabetes, often presenting in a chronic wound state. Adjuvant therapies may be used to kick-start the healing process in hard-to-heal and chronic wounds, but specific placement of these therapies in the care pathway is not always clear. A group of experienced clinicians developed the following consensus statement and treatment algorithm on the use of the extracellular matrix protein therapy Xelma (Mölnlycke Health Care, Dunstable) specifically in diabetic foot ulcers.

For both the patient and the clinician, the challenges of healing a diabetic foot ulcer (DFU) are multiple. In these frequently chronic wounds, sustained, optimal, traditional wound care on its own may not be enough to achieve healing. A decision may then be made to introduce an adjuvant wound healing therapy into the regimen.

While randomised controlled trials are widely considered to be the most clinically informative measure of a product's efficacy, wound and patient-group heterogeneities in DFU populations – in addition to the costs associated with clinical trials – frequently hinder the design and execution of such investigations. In the absence of clinical trials, questions about the most appropriate use of adjuvant wound healing therapies (which subset of patients will benefit? When should therapy be commenced or withdrawn?) are left to the individual clinician to answer. In such circumstances, the guidance of experienced clinicians can be a useful resource.

One adjuvant therapy designed to treat hard-to-heal and chronic wounds is Xelma (Mölnlycke Health Care, Dunstable). Here, the proceedings of a roundtable discussion on the use of Xelma in DFUs, attended by key opinion leaders in diabetic foot care, are reported. The group drew on their various experiences using Xelma in DFUs, their wider clinical experience and the available literature to develop the following consensus statement and treatment algorithm.

PRODUCT BACKGROUND

Xelma's active ingredient, the protein amelogenin, aggregates into ball-shaped units at the body's pH and provides a temporary, biological, degradable extracellular matrix for cell attachment and proliferation, allowing for the synthesis of growth factors and endogenous extracellular matrix components. When functioning properly, this process triggers the normal wound healing cascade (Mölnlycke Health Care, 2009).

LITERATURE

A pan-European randomised controlled trial assessed the efficacy of Xelma in venous leg ulcers (Vowden et al, 2007). The investigators reported that those randomised to receive Xelma experienced a greater percentage reduction in ulcer size compared with the control group from baseline to the last visit (mean –33.11% vs –11.07%, respectively; P=0.06). In a 12-week post-treatment follow-up study of the Vowden et al (2007) cohort, Romanelli et al (2008) found that significantly more people treated with Xelma continued to show a reduction in ulcer size from baseline than in the control group (P=0.02).

In 2009, Guest et al reported on the cost-effectiveness of Xelma therapy in conjunction with compression bandaging versus compression bandaging alone in venous leg ulcers. A 12-month Markov model revealed a 10% reduction in NHS costs per wound over 12 months (£4261 [95% CI, £3409–5114] to

£3816 [95% CI, £3227–£4405]) in the Xelma treatment group.

Similar data are not yet available for Xelma in DFUs. However, a case series found a reduction in ulcer area in 80% (8/10) of previously static DFUs treated with Xelma (McCardle et al, 2009).

TABLE 1. Generalised elements of optimal care for the person with diabetes and their wound that should be considered in light of local and national guidance.

Wound care – Infection control; vascular supply optimisation; pressure management (offloading); cleansing (as appropriate); debridement (as appropriate); exudate management; patient or carer education (as appropriate).
Care of the patient – Metabolic control; cardiovascular risk reduction; comorbidity management (weight control; smoking cessation, etc.); support and care issues (involvement of family/carers and community services as appropriate).

CONSENSUS STATEMENT

Individual clinics, trusts and countries will have their own protocols regarding wound care, including infection control and dressing choice. This consensus statement and algorithm for the use of Xelma in DFUs should be considered with these protocols in mind.

Gold-standard care

The group stressed that the principles of optimal care (described in brief in *Table 1*) for the patient and their wound are central to achieving wound healing. Consistent optimal care, initiated and maintained from presentation, should be given time to achieve healing before changes to the care plan are made. However, many DFUs present as chronic wounds and the need for prompt intervention with modalities that kick-start wound healing should not be overly delayed. Once a period of at least 2 weeks of optimal care has been undertaken and the wound has remained static, the group suggest that clinicians may consider the use of Xelma (*Figure 1*; see overpage).

Wound classification as a guide to care

Wound classification systems are used to categorise, and subsequently describe, a wound for the purposes of audit, research and clinical management. Here, a colour-coded version of the University of Texas classification of diabetic foot wounds (Lavery et al, 1996) provides a "traffic-light" system to help clinicians identify wound types that the group considered possibly appropriate for treatment with Xelma (*Figure 2*).

Wound infection

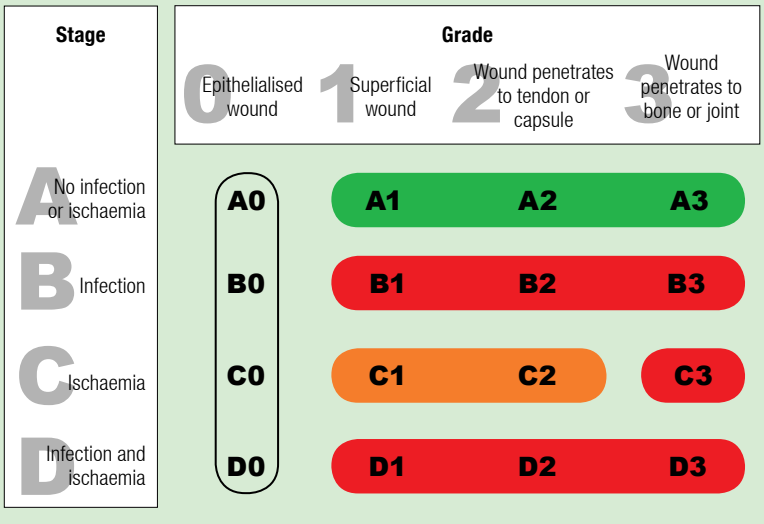
Careful examination for clinical signs of infection should be undertaken in all wounds. The Infectious Diseases Society of America provide useful guidance for infection in the diabetic foot (Lipsky et al, 2004). Xelma is contraindicated for clinically infected wounds (DUFs in Texas stages B and D are not appropriate candidates for Xelma; *Figure 2*). Should infection occur during a course of Xelma, local infection control protocols should be enacted and Xelma maintained with careful review.

Vascular insuffiency

Use of Xelma in ischaemic wounds is contraindicated (*Figure 2*; C3, D1–3). However, the group suggested that people with ischaemia and DFUs that are superficial or extend to tendon or capsule (*Figure 2*; C1–2) for whom revascularistation is not possible or has failed, may benefit from the addition of Xelma to their wound care regimen. The use of Xelma in these wound types may be considered by the clinician experienced in the product's use.

Slough

Xelma is not recommended for use in wounds with >50% slough. This indication is the result



Key: ■ appropriate wound types for use of Xelma, with consideration of other indications; ■ use of Xelma in these wound types is not routinely recommended, but may be appropriate for use by experienced clinicians when revascularisation in not possible, or has failed; ■ use of Xelma not appropriate; □ Xelma is not for use in epithelialised wounds (i.e. grade 0). Note: Should infection occur during a course of Xelma, local infection control protocols should be enacted and Xelma maintained with careful review.

FIGURE 2. University of Texas classification of diabetic foot wounds (Lavery et al, 1996) that has been colour-coded using a traffic-light system to suggest in which wound types Xelma may be suitable.

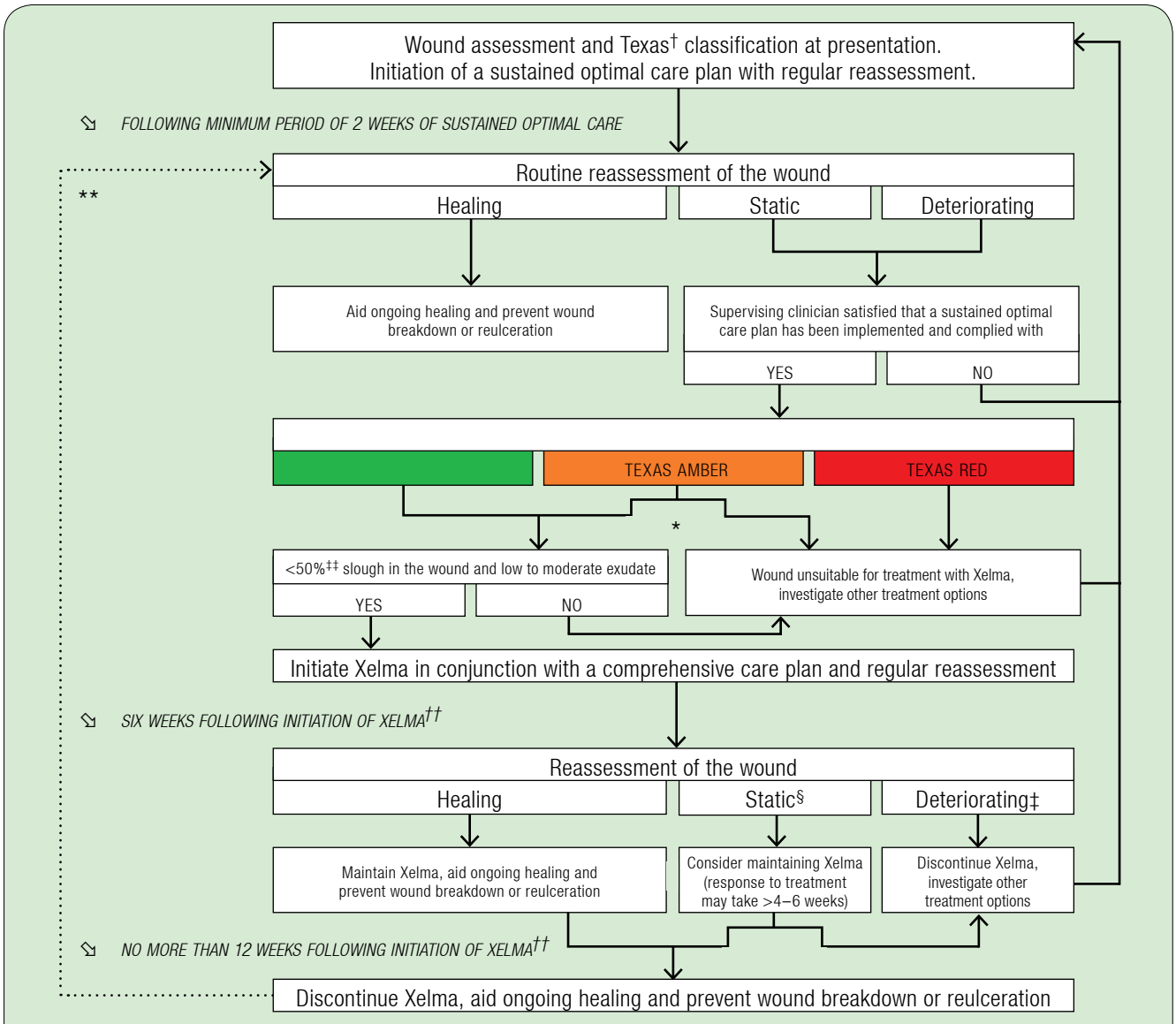
of evidence from trials of the product in venous leg ulcers and the group believes that this indication is less appropriate for DFUs. Slough up to 50% in DFUs is likely to be indicative of poor wound-bed preparation or high bacterial load. The group agreed that DFUs with >50% slough are inappropriate for Xelma and that "clean is best". The achievement of 0–20% slough prior to Xelma commencement should be a goal.

Exudate

Xelma is contraindicated in highly-exuding wounds. In wounds that have been commenced on Xelma, the group's clinical experience suggested that an increase in exudate can be expected and should be anticipated with the use of an appropriately absorbent secondary dressing (e.g. a hydrofibre or foam dressing) to avoid maceration. However, a rapid increase in exudate can be indicative of developing infection and should be carefully monitored.

Debridement

Sharp debridement should be continued as appropriate during Xelma. Use of hydrogels or larval debridement is contraindicated. If Xelma



†University of Texas classification of diabetic foot wounds (Lavery et al, 1996). ‡Find the colour-coded Texas classification in *Figure 2*. ††Wounds that epithelialise should have Xelma discontinued. ‡‡0–20% slough prior to Xelma commencement should be a goal. §A marginal increase in wound area may occur just prior to the wound responding to Xelma and should not be confused with wound deterioration. *Initiation of Xelma in the Texas Amber group (*Figure 2*) should only be undertaken by an experienced clinician. **A second course of Xelma may be appropriate in some cases. **Deteriorating**, significant increase in ulcer area from previous assessment; **healed**, complete epithelialisation of the ulcer; **healing**, significant reduction in ulcer area from previous assessment; **static**, no change, or very minor change, in wound area since previous assessment.

FIGURE 1. Algorithm for the use of Xelma in diabetic foot ulcers, in light of local or national protocols.

is to be commenced following a period of larval debridement, the larvae should be removed 48 hours prior to the initial application of Xelma.

Irrigation

Wound-bed irrigation should not be undertaken during the use of Xelma as it may interrupt the wound healing cascade. The group highlighted that there may be some "crusting" on the wound as a result of Xelma, but clinicians should not attempt to irrigate, rather regular sharp debridement will remove wound debris (see above). However, careful cleansing of the ulcerated limb may be undertaken up to the periwound margin.

There are continuity of care implications for the irrigation moratorium during Xelma. The clinician should ensure that the person whose ulcer is being treated with Xelma, and any healthcare professionals or carers involved in the day-to-day management of the ulcer, are informed that no washing of the wound is to take place during the treatment period.

Seamless care

For many people with DFUs their care will be carried out by a range of people, in a range of settings, during their ulcers' duration. Xelma is available on the Drug Tariff, allowing for easy continuation of treatment across traditional healthcare boundaries (e.g. Xelma commenced during an inpatient stay can be continued on discharge to the community).

It is important that information on continuation of the therapy and its indications (e.g. no irrigation, see above) be passed by the clinician initiating Xelma to the patient, carers and healthcare professionals involved. The group suggested that a letter or information sheet on Xelma be given by the initiating clinician to appropriate parties.

Application

Xelma is a topical gel that should be applied to suitable wounds at weekly intervals. It should be refrigerated during storage and warmed to body temperature just prior to application. Xelma should be applied inside the wound margins as demonstrated in *Figure 3*.

The group stressed that clinicians should not be tempted to over use the product in a single application. Even wound-bed coverage should be achieved without excess product that would, especially in plantar ulcers, risk an overly wet wound and could be deleterious.

Wound area reduction

To allow sufficient time for the wound to respond, Xelma should not be withdrawn (unless in the instance of an adverse event) during the first 6 weeks of treatment, even if no initial decrease in wound area is measurable. The group's experience suggested that the duration of treatment with Xelma before a reduction in wound area could be measured is specific to the individual wound and may be expected to occur between 4 and 8 weeks after initiation, but could happen earlier or later in the treatment course. The group also found that a marginal increase in wound area may occur just prior to the wound responding to Xelma (McCardle et al, 2009) and should not be confused with wound deterioration.

A single course of treatment with Xelma should not exceed 12 weeks. The group suggested that in some cases, following careful reassessment, a second course of Xelma – again, for no more than 12 weeks – may be undertaken.

Wound care costs

While the cost of Xelma (£56/0.5 mL syringe for wounds <10 cm^2; £98/1.0 mL syringe for wounds 10–20 cm^2; available on the Drug Tariff) is higher than that of traditional wound care products, this must be weighed against the total cost of traditional treatments and periods of hospitalisation, during the months, or even years, that a chronic DFU may persist. The group suggested that introduction of a more expensive adjuvant wound healing therapy such as Xelma could also be viewed as an opportunity to refocus the patient's concordance and adherence.

CONCLUSION

The group stressed that algorithms do not replace the careful, ongoing clinical assessment and decision making that are the responsibility of the clinician. However, it is hoped that the guidance provided here will be of assistance, or help to confirm decisions, for the clinician at the initiation, or during use, of Xelma. ■

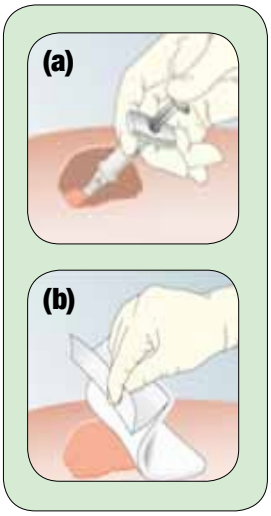


FIGURE 3. Having attached the silicone applicator, (a) carefully apply a thin layer of Xelma to the wound bed (approximately 1 mL/20 cm^2) then (b) cover the wound with an appropriate secondary dressing, taking into consideration a possible increase in exudate. Depending on exudate levels, secondary dressings can be changed between applications of Xelma.

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