National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT380 UrgoStart for treating diabetic foot ulcers and leg ulcers

Consultation comments table

Final guidance MTAC date: 16 November 2018

There were 11 consultation comments from 3 consultees (2 NHS professionals, 1 manufacturer). The comments are reproduced in full, arranged in the following groups according to the main issue raised in the relevant comment:

- General note from consultee (comment 1)
- Technology description (comments 2 to 3)
- Draft recommendation (comment 4)
- Cost modelling (comments 5 to 6)
- User experience (comments 7 to 8)
- Other comments (comments 9 to 11)

General note from consultee

#	Consultee ID	Role	Section	Comments	Response
1	3	Manufacturer	General	We wish to submit the following comments consistent with the advisory committee's areas of interest as follows: A. Has all of the relevant evidence been taken into account? B. Are the summaries of clinical and resource savings reasonable interpretations of the evidence? C. Are the recommendations sound and a suitable basis for guidance to the NHS? D. Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?	Thank you for your comment.

Technology description

#	Consultee ID	Role	Section	Comments	Response
2	3	Manufacturer	2.2	*"The TLC-NOSF layer is a combination of the patented TLC technology, which is intended to create a moist protective wound healing environment, and the NOSF, which inhibits protease activity, specifically matrix metalloproteinases, and this is designed to accelerate healing"* **Urgo Medical Opinion**: We believe that, UrgoStart is not innovative just because it "inhibits protease activity." In addition, it also has the *neovascularisation mode of action specified in the original submission (decision Problem Section 2.2). Thus, by not specifying the important and additional role of restoration of neovascularisation by reactivating vascular cells proliferation and migration, and the promotion of angiogenesis through proliferation and migration of endothelial cells,* the section is in violation of items **A, and B** of the committee's comments area of interest **Evidence:** As noted in the Explorer RCT "the potassium salt of sucrose octasulfate, a key component of UrgoStart has a unique structure that interacts with growth factors	Thank you for your comment. The EAC did not identify any evidence reporting specicifically on UrgoStart's effect on neovascularisation by promoting fibroblast growth and proliferation. There is evidence that highlights the generic mechanism however it is does not relate specifically to wound healing. The committee considered this comment carefully and the description of the innovative aspects of the technology and decided not to change it.

				and thus restores their biological functions contributing to tissue formation" (ref 22–24 of the Explorer Lancet Publication). **Urgo Medical's Recommendation:** The relevant statement for Section 2.2 should be modified to also include: *"The TLC-NOSF layer is a combination of the patented TLC technology, which is intended to create a moist protective wound healing environment, and the NOSF, which inhibits protease activity, specifically matrix metalloproteinases, whilst also restoring neovascularisation. This is designed to accelerate healing."*	
3	3	Manufacturer	General	**Terminology to be clarified** • Section 2.1 states *"UrgoStart (Urgo Medical) is an advanced dressing for treating chronic wounds".* This could read 'UrgoStart is an advanced dressing for treating Diabetic Foot Ulcers, Leg Ulcers and Pressure Ulcers' – use of the term chronic here may be confusing for clinicians, who may associate it with duration the wound has been present rather than chronic due to pathology. • Paragraph 1.1. The term *"basic dressings"* is used here, and throughout the document. We disagree slightly with this. We believe the most appropriate terminology would be 'neutral dressings', as basic implies cheap, older dressings whereas the evidence for UrgoStart is vs. UrgoTul. UrgoTul is not a 'basic' dressing, but it is a 'neutral' dressing with clinical data showing its efficacy as such.	Thank you for your comment. The committee sought expert advice about terminology which would be easily understood in clinical practice in the NHS and decided tp remove the term 'chronic' and to use the terms 'interactive' and 'non-interactive' throughout the guidance to describe different types of dressings.

Draft recommendation

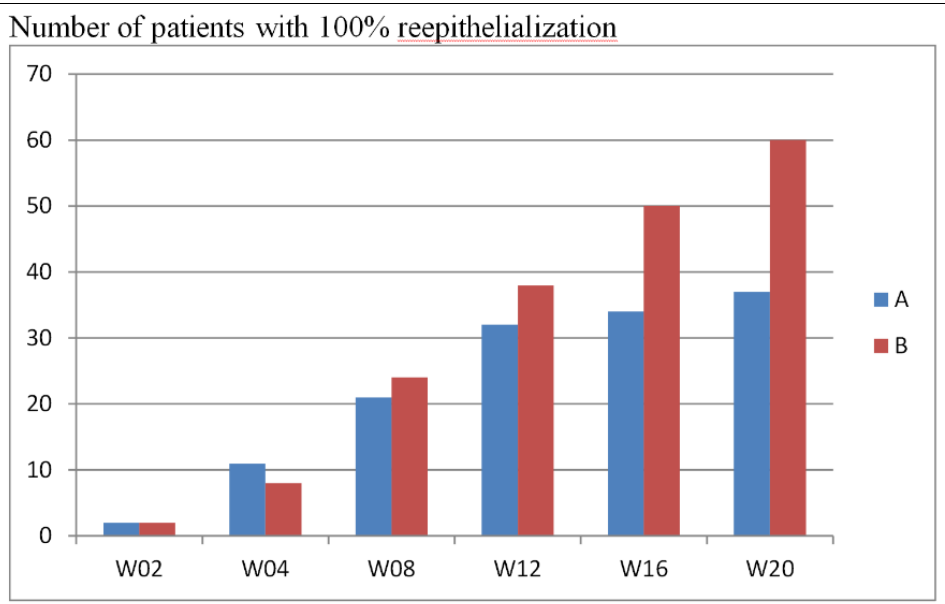
#	Consultee ID	Role	Section	Comments	Response
4	3	Manufacturer	1.2	Urgo Medical Opinion: The strength of the statement in its current form is in violation of items A, B and C of the committee's areas of interest Urgo Medical's Recommendation: The wording of this statement should either:	Thank you for your comment. The committee consideredyour comment carefully and decided not to change the guidance.

				a) Follow that in section 4.7 - *"The committee concluded that UrgoStart should be recommended for people with chronic, non-infected diabetic foot ulcers or venous leg ulcers."* or b) As these are different pathologies, and often treated by different groups of clinicians, the recommendation could be clearer in two separate statements, such as: ○ *UrgoStart dressings are strongly recommended for people with non-infected diabetic foot ulcers* ○ *UrgoStart dressings are recommended for people with venous leg ulcers*	

Cost modelling

#	Consultee ID	Role	Section	Comments	Response
5	3	Manufacturer	1.3	"*Cost modelling shows that, compared with standard care, using UrgoStart dressings to treat diabetic foot ulcers is associated with a cost saving of about £342 per patient after 1 year.* ***It also shows that UrgoStart is likely to be cost saving for treating venous leg ulcers, but by how much is less certain***" **Urgo Medical Opinion**: We believe that by not specifying the average cost savings per patient for VLUs in the recommendation, this section is in violation of items **A, B and C** of the committee's areas of interest **Evidence:** The results of the EAC's revised base-case model showed that on average, the use of UrgoStart in VLU results in a higher £541 per patient per year compared to £342 for DFU (see section 3.7 of consultation document). Significantly, the EAC probabilistic sensitivity analyses for VLU models suggests that over 98% of patients would benefit from savings. Given the robustness of the evidence as confirmed by the probabilistic sensitivity analyses, by not specifying this significant cost saving here, readers might be misled that the cost savings from the use of UrgoStart compared to neutral	Thank you for your comment. The committee considered your comment carefully and concluded that although UrgoStart is likely to be cost saving for treating venous leg ulcers, but the robustness of this conclusion is less certain from the evidence available, therefore the committee did not feel able to provide a cost saving figure. The committee decided to amend the guidance to provide further clarification.

				dressings is insignificant. Furthermore, the budget impact of such savings, despite the expressed uncertainties for the NHS, when extrapolated to the national population of VLU's, would probably run into several millions of pounds annually. **Urgo Medical's Recommendation:** The relevant statement for VLUs in Section 1.3 should be modified to read: ***"It also shows that using UrgoStart dressings to treat venous leg ulcers is associated with a cost saving of about £541 per patient after 1 year, except for in a small minority of patients"***	
6	3	Manufacturer	4.8	*"in these instances UrgoStart would be changed to a different product after 6.09 weeks (DFU) or 8.26 weeks (VLU)"* **Urgo Medical Opinion**: We believe the Explorer trial data contradicts this, hence the Section is in violation of items **A and B** of the of the committee's comments of interest **Evidence:** The Explorer data shows that some wounds will heal in few weeks, others in a longer time, but the mean estimated time to heal (Kaplan Meier method) is around 120 days. If treatment with UrgoStart is stopped at 6 weeks as above, this is not a suitable cut off for all patients. As illustrated by the table below, after 12 weeks, the difference between the 2 groups is marked (with a plateau for the control group between 12 and 20 weeks). Please find below the graph (from Explorer) with the cumulative rate of closure between baseline and Week 20 (A = Control and B = TLC-NOSF):	Thank you for your comment. The EAC explained that the data used to calibrate the model was taken from the Guest et al. (2018a) and Guest et al. (2018b) papers, which summarised resource-use data from patients at 562 GP practices. The committee understood that the product change times used in the model were averages calculated so that the healing outcomes matched the Guest et al. real world data. Clinical experts agreed that if a wound showed no improvement after a few weeks a different product would be tried and the length of time depended on a number of factors related to the wound and patient. The committee considered the assumptions in the model were appropriate but it was aware that they represent a simplification of the complex process of managing wound healing processes. It decided not to changethe guidance.

				 **Urgo Medical's Recommendation:** The relevant statement in Section 4.8 should be modified to read: *"The EAC explained that the calibration of the model was an attempt to address this by recognising that not all wounds will improve with treatment and in these instances UrgoStart could be changed to a different product. Please note that in clinical practice, many more patients continue to achieve wound healing well past these cut-off model points."*	

User experience

#	Consultee ID	Role	Section	Comments	Response
7	1	NHS Professional	-	We as a vascular unit have been using the urgo start product on outpatients and also inpatients. I have found the product to be easy to use, easy to explain to the patient and has also shown some fantastic results in a short period of time. The patients have also been noticing the difference, which for me is one of the best positives. In one of my patients it has shown a reduction in wound size over 4 weeks of approximately 30 % and the wound is also clean with epithelisation present to ulcer bed.	Thank you for your comment. The committee welcome comments on experience with the technology in the NHS.
8	2	NHS Professional	-	The podiatry team at MFT North Manchester community have used Urgostart successfully in a number of patients who have had wounds that have been slow to heal and stuck in the inflammatory phase of healing. This has helped kick start the healing process which has been beneficial to both patient and clinician.	Thank you for your comment. The committee welcome comments on experience with the technology in the NHS

Other comments

#	Consultee ID	Role	Section	Comments	Response
9	3	Manufacturer	General	**Equality Statement and Quality of Life of Chronic Wound Patients** • Patient representatives highlighted the grave plight of chronic wounds as part of the technology appraisal, but this has not been included in the draft consultation document. • In support of the poor quality of life of chronic wound patients, we submitted in our report a study we conducted in several wound clinics in the UK, but this has not been reported either (see attached QoL ISPOR Poster). The benefits of earlier wound healing conferred on patients following the use of UrgoStart would be better appreciated as shown in the ISPOR poster, illustrating that DFU and VLU patients endure poorer QoL compared to patients with other chronic diseases such as Asthma, COPD, Diabetes, Epilepsy, Heart Disease and even Stroke.	Thank you for your comment. The committee acknowledged that diabetic foot ulcers and venous leg ulcers are associated with a high level of morbidity that has an impact on daily living. The committee decided to make a minor amendment to the guidance.

10	3	Manufacturer	4.7	**Urgo Medical Opinion**: We believe that there is no clinical evidence to support a 6 week treatment delay after clearing of infection. We believe that in practice adding in this statement could block DFU patients from receiving UrgoStart as a treatment, hence the Section is in violation of items **A, B and C** of the of the committee's comments of interest **Evidence:** The Explorer RCT Lancet data shows evidence that 'the sooner UrgoStart is used the better the results', with early intervention demonstrating even faster healing rates using the product. Please find attached a poster presented by Pr. Gerry Rayman at the European Association for the Study of Diabetes specifically addressing this topic (both in pdf poster format as presented, also in Word document format containing all the data). **Urgo Medical's Recommendation:** The relevant statement in Section 4.7 should be modified to read: ***"**UrgoStart would be used as soon as a wound is cleared of infection**"***	Thank you for your comment. The considered your comment and expert advice and decided to amend the guidance.
11	3	Manufacturer	General	**Update of Existing Guidelines and NICE Pathways** **Urgo Medical Opinion**: We strongly believe this should be routed to the topic selection oversight group/the NICE guidelines programme in order to update the guideline NG19 for Diabetic Foot Ulcers and the NICE pathway. **Evidence:** We believe it meets the criteria based on: a- There are a number of equivalent technologies available b- The equivalent technologies have been available in clinical practice for some time c- The benefits of the technology are likely to be best evaluated in the context of a care pathway already developed by NICE The guideline/pathway in its current format from 2016 states the following, which are no longer appropriate considering the strength of evidence and quality of the Explorer RCT showing the efficacy of using UrgoStart for Diabetic Foot Ulcers: *2.5 "The evidence surrounding different dressing types for diabetic foot ulcer was often limited or inconclusive. It is proposed that more randomised controlled trials are undertaken to explore this question, but alternative methodologies may*	Thank you for your comment. Updating of existing clinical guidelines is outside the remit of the medical technologies advisory committee.

				also be considered in the case of treating a complex wound. The proposed study would monitor and evaluate the cure rates of foot ulcer resulting from diabetes, rates and extent of amputation (major or minor), health-related quality of life, adverse events and hospital admission rates and length of stay"……. 1.5.10 When deciding about wound dressings and offloading when treating diabetic foot u account the clinical assessment of the wound and the person's preference, and use with the lowest acquisition cost appropriate to the clinical circumstances. **Urgo Medical's Recommendation:** The current guideline should be updated to reflect the recommended usage of UrgoStart in the treatment of these wounds	

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