NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

UrgoStart for treating leg ulcers and diabetic foot ulcers

The National Institute for Health and Care Excellence (NICE) is producing guidance on using UrgoStart in the NHS in England. The medical technologies advisory committee has considered the evidence submitted by the company and the views of expert advisers.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the public. This document should be read along with the evidence (see the committee papers).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and resource savings reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?

Note that this document is not NICE's final guidance on UrgoStart for treating leg ulcers and diabetic foot ulcers. The recommendations in section 1 may change after consultation.

After consultation the committee will meet again to consider the evidence, this document and comments from the public consultation. After considering the comments, the committee will prepare its final recommendations which will be the basis for NICE's guidance on the use of the technology in the NHS in England. For further details, see the medical technologies evaluation programme process and methods guides.

The key dates for this guidance topic are:

Closing date for comments: 08 November 2018

Second committee meeting: 16 November 2018

Details of the advisory committee are given in section 5.

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice.

If the case for adopting the technology is supported, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. If the technology is recommended for use in research, the recommendations are not intended to preclude the use of the technology in the NHS but to identify further evidence which, after evaluation, could support a recommendation for wider adoption.

1 Recommendations

1.1 Evidence supports the case for adopting UrgoStart dressings to treat venous leg ulcers and diabetic foot ulcers in the NHS. UrgoStart dressings are associated with increased wound healing compared with basic dressings. For people with non-venous leg ulcers, there is insufficient evidence to support routine adoption.

1.2 UrgoStart dressings should be considered as an option for people with chronic and non-infected venous leg ulcers or diabetic foot ulcers.

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. For both types of ulcers, potential cost savings mainly come from better healing with UrgoStart dressings.

Why the committee made these recommendations

UrgoStart is a type of advanced wound dressing. Clinical trial evidence shows that using UrgoStart to treat diabetic foot ulcers increases wound healing compared with basic dressings. For venous leg ulcers, the evidence shows that UrgoStart increases the rate of wound healing in the short term compared with basic dressings when used with standard care, but the impact on complete wound healing is less certain. There is less evidence for non-venous leg ulcers so, although clinical and patient benefits are plausible, there is no positive recommendation in this patient group. Cost analyses suggest that using UrgoStart could save costs for the NHS.

2 The technology

Technology	UrgoStart (Urgo Medical) is an advanced dressing for treating chronic wounds. It consists of a layer of open-weave polyester mesh impregnated with hydrocolloid polymers within a petroleum jelly known as technology lipido-colloid (TLC). It also contains nano-oligosaccharide factor (NOSF) and has an absorbent pad and a semi-permeable backing. There are 5 formats of the dressing and each comes in different sizes: UrgoStart Contact Layer, UrgoStart Non-Adhesive, UrgoStart Plus Pad, UrgoStart Border and UrgoStart Plus Border.
Innovative aspects	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.
Intended use	UrgoStart is intended for treating chronic wounds. The indications addressed in this evaluation are leg ulcers and diabetic foot ulcers.
Costs	UrgoStart has a typical list price of £4.28 per dressing.
For more details, see the Urgo Medical website.	

3 Evidence

Clinical evidence

Relevant evidence comes from 5 studies, 3 of which are randomised controlled trials

3.1 Of the 5 studies that met the inclusion criteria defined in the scope, 2 were randomised controlled trials (RCTs) in venous and mixed leg ulcers and 1 was an RCT in diabetic foot ulcers. There is also a non-comparative study in diabetic foot ulcers and a pooled analysis of non-comparative observational studies, which included both patient groups. For full details of the clinical evidence, see section 3 of the assessment report.

Results from the EXPLORER RCT show an increase in wound closure for diabetic foot ulcers

3.2 In the multi-centre double-blind international EXPLORER (n=240) RCT with a 20-week follow-up, UrgoStart was compared with UrgoTul, a basic

non-adherent dressing (Edmonds et al. 2018). The results reported a statistically significant increase in complete wound closure in favour of UrgoStart (p=0.002), as well as a statistically significant increase in absolute wound area reduction (p=0.022). Safety and quality of life were similar in the 2 groups. The external assessment centre (EAC) noted that this was a European international study with some patients recruited from UK centres, but the number of patients recruited per centre was low (median=3) and the study only included people with neuro-ischaemic ulcers.

Results from the CHALLENGE RCT in venous leg ulcers show an increase in wound area reduction in the first 8 weeks

3.3 In the multi-centre double-blind international CHALLENGE (n = 187) RCT with an 8-week study period, UrgoStart was compared with UrgoTul Absorb, a basic non-adherent dressing (Meaume et al. 2012, Meaume et al. 2017). Compression therapy was used in both the intervention and control groups (more than 96% at week 6). The results reported a statistically significant increase in relative wound area reduction (p=0.002) and in absolute wound area reduction (p=0.003), in favour of UrgoStart. Use of UrgoStart also resulted in a statistically significant improvement in the pain and discomfort dimensions of the EQ-5D quality-of-life assessment (p=0.022). Safety and patient acceptance were similar in the 2 groups. The EAC noted that the follow-up period of 8 weeks was potentially too short to assess healing in complex wounds, and only 13 wounds in total were completely healed by the end of the study (equally in the 2 treatment arms). No UK sites were included in this study, and there was a small number of patients having treatment per centre (mean=4.2).

Pooled analysis of non-observational studies broadly supports the evidence from the RCTs

3.4 The healing rates of venous leg ulcers and diabetic foot ulcers was broadly supported by evidence from a pooled analysis of non-comparative data from 8 observational studies (Munter et al. 2017). The EAC noted

that there was substantial heterogeneity in the follow-up period (4−20 weeks), outcome measures and distribution of ulcer-type in this study. The analysis, however, included a large patient population with more than 10,000 patients with chronic wounds of whom 7,903 had venous leg ulcers and 1,306 had diabetic foot ulcers.

Cost evidence

The company's cost analyses include separate models for leg ulcers and diabetic foot ulcers, both of which show cost savings

3.5 The company presented separate de novo cost-effectiveness models for leg ulcers and diabetic foot ulcers. The leg ulcer model was a Markov model with a 1-week cycle length, which incorporated 3 health states. The diabetic foot ulcer model was more complicated and included 6 health states. The base-case results were presented for a time horizon of 1 year. When UrgoStart was compared with basic dressings, the results showed a saving of £274.25 per patient per year for leg ulcers and £666.51 per patient per year for diabetic foot ulcers.

The EAC revisions of some of the parameters and its calibrations of the company's models to more accurately reflect NHS costs and consequences

3.6 The EAC considered that both model structures presented by the company adequately captured all the relevant health states, and that the assumptions were valid and reasonable. It did not agree, however, with the company values for some parameters, which were revised. The EAC also calibrated the models to align with the healing outcomes and resource use from published UK studies (Guest et al. 2018a and Guest et al. 2018b). The EAC assumed 20% of people with a diabetic foot ulcer would not heal and treatment would proceed for 1.4 months (6.09 weeks) on average before the dressing was changed to a different product. The EAC assumed 37.6% of people with a leg ulcer would not heal and treatment for these patients would proceed for 1.9 months (8.26 weeks) on average before the dressing was changed to a different product.

Results from the EAC's cost analysis show UrgoStart is likely to be cost saving

3.7 Results from the EAC's base-case analysis showed UrgoStart to be cost saving by £541 per patient per year for leg ulcers and by £342 per patient per year for diabetic foot ulcers compared with standard care. Key drivers of the savings were the cost of dressings, the transition parameters for healing and infection or complications, and the cost of community nursing and hospital visits. The EAC conducted sensitivity analyses and found that UrgoStart was always cost saving for leg ulcers. It also found that UrgoStart only incurred costs for diabetic foot ulcers if the healing rate was assumed to be half of that reported in the EXPLORER trial. For full details of the cost evidence, see section 4 of the assessment report.

4 Committee discussion

Clinical-effectiveness overview

Results from the EXPLORER trial show faster complete healing with UrgoStart dressings in diabetic foot ulcers

4.1 The committee concluded that the EXPLORER study provided convincing evidence that UrgoStart dressings improve complete wound healing in patients with diabetic foot ulcers. It noted the EAC conclusions that there was a low risk of bias in this study, and that the reported benefits associated with UrgoStart were also supported by the pooled data analysis of non-comparative observational data. Although most of the evidence came from people with neuro-ischaemic ulcers, a clinical expert advised that similar care is used for both neuropathic and neuro-ischaemic diabetic foot ulcers. The committee concluded that the use of UrgoStart improves wound healing in people with diabetic foot ulcers.

Results from the CHALLENGE study show a faster rate of early healing with UrgoStart dressings in venous leg ulcers

4.2 The committee concluded that the results of the CHALLENGE study showed an increase in the rate of early wound healing with UrgoStart in

patients with venous leg ulcers compared with standard treatment. It noted, however, that the study period of 8 weeks was relatively short, and that the observed treatment benefit was based on measuring increased wound area reduction rather than complete wound closure. Clinical experts confirmed that rapid wound area reduction in the first 8 weeks is a good surrogate for ultimately complete wound closure, but that this is not definitive. The experts stated that venous leg ulcers typically heal completely within 18 to 24 weeks. The committee noted the EAC conclusion that there was a low risk of bias in this study, and also that the benefits associated with UrgoStart were supported by the observational data. It concluded that UrgoStart improves wound healing in venous leg ulcers when used with standard care, although it was uncertain if this would be translated into complete wound closure.

UrgoStart may lead to benefits that are important in improving day-to-day living in people with diabetic foot ulcers or venous leg ulcers

4.3 The committee concluded that there was limited published evidence to support quality-of-life benefits with UrgoStart use. It heard from clinical experts, however, that an increase in wound closure and in the rate of wound area reduction are likely to be associated with improvements in day-to-day living for people with diabetic foot ulcers or venous leg ulcers. The experts explained that, for people with diabetic foot ulcers, complete wound closure is usually necessary for them to be able to return to unhindered walking. They also explained that, for people with venous leg ulcers, a reduction in the wound area may translate into important benefits including earlier transition to less cumbersome dressings and treatment in the community. This was corroborated by comments from a small sample of people who have used UrgoStart dressings and reported quality-of-life benefits associated with improved wound healing. The committee concluded that it was plausible that UrgoStart leads to benefits that are important in improving day-to-day living in people with diabetic foot ulcers or venous leg ulcers.

Relevance to the NHS

The evidence for UrgoStart is broadly generalisable to the NHS

4.4 Only a small proportion of the patients with diabetic foot ulcers in the European EXPLORER study were recruited from a UK centre. There were no patients from the UK in any of the studies that investigated the benefits of UrgoStart in patients with leg ulcers. Clinical experts stated that the demographics of patients having treatment and the fundamentals of wound care are likely to be similar across Europe. However, the experts also explained that some differences in care may exist including, for example, the type of health professional giving the treatment and the compression pressure used to treat patients with venous leg ulcers. The committee concluded that the evidence for UrgoStart is broadly generalisable to the NHS.

The evidence for benefits for leg ulcers is focussed on venous leg ulcers

4.5 The committee noted that most of the evidence of benefit in patients with leg ulcers was in people with venous leg ulcers. Clinical experts confirmed that about 70% of leg ulcers are caused by venous disease. The experts also stated that compression is an important part of standard care for venous leg ulcers but that treatment of non-venous leg ulcers relies on dressings alone. It concluded, however, that even though it is plausible that there are benefits with UrgoStart in non-venous leg ulcers, there is insufficient evidence to make a definitive recommendation in this group.

NHS considerations

UrgoStart can be incorporated in care pathways by including it on local formularies

4.6 Clinical experts advised the committee that the management of diabetic foot care, including ulcer management, varies across different regions of the NHS. In most areas, patients are managed by a multi-disciplinary team and move between GP practice, secondary care and community care depending on their needs. Treatment of venous leg ulcers, on the other hand, is mostly done in a community setting. Clinical experts

advised that new and novel dressings are usually incorporated into local care pathways through their inclusion in dressing formularies. The committee did not consider that the use of UrgoStart should be restricted to any particular setting in the NHS.

UrgoStart should be considered for people with chronic, non-infected ulcers

4.7 Clinical experts confirmed that UrgoStart would only be used after a thorough wound and patient assessment, and after interventions to control other modifiable factors including debridement and treatment of wound infection. They also indicated that UrgoStart would only be used for a wound that had been clear of infection for at least 6 weeks. The experts also agreed that if the use of UrgoStart dressings did not lead to progress in wound healing, they would change to a different product. The committee concluded that UrgoStart should be recommended for people with chronic, non-infected diabetic foot ulcers or venous leg ulcers.

Cost-modelling overview

The EAC's updated model is more plausible than the company's model and most appropriate for decision-making

4.8 The committee agreed that the 2 patient groups should be considered separately in the cost model and concluded that the EAC updated model was more appropriate for decision-making than the company's model. The committee expressed concerns about the observed variability in wound healing rates, and questioned whether this was correctly reflected in the model. 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 would be changed to a different product (6.09 weeks for diabetic foot ulcers and 8.26 weeks for venous leg ulcers). The calibration process included the use of data from the Guest et al. (2018a) and Guest et al. (2018b) papers, which summarised resource-use data taken from an electronic database of patients in 562 GP practices across the UK. These data were used to

estimate the proportion of patients whose ulcers had not healed after 1 year in the comparator arms of both analyses.

Main cost drivers

Cost savings are likely to be robust for treating diabetic foot ulcers but are uncertain for treating venous leg ulcers

4.9 The committee noted the importance of healing-rate parameters in determining the outcome of the cost modelling. It expressed confidence that there was improved complete wound healing in diabetic foot ulcers with UrgoStart. The committee, however, was uncertain about the reliability of using an extrapolation method to derive complete wound healing rates from partial healing at 8 weeks in people being treated for venous leg ulcers. In view of this, the committee concluded that the cost savings are likely to be robust when UrgoStart is used to treat diabetic foot ulcers, but that uncertainty remains about the cost savings when UrgoStart is used to treat venous leg ulcers.

Cost savings

UrgoStart is estimated to be cost saving compared with standard care, but there are uncertainties in the size of those savings in people with venous leg ulcers

4.10 The EAC's sensitivity analyses showed the estimated cost savings were fairly robust. It conducted deterministic sensitivity analyses for key model parameters in both cost models. Results showed that the technology remained cost saving in most cases. The committee concluded that, based on the published evidence, cost modelling and expert opinion, UrgoStart is likely to be cost saving compared with basic dressings. It accepted the estimate from the EAC's updated model for diabetic foot ulcers of a £342 saving per patient per year as a realistic estimate. For venous leg ulcers, it accepted that use of UrgoStart is likely to be cost saving but considered that the magnitude of the savings is less certain.

5 Committee members and NICE project team

Committee members

This topic was considered by the medical technology advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more technical analysts (who act as technical leads for the topic), a technical adviser and a project manager.

Sarah Douglas

Liesl Millar
Technical analysts

Bernice Dillon
Technical adviser

Jae Long
Project manager

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