NICE National Institute for Health and Care Excellence

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

HEALTHTECH PROGRAMME

Draft guidance

Topical antimicrobial dressings for infected leg ulcers in people 16 years and over: late-stage assessment

Guidance development process

NICE late-stage assessment (LSA) guidance evaluates categories of technologies that are already in widespread use within the NHS. It assesses whether price variations between technologies in a category are justified by differences in innovation, clinical effectiveness and patient benefits. This will support NHS commissioners, procurement teams, patients and healthcare professionals to choose technologies that maximise clinical effectiveness and value for money.

Find out more on the NICE webpage on late-stage assessment (LSA) for medtech.

NICE is producing this guidance on topical antimicrobial dressings for infected leg ulcers in people aged 16 years and over in the NHS in England. The medical technologies advisory committee has considered the evidence and the views of clinical and patient experts.

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

The committee is interested in receiving comments on the following:

Issue date: February 2025

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

After consultation:

- Based on the consultation comments received, the committee may meet again.
- If committee meets again it will consider the evidence, this evaluation consultation document and comments from stakeholders.
- The committee will then prepare the final draft guidance, which will go through a resolution process before the final guidance is agreed.

Note that this document is not NICE's final guidance on Topical antimicrobial dressings for infected leg ulcers in people aged 16 years and over. The recommendations in section 1 may change after consultation.

More details are available in NICE's health technology evaluations: the manual and NICE's late-stage assessment interim process and methods statement.

Key dates:

Closing date for comments: 28/02/2024

Second committee meeting: 20/03/2024

1 Recommendations

1.1 There is not enough evidence to determine whether price variations between different antimicrobial agents in topical antimicrobial dressings for infected leg ulcers are justified. So, if an antimicrobial dressing is needed to treat an infected leg ulcer, use the least expensive option that is:

- clinically appropriate, and
- meets the preferences and needs of the person with the infected leg ulcer.

1.2 A healthcare professional and the person with the leg ulcer should reach a joint decision on which dressing to use (see the NICE page on shared decision making). Decisions should take into account how the choice of dressing might impact the person's:

- physical health
- mental health and wellbeing
- relationships with others
- ability to complete activities of daily living.

1.3 When deciding on the least expensive option, consider the following factors:

- the cost of the primary dressing
- the need for and cost of additional products
- the frequency of dressing changes needed
- if a person can change their own dressing or if a visit by a healthcare professional is needed.

What information is needed

More information is needed to determine whether price variations between different antimicrobial agents in topical antimicrobial dressings can be justified. Evidence should compare agents with each other and in similar

dressing types. Evidence should be statistically powered, report details of concomitant treatments and ideally be done in a community setting in the NHS.

Key outcomes that should be captured include:

- clinical performance outcomes of the dressings to evaluate clinical and cost effectiveness, including:
  - health-related quality of life
  - time taken to clear signs and symptoms of infection
  - time to complete wound healing
  - duration of antimicrobial dressing use and any other leg ulcer treatments
  - short- and long-term toxicity of the antimicrobial agents in the dressings
  - other adverse events or sensitivities to the dressing, including the number of people who have contraindications to particular antimicrobial agents
  - infection load and the type of bacteria killed or removed by the dressing
  - the number of people who progress to needing oral antibiotics
- healthcare professional preferences, including:
  - dressing conformability
  - ease of application
  - ease of removal.

What this means in practice

Considerations for procurement and commissioning

According to the National Wound Care Strategy Programme, in 2019 there were an estimated 739,000 leg ulcers in England with estimated associated healthcare costs of £3.1 billion per year. The focus of this assessment is the subset of leg ulcers with a local infection. The prevalence of infection in

2 UK-based studies was reported to be 18% (in leg ulcers of any cause) and 41% (in venous leg ulcers).

Considerations for wound management formulary groups

These recommendations are not intended to restrict choice. When developing a formulary, if dressings have similar technical specifications but different agents or prices, decision making should consider cost and the factors listed in recommendation 1.3.

Information on the cost of dressings should be available to healthcare professionals so that they can decide, using the factors listed in recommendation 1.3, which of the clinically appropriate options is the least expensive.

Considerations for healthcare professionals

These recommendations do not replace clinical reasoning. If more than one type of dressing is clinically appropriate, the choice of dressing should be based on patient preferences and cost, taking into account the factors listed in recommendation 1.2 and 1.3.

Considerations for people with infected leg ulcers

People with infected leg ulcers should be involved when deciding which antimicrobial dressing to use. They should be given information on the antimicrobial dressing that is being prescribed and, where possible, offered options that meet their needs. They should be given support if they experience any issues and wish to change to another type of antimicrobial dressing.

Why the committee made these recommendations

There are many topical antimicrobial dressings available with a variety of antimicrobial agents, which vary in technical specification and cost. This

assessment aimed to determine whether the differences in clinical, economic and non-clinical outcomes attributed to those antimicrobial agents could justify price variation.

Given the uncertainties in the clinical evidence, it is not possible to say whether any antimicrobial agent works better than the others. These uncertainties include:

- a lack of direct comparisons of antimicrobial agents
- differences in:
  - the outcomes measured and
  - when the outcomes were measured.

So it is not possible to say whether price differences are justified.

A user preference assessment of healthcare professionals shows that there are multiple criteria that healthcare professionals consider when selecting antimicrobial dressings. These include a holistic assessment of the person's clinical and social needs. Healthcare professionals also consider criteria relating to the cost of the dressing and treatment of the leg ulcer. Once clinically appropriate dressings are identified, the decision on which to use should be based on cost and patient preference.

Evidence shows that people with infected leg ulcers are often not involved in selecting their antimicrobial dressing. There are many personal factors that could be impacted by using an antimicrobial dressing and these should be discussed with the person when choosing a dressing.

More evidence is needed to show whether price variations can be justified by differences in how well different antimicrobial dressings work. Evidence should be collected for outcomes that are important to the people using the dressings, and that allow clinical and cost benefits to be assessed.

2 The technology

2.1 Topical antimicrobial dressings are dressings that contain an antimicrobial agent, which they deliver directly to the wound or wound bed to provide sustained antimicrobial effects. They are one of the options available to healthcare professionals when treating infected leg ulcers. There are various types of wound care dressings, with different intended clinical benefits. These are shown in table 1.

Table 1 Types of dressings and their uses

Dressing types	Uses
Alginate, gelling fibre and absorbent fibre	Exuding wounds, to act as an absorbent while maintaining a moist environment
Foams and absorbent pads	Moderate to high exuding wounds
Wound contact layers, for example gauze	Superficial or partial thickness wounds
Ointments, hydrogels, gels or pastes containing the antimicrobial agent, or ribbons made from one of the materials from another dressing type	Deeper wounds and wounds requiring debridement of thick slough
Hydrocolloid	Aiding debridement of devitalised tissue

2.2 As well as different types of dressing, there are different antimicrobial agents used in dressings. These are the focus of this assessment. Chemically or pharmacologically active antimicrobial agents include:

- silver
- chitosan
- honey
- iodine
- copper
- chlorhexidine
- enzyme alginogel
- octenidine and

- polyhexamethylene biguanide (PHMB).

Non-active agents with a physical mode of action include dialkylcarbamoyl chloride (DACC).

2.3 Some agents are available in different forms (described as subagents). For example:

- honey:
  - Manuka
  - monofloral
  - polyfloral
- iodine:
  - cadexomer iodine
  - povidone iodine
- silver, the subagents of which can be categorised into 3 subgroups:
  - silver salts and compounds:
    - ionic silver
    - silver sulphate
    - silver sulphadiazine
    - silver oxysalts
    - ionic silver complex
  - elemental silver:
    - metallic or elemental silver and
    - nanoparticulate silver and
  - ionic silver with antibiofilm agents
- copper: cupric oxide.

2.4 There are many antimicrobial dressings available to the NHS. For this assessment NICE considered antimicrobial dressings listed on the NHS Drug Tarriff Part IX.

3 Committee discussion

The medical technologies advisory committee considered evidence on antimicrobial agents in topical antimicrobial dressings for infected leg ulcers in people 16 years and over. Evidence was taken from several sources and used to determine whether price variation between agents could be justified by differences in their clinical and cost effectiveness or in non-clinical outcomes important to users. These included a review of the published literature, evidence submitted by the companies, responses from stakeholders, lived experience of people who have used antimicrobial dressings and a user preference assessment. The committee also considered the economic evidence from a review of the published literature, a resource impact assessment and an economic evaluation done by the external assessment group (EAG). Full details are available in the project documents for this guidance.

The condition

3.0 The National Wound Care Strategy Programme defines a leg ulcer as an ulcer between the knee and ankle that has not healed within 2 weeks. Most leg ulcers are caused by venous insufficiency, although they can also be caused by peripheral vascular disease, reduced mobility, cardiac failure, diabetes or sickle cell disease. Ulcers heal slower when they are infected.

Current practice

3.1 Antimicrobial dressings can be used to treat leg ulcers that have signs and symptoms of local infection. The choice of dressing is informed by the wound presentation and the person's individual needs. So, dressing choice often changes throughout the duration of a wound. In general, a dressing should be used for no more than 2 weeks before the wound and dressing are reassessed. Subsequent dressings may be of the same type or there could be a step down to a non-antimicrobial dressing or step up to a second-

line option. If there is still evidence of local infection after 2 weeks, further escalation for advice from the tissue viability team may be necessary, as per local guidance. There is no national guidance on using topical antimicrobial dressings to treat infected leg ulcers. This has led to the development of local guidance within formularies (where these exist), and a wide variation in practice and available dressings across the NHS. Other measures aimed at reducing the microbial burden of the wound can include using compression products and systemic antimicrobial therapy.

Lived experience

3.2 A survey of people with infected leg ulcers showed that most respondents (10 out of 12) reported that they were not involved in the decision making process to select an antimicrobial dressing. The committee heard from a patient expert how using an antimicrobial dressing for an infected surgical wound had impacted their life. They explained that the dressing caused discomfort and embarrassment, and that there was sometimes a smell from the infected wound. Using the dressing had also had a negative impact on their mental health and their relationships. They also described the lack of shared decision making when being prescribed an antimicrobial dressing. The committee acknowledged that the patient expert had used antimicrobial dressings for an infected surgical wound and not an infected leg ulcer. But, it agreed that a wound infection could have a significant impact on a person's health and quality of life. The committee concluded that a shared decision should always be made, and that the impact of the dressing selection should be considered when deciding which antimicrobial dressing to use.

Healthcare professional preferences

3.3 The committee considered evidence from a user preference assessment completed by healthcare professionals. This aimed to

explore which criteria are most important to healthcare professionals when choosing an antimicrobial dressing to treat an infected leg ulcer. This included all aspects of an antimicrobial dressing and not just the antimicrobial agent. Healthcare professionals were selected for the user preference assessment because it became evident during scoping, that while shared decision making is promoted and patient preference is considered, the choice is ultimately made by the healthcare professional. This is mainly driven by clinical reasoning. The group comprised 15 healthcare professionals who had experience of prescribing antimicrobial dressings. The group developed 2 sets of criteria that they used when selecting a dressing. These were criteria based on clinical presentation and criteria that are independent of clinical presentation.

Criteria based on clinical presentation

3.4 The group identified 5 main criteria related to clinical presentation:

- wound presentation
- medical history and patient characteristics
- previous dressing regimes and efficacy
- mode of action of agent or dressing
- cytotoxicity of antimicrobial agent.

Criteria independent of clinical presentation

3.5 The group also identified 5 criteria that are independent of clinical presentation. Ranked in order of importance, they were:

- conformability
- ease of removal
- application directions
- cost
- sustainability.

None of these criteria are specific features of individual branded dressings or antimicrobial agents but are generic and relate to general dressing performance. The committee noted that apart from cost and, to a lesser extent, ease of removal, these preferences are not captured by the evidence. The committee concluded that future evidence collection should evaluate the performance of dressings in these criteria.

Equality considerations

3.6 Many different groups could be affected by infected leg ulcers. Some of these groups have protected characteristics. The committee heard that older people are more likely to have a leg ulcer. Also, people from lower socioeconomic groups will have longer healing times with a higher chance of the ulcer recurring. The committee was made aware that the chance of having a leg ulcer is higher in people who are seriously ill, have a neurological condition, impaired mobility, impaired nutrition or obesity. The risk of infection is also higher in people with conditions such as anaemia, cardiac disease, respiratory disease, peripheral arterial disease, renal impairment or rheumatoid arthritis. The committee also heard that people from certain ethnic backgrounds (South Asian, Chinese, black African and African-Caribbean) have an increased risk of diabetes, which increases the risk of infection. Leg ulcers are also more common in people with haemoglobinopathies such as sickle cell disease and thalassaemia. Signs of infection may also be less visible on darker skin. The committee was made aware that smoking, dependence on alcohol, drug use and nutritional deficiencies can be contributing factors to delayed wound healing. When people are less adherent to their treatment plan, they can be at a higher risk of developing an infection. The committee heard that this may be a risk for people with mental health conditions and learning disabilities. When discussing access to services, the committee heard that people with no fixed address

may experience difficulties if they need frequent dressing changes. The committee was made aware that while some of the antimicrobial agents in scope contained animal products, some do not and can be used by people in all faith groups and vegans. The committee also heard that some dressings and agents may be contraindicated for women who are pregnant or breastfeeding, or people with thyroid dysfunction. But some non-active agents may be suitable for pregnant or breastfeeding women. The committee understood that people who have infected leg ulcers will have individual needs and that these should be considered when selecting an antimicrobial dressing.

Clinical effectiveness

Key evidence is limited

3.7 The evidence for antimicrobial dressings to treat infected leg ulcers in people 16 years and over is heterogeneous and limited in quality. The EAG could not determine the relative efficacy of the different antimicrobial agents, despite there being an indication of some benefits in treating infection and wound healing. It identified 34 studies for inclusion in the review. But not all of these were in people with infected leg ulcers. If there was no evidence for an antimicrobial agent in people with infected leg ulcers, the EAG included studies in people with infected wounds elsewhere on the body. If there was still no evidence for the agent, the EAG included studies in people with leg ulcers that were not infected or where the infection status was unclear. This allowed the EAG to evaluate all but 1 of the agents (no evidence was identified for chlorhexidine) but meant that some evidence was less generalisable to people with infected leg ulcers. Of the 34 studies, 21 were in people with infected leg ulcers. Of these, 18 evaluated silver, 2 iodine, 1 octenidine, 1 DACC and 2 honey. There were 8 studies in people with infected wounds that were not leg ulcers. Of these, 1

evaluated DACC, 2 honey, 3 enzyme alginogel and 2 chitosan. There were 5 studies in people with leg ulcers that were not infected or where the infection status was unclear. Of these, 2 evaluated PHMB and 3 evaluated copper. There was evidence for:

- 2 of the 3 subagents of honey (Manuka and monofloral)
- 1 of the 2 subagents of iodine (cadexomer iodine)
- the following 7 of the 8 subagents of silver:
  - ionic silver with antibiofilm agents
  - ionic silver
  - silver sulphate
  - silver sulphadiazine
  - metallic or elemental silver
  - silver oxysalts and
  - ionic silver complex
- the subagent of copper (cupric oxide).

No evidence was available for polyfloral honey, povidone iodine or nanoparticulate silver. There was no evidence available for any population subgroups such as type of leg ulcer or wound presentation.

Additional limitations of the evidence

3.8 There is limited evidence comparing the effectiveness of the different agents in the relevant outcomes. Most outcomes were not well reported or were measured using different tools across studies, making it difficult to draw conclusions from the data. Key outcomes with the most evidence were infection status, complete or partial wound healing and change in size or area of ulcer or wound. Minimal quality-of-life data was found. The included studies varied in design and healthcare setting. Only 8 of the studies were done at least partially in the UK, so the evidence is less

generalisable to the NHS. The studies also lack statistical power and agents were not compared in similar types of dressing. The EAG found most studies in people with infected leg ulcers have a moderate to high risk of bias. The committee concluded that there was not enough evidence to make conclusions on the relative performance of the different agents and subagents in all outcomes.

Cost effectiveness

Model structure

3.9 The EAG developed a Markov model that included 4 health states:

- infected, unhealed wound
- non-infected, unhealed wound
- healed wound
- death.

The EAG compared 6 agents with each other in a fully incremental analysis and a pairwise analysis between agents. These were iodine, copper, chitosan, silver, honey and PHMB. There was not enough evidence available to include chlorhexidine, enzyme alginogel, octenidine, or DACC in the analysis. Subanalyses were done using the same methods to compare relevant subagents with each other. The results of the main and subanalyses were presented as total costs and associated quality-adjusted life years (QALYs). The EAG used a 1-year time horizon with a 1-week cycle length.

Model inputs

3.10 The EAG's model included parameters of clinical performance, resource use and cost of dressings. It used the evidence identified in the review for clinical performance, other published literature for resource use, and the NHS Drug Tariff Part IX and registry data for the cost of the dressings. Because of the limited evidence, and to

avoid assuming clinical equivalence of different antimicrobial agents, the EAG made the following assumptions to inform parameters:

- the rate of complete healing was used to estimate:
  - a per-week healing rate and
  - the rate of infection resolution
- after their first-line antimicrobial dressing, people progressed to a weighted second-line 'basket' of treatments that were assumed to be clinically equivalent regardless of the first-line treatment used
- no recurrence of leg ulcer infection within the 1-year time horizon
- the 'infected, unhealed' health state had more per-person dressing changes than the 'non-infected, unhealed' health state
- people in the 'infected, unhealed' and the 'non-infected, unhealed' health states need the same amount of resources
- the EAG calculated from the literature that unhealed ulcers use 4.5 times more resources than healed ulcers, and so resource use was adjusted accordingly if a person was in the 'healed' state or not.

The EAG did scenario analyses to explore these assumptions. The clinical experts advised that discontinuation from antimicrobial dressings was considered best practice once an infection had resolved. The clinical experts also advised that linking the rate of infection resolution to complete healing has limitations but that another more appropriate alternative was not available. The committee agreed that to avoid assuming clinical equivalence, and in the lack of better options, that the EAG's approach was acceptable.

3.11 Costs of antimicrobial dressings were sourced from Part IXa of the Drug Tariff. A weighted average cost of all dressings containing the

agent or subagent was calculated using registry data. The clinical experts advised that costs may vary between acute and community care because of variation in modes of procurement, such as bulk billing, that can be used by acute trusts. The committee felt that costs may not be accurately captured in the model. This was because of the different models of delivery between services, which make it difficult to capture overall costs and spending nationally. The committee also noted that healthcare professionals may be unaware of the costs of dressings. The committee emphasised that cost information should be made more readily available to healthcare professionals via formularies. This would help inform their decision making on which clinically appropriate dressing to use.

Model limitations and scenario analyses

3.12 The committee considered that there were several limitations in the model. These were caused by the uncertainty in, or the lack of, available data to inform the parameters and the assumptions that the EAG had to make. The results from the economic evaluation should therefore be interpreted with caution. The EAG did several additional scenario analyses to explore these uncertainties. They included:

- varying the weighted cost of the antimicrobial dressing per agent to the maximum and minimum possible
- varying frequency of dressing changes
- aligning the cost of iodine to cadexomer iodine (base case used povidone iodine cost and cadexomer iodine efficacy)
- varying the resource requirements, costs and utilities of different health states
- assuming clinical equivalence between agents
- applying different rates of infection.

There was not enough evidence to do analysis of any of the subgroups, including:

- type of leg ulcer
- wound presentation
- location of ulcer, or
- complexities that may impact the treatment of leg ulcer infections.

Results of the economic evaluation

3.13 Because of the uncertainty in the evidence used to inform it, the results from the economic model are highly uncertain. The difference in costs and QALYs are small and the 95% confidence intervals overlapped for all agents in both costs and QALYs. As a result, the EAG could not conclude whether there are clinically meaningful differences between the agents. The high level of uncertainty remained for all of the EAG's scenario analyses. It also remained for the analysis of subagents, which compared 2 honey subagents with each other, and silver subagents with each other. The cost of a dressing and the effectiveness of a dressing to clear an infection were 2 of the main drivers of cost effectiveness in the model. Prescription time and the frequency of dressing changes were also drivers of cost effectiveness. Because of the high uncertainty and lack of data, the committee concluded that more evidence was needed to determine if one antimicrobial agent offered more value than another to the NHS.

Resource impact assessment

3.14 There is not enough evidence to determine if price variations between agents are justified. Resource impact analysis indicated that using clinically appropriate but less expensive options could make savings for the NHS. But, the committee understood that there were a number of limitations in the analysis, including that:

- the data was for antimicrobial dressings in all indications, and not just infected leg ulcers
- procurements via wound care formularies and off-medical prescribing platforms were not included
- the analysis assumed that:
  - antimicrobial agents were clinical equivalent
  - dressings would be used for the same amount of time
  - dressings would be changed with the same frequency
  - all infected leg ulcers are the same grade.

The committee noted difficulties in accurately capturing overall costs and national spending. It concluded that, because of these difficulties, the savings it saw may not accurately reflect the use of antimicrobial dressings to treat infected leg ulcers. Further analyses exploring different assumptions are being prepared and will be presented to committee for their consideration.

Justification for price variation

3.15 The committee discussed the clinical and economic evidence, the user preference assessment and the patient expert's lived experience. It concluded that it was not possible to determine if the price variation between antimicrobial agents was justified by differences in clinical or cost benefits. The committee emphasised that an appropriate range of antimicrobial dressings should be available for healthcare professionals to meet the needs of people with infected leg ulcers.

Evidence needed to show additional value

3.16 The committee concluded that more evidence is needed to justify the price variation between antimicrobial agents used in antimicrobial dressings to treat infected leg ulcers. It noted that it was not possible to determine the value of individual antimicrobial agents because the available evidence lacked head-to-head

comparisons of similar dressings. The committee asked for more evidence using clinical and cost outcomes that can inform a health economic evaluation. It also asked that evidence be collected to evaluate the performance of dressings in the criteria identified in the user preference assessment.

4 Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be evaluated. 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.

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