NICE National Institute for Health and Care Excellence

Late-stage assessment

GID-HTE10041
Topical antimicrobial dressings for infected leg ulcers in people aged 16 and over

Scope

1 Introduction

The topic has been identified for late-stage assessment (LSA) by NICE, in collaboration with the Department of Health and Social Care. LSA aims to assess technologies that are in widespread or established use in the NHS. Over time, technologies in use often undergo continuous or incremental innovation and adaptation. LSA will assess whether price variations between technologies are justified by the incremental differences and advancements, and which technologies represent value for money. It will support clinical practitioners, managers and commissioners in using NHS resources as effectively as possible and ensure that patient and system benefits are maximised.

The technologies identified for this assessment are topical antimicrobial dressings available for use in the NHS. The evaluation will assess the clinical and economic benefits of innovations in antimicrobial dressings for local leg ulcer infections in people aged 16 and over, as well as evaluating how product features impact outcomes and user preferences. The innovations in antimicrobial dressings that will be evaluated are the different antimicrobial agents used (see section 2.2 for further definition).

1.1 Population

The National Wound Care Strategy Programme (NWCSP) defines a leg ulcer as an ulcer between the knee and ankle that has not healed within 2 weeks (NWCSP 2023). 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. Most leg ulcers with delayed wound healing are not clinically infected but are likely to be colonised with bacterial biofilm.

According to the NWCSP, in 2019 there were an estimated 739,000 leg ulcers in England with estimated associated healthcare costs of £3.1 billion per year (NWCSP 2023). A cohort study, where data was entered by GPs at practices across the UK and included information on community and secondary care, included 3,000 people in 2017 to 2018 (Guest 2020). Analysis led to an estimate of 3.8 million adults with a wound managed by the NHS, 28% of which were leg ulcers (15% were venous leg ulcers and 13% were other or unspecified types of leg ulcer). Infection was recorded in 41% of the venous leg ulcers. The rate of healing was lower in the presence of infection, with 18% of venous leg ulcers that had recorded evidence of infection healing during the study period compared with 50% of those without evidence of infection. The annual amount of NHS resource spent on dressings for venous leg ulcers was estimated at nearly £80 million. People with a venous leg ulcer had an average of one nursing visit or dressing change every 2 to 3 days. People with other kinds of leg ulcer had an average of one nursing visit or dressing change every 3 to 4 days. Less than 1% of all patients with a wound were prescribed the same dressing for the duration of their wound or study period. On average, patients were prescribed a mean of 8 different dressing types over the study period, which varied according to the wound type. A more recent study derived a point prevalence for venous leg ulcer of 3.2 per 10,000 people in the UK and estimated that the national cost of treating them was £102 million with a per person annual cost of £4,790 (Urwin 2022). While this study did not distinguish between infected and non-infected leg ulcers, the authors found that on average, treatment with an antimicrobial primary dressing containing honey, silver or other antimicrobial agent was associated with higher costs compared with use of a non-antimicrobial dressing.

The risk of wound infection is influenced by various characteristics of the individual, their wound, and the environment. Antimicrobial dressings are indicated for wounds that are infected or for wounds at risk of infection. The

focus of this assessment is on infected leg ulcers, based on clinical advice and guidelines. There is considerable variation in the cost of dressings between categories of dressings and within each category.

1.2 Current management

For ongoing care of leg ulcers, the NWCSP recommends cleansing the wound bed, the surrounding skin and the whole limb, and considering debridement if needed (NWSCP 2023). An emollient should be applied to surrounding skin as needed before applying a “simple, low adherent dressing with sufficient absorbency”. It recommends that infected leg ulcers are treated according to the NICE guideline on leg ulcer infection: antimicrobial prescribing (NICE 2020) and advises that people with acute infections should not be offered compression as part of their immediate and necessary care. But this may be considered after assessment and appropriate management of the infection. Within 14 days, causes and risk factors for non-healing wounds should be identified and assessed. A treatment plan should be formulated to address the cause of the leg ulcer and compression therapy should be offered as appropriate to the person’s needs. Leg ulcers that remain unhealed should be escalated for advice in line with local care pathways.

The International Wound Infection Institute (IWII) describes a wound infection continuum of 5 stages: contamination, colonisation, local infection (covert and overt stages), spreading infection and systemic infection (IWII 2022). Steps to reduce the wound microbial burden include managing exudate, optimising the wound bed with therapeutic cleansing and debridement and using antimicrobial dressings when indicated. It notes that topical antimicrobials play a role in treating a wound when it is likely to be clinically infected.

The assessment, diagnosis and management of infected leg ulcers is a nurse-led discipline typically managed in the community (Guest 2020). Diagnosing wound infection is a clinical judgement based on the presence of signs and symptoms of infection alongside wound chronicity. Assessment of a person with a wound infection should be approached holistically considering the person, their history and comorbidities alongside the wound presentation. According to the IWII, signs and symptoms of local infection can be subtle

(covert) or more overt (classic) (IWII 2022). Covert signs and symptoms include hypergranulation, bleeding or friable granulation, epithelial bridging and pocketing in granulation tissue, increasing exudate and delayed wound healing beyond expectations. Overt signs and symptoms include erythema, local warmth, swelling, purulent discharge, wound breakdown and enlargement, new or increasing pain and increasing malodour.

Biofilms also contribute to delayed wound healing (IWII 2022). A biofilm is a community of microorganisms in which cells stick together or to a surface and become embedded in a slimy matrix. Wound biofilms can be embedded in slough, debris, necrotic and other tissues and can be difficult to identify. Signs and symptoms of biofilm include failure to heal despite appropriate antibiotic therapy, recalcitrance to appropriate antimicrobial therapy, delayed healing despite optimal treatment, increased exudate, increased poor granulation or friable hypergranulation, low level erythema or low-level chronic inflammation, secondary signs of infection.

Once an infection has been identified, a topical antimicrobial dressing can be used to reduce the level of bacteria at the wound surface. Dressing products are chosen to suit a particular wound presentation and individual patient needs at a particular stage of healing. The ideal dressing should provide the optimum environment for wound healing and protection from further injury or infection. There are various forms of wound care dressing, including gauze, film, hydrocolloid, hydrogel, foam and alginate, each with intended clinical benefits. As well as having different forms, dressings can contain different antimicrobial agents such as silver, honey, copper, iodine, and enzyme alginogel.

There is currently a lack of national guidelines on the use of antimicrobial dressings to treat leg ulcer infections. The NICE guideline on leg ulcer infection: antimicrobial prescribing (NICE 2020) recommends that underlying conditions, such as venous insufficiency and oedema, should be managed to promote healing. It recommends that an antibiotic should be offered for adults with a leg ulcer when there are symptoms or signs of infection. Oral antibiotics should be offered if a person can take oral medicines and the severity of their condition does not require intravenous antibiotics. It acknowledged that the

criteria for identifying infection in leg ulcers was not consistent between studies but agreed that signs or symptoms may include redness or swelling spreading beyond the ulcer, localised warmth, increased pain or fever. These overlap with the overt signs of local wound infection, spreading infection and systemic infection on the IWII wound infection continuum. The guideline does not include any recommendation on using topical treatments (antibiotics and antiseptics). It noted that topical antiseptics are used for leg ulcers in clinical practice, often to manage minor, localised infections. However, the committee agreed that they could not make any recommendations on the use of topical antiseptics for treating infected leg ulcers because of the limitations of the evidence and the unclear benefit.

Due to the lack of national guidelines, local formularies have developed local guidance on the use of antimicrobial dressings. This has resulted in a wide variation in practice across the NHS, particularly in first line treatment. The NWCSP work and the IWII consensus update aim to address this variation in practice to improve wound care services nationally (NWCSP, IWII 2022). The IWII advise using topical antimicrobial treatments to manage wounds with signs and symptoms of local wound infection and wounds suspected or confirmed as having biofilm. For wounds with signs and symptoms of spreading or systemic infections, it advises topical antimicrobial treatments in combination with systemic antibiotics (IWII 2022).

Local formularies often recommend appropriate first line options for an infected wound. In general, the maximum time a dressing should be used is 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 continues to be evidence of local infection after 2 weeks, local guidance typically recommends escalation for advice from the Tissue Viability Team which is in line with recommendations from the NWCSP (NWCSP 2023).

1.3 Antimicrobial stewardship

Antimicrobial resistance occurs when microorganisms naturally evolve in ways that cause medications used to cure infections to be ineffective. Antimicrobial

stewardship refers to the supervised and organised use of antimicrobial agents. The NICE guideline on antimicrobial stewardship (NICE 2015) recommends that commissioners ensure stewardship operates across all care settings. Healthcare practitioners should consider the risk of antimicrobial resistance for individual people and the population as a whole when considering whether or not to prescribe an antimicrobial. Wounds UK outlined 5 key components as part of the best practice statement for antimicrobial stewardship which include ensuring the right diagnosis and care plan for people, the right antimicrobial and delivery system, the right time to initiate antimicrobial treatment and the right dose and duration of antimicrobial treatment (Fletcher 2020).

2 Technologies

This section is based on information provided to NICE by companies, commissioning and clinical experts, and information available in the public domain.

2.1 Purpose of the technologies

Topical antimicrobial dressings are dressings that contain or deliver an agent directly to the skin to provide sustained antimicrobial effects. The British National Formulary (BMJ Publishing Group and the Royal Pharmaceutical Society of Great Britain 2024) states that an antimicrobial dressing may be used for local wound infection “to reduce the level of bacteria at the wound surface but will not eliminate a spreading infection”.

There are various forms of wound care dressing, including gauze, film, hydrocolloid, hydrogel, foam and alginate, each with different intended clinical benefits. Some will be more appropriate for a particular type of wound presentation. For example, wounds with heavy exudate may need a more absorbent dressing. As well as different forms of dressing, there are different antimicrobial agents available.

Dressings vary in their mechanism of action, with some dressings designed to release the antimicrobial into the wound to inhibit or kill the growth of

microorganisms. Others have no active pharmaceutical component and aim to physically remove microorganisms from the wound to reduce infection.

Antimicrobial dressings are one form of intervention that aim to reduce bacterial load or combat biofilm, but additional complementary interventions such as compression therapy may be required alongside them in order to optimise patient outcomes (NICE 2020).

2.2 Technology features

Part IX of the Drug Tariff contains a list of antimicrobial dressings that have been approved by NHS Prescription Services for prescribing at NHS expense by an appropriate practitioner in primary or community care. The list of technologies included in this evaluation is not exhaustive and other technologies may be available to the NHS currently or in the future.

Basic technology requirements

Antimicrobial dressings available on the Drug Tariff have the following basic requirements:

- Inclusion of an antimicrobial agent.
    - Chemically or pharmacologically active antimicrobial agents used in dressings include silver, honey, iodine, copper, chlorhexidine, enzyme alginogel, octenidine and polyhexamethylene biguanide (PHMB).
    - Non-active agents with a physical mode of action include chitosan and dialkylcarbamoyl chloride (DACC). These bacterial binding agents are being included in the scope because while they are not antimicrobials, they may have an antimicrobial effect. So, they are often recommended by local formularies and used as alternatives to active antimicrobial agents.
- A form of dressing containing the antimicrobial agent, or a dressing used alongside the antimicrobial agent. The following categories were informed by a list provided to NICE by the Surgical Dressing

Manufacturers Association (SDMA) and clinical experts, and are grouped by clinical indication based on clinical expert opinion:

- Alginate, gelling fibre, absorbent fibre - for exuding wounds, to absorb whilst maintaining a moist environment
- Foams, absorbent pads - for moderate to high exuding wounds
- Wound contact layers, e.g. gauze - for superficial or partial thickness wounds
- Ointments, hydrogels, gels or pastes containing the antimicrobial agent, or ribbons made from one of the above materials - for deeper wounds and wounds requiring debridement of thick slough
- Hydrocolloid – to aid debridement of devitalised tissue
- Additional features may include low adherence, odour absorbent, perforated, semi permeable, high absorbency, conformable, sustained release of antimicrobial agent, haemostatic effect, debridement properties, or extended wear time.

2.3 Current NHS market for the technologies

There are a large number of wound dressings available to the NHS with a wide range of physical performance characteristics (such as size, adhesion, conformability, dressing material, and fluid-handling properties).

There are at least 25 companies providing over 250 antimicrobial dressings (including different sizes and variants) to the NHS across a range of procurement routes.

- Antimicrobial dressings are listed as lot 10 in the NHS Supply Chain advanced wound care framework. The framework started on 1 November 2021 and ends on 31 August 2025. Data supplied to NICE indicate an annual spend on antimicrobial dressings via NHS Supply Chain in excess of £16 million.

- Antimicrobial dressings are listed in Part IXA of NHS Drug Tariff (NHS Business Services Authority 2017).

- Local formularies provide access to antimicrobial dressings, often with guidance on first- and second-line options, and placing some dressings unavailable unless they are ordered by a specialist such as a tissue viability nurse.

- There are also known alternative off-medical prescription procurement platforms in use for antimicrobial dressings. These include Onpos (Coloplast), Formeo (Smith &Nephew), CComms (Convatec) and Halo (Hartmann).

For this assessment NICE will consider antimicrobial dressings indicated for leg ulcers in people aged 16 and over and currently available for NHS Prescription as part IX of the Drug Tariff. Although NHS supply Chain also procure antimicrobial dressing products for secondary care, the focus of this evaluation will be on primary and community care as this is the key area of use of these technologies across the NHS. There is price variation both between types of dressings and within types of dressings on part IX of the Drug Tariff. For example, a 10 x 10 cm foam silver dressing can range from £5.11 to £6.71. Similarly, a 10 x 10 cm alginate honey dressing can range from £3.55 to £4.38.

Data supplied to NICE by two off-medical prescription procurement platforms used in NHS England suggests that antimicrobial dressings containing silver account for the largest spend compared to other agents.

The Clinical Practice Research Datalink (CPRD) collects anonymised patient data from a network of GP practices across the UK (CPRD 2024). This was used to identify instances of antimicrobial dressing use in primary care associated with leg ulcers. Dressings issued within 6 months of the leg ulcer being recorded were included but it is unknown if the specific indication was a local infection in the leg ulcer. According to this data, the most commonly used agent in antimicrobial dressings issued between 1st October 2018 and

31st March 2024 for leg ulcers was iodine closely followed by silver. These 2 agents accounted for more than half the dressings.

3 Decision problem

Due to the large number of similar type antimicrobial dressings available on Part IX of the Drug Tariff, this late-stage assessment will be based on features. These features will be the antimicrobial agent used.

Population	People aged 16 and over with a leg ulcer that shows signs and symptoms of local wound infection as per the IWII continuum
Subgroups	If the evidence allows the following subgroups may be considered: • By type of leg ulcer: venous, vasculitic, phlebolymphoedema • By wound presentation • Location of ulcer • Complexities (e.g., comorbidities or medical history) that may impact treatment of leg ulcer infections
Healthcare setting	Primary and community care settings in the UK If there is no evidence in these settings, relevant evidence in other healthcare settings or outside the UK may be considered where appropriate.
Intervention	Antimicrobial dressings available to the NHS on Part IX of the Drug Tarriff. Interventions will include dressings using an active antimicrobial or bacterial-binding agent: • honey • iodine • silver • chlorhexidine • copper • PHMB • octenidine • enzyme alginogel • DACC • chitosan. Details on technology features can be found in Section 2.2
Comparator(s)	An antimicrobial dressing that is considered current standard of care in the NHS (for example, based on clinical expert advice and clinical evidence). In most

	cases the comparator will not feature the additional agent included in the intervention. The comparator may differ between subgroups.
Outcomes	Outcome measures for consideration, informed from a recent core outcome set developed for leg ulcers (Hallas 2024), may include but are not limited to: **Healing:** (Intermediate outcomes) • Reduction in signs of local infection (covert: pocketing, epithelial bridging, and hyper granulation; overt: erythema, warmth, swelling, purulent discharge, malodour) • Changes to wound bed condition including slough, exudate, granulation and oedema • Condition of peri-wound skin • Reduction in wound size or area • Frequency of dressing changes (Clinical outcomes for infection) • Complete infection healing • Time to healing • Infection recurrence • Prescription of antibiotics (Clinical outcomes for wound healing) • Complete wound healing • Time to healing • Wound recurrence • Prescription of antibiotics • Scar formation **Pain** (patient reported outcome) • Pain and discomfort levels **Quality of life** (patient reported outcomes) • Health-related quality of life • Functional status **Resource use** • Cost of the technology and associated products • Cost of other resource use including: ○ health care professional appointments or visits (primary, community and secondary care)

	○ costs associated with managing wound infection related complications ○ costs of wound care complications due to underlying conditions or diseases **Adverse events and safety** • Allergic reaction, including sensitivity and irritation • Increased pain due to dressing • Skin discolouration • Negative impact on antimicrobial stewardship • Other intervention-related adverse events User preference and non-clinical outcome measures will be based on the prioritisation of outcomes important to users, if considered appropriate for the assessment.
Economic analysis	A health economic model will be developed, where possible, comprising a cost-comparison or cost utility analysis. Costs will be considered from an NHS and Personal Social Services perspective. Sensitivity and scenario analysis should be undertaken to address the relative effect of parameter or structural uncertainty on results. The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.
Other issues for consideration	• There is known variation in practice across local formularies and care pathways in the NHS. • There are varied active components across the antimicrobial dressings included in this scope and some may be contraindicated in certain groups (such as those with known sensitivities or people who are breastfeeding). • The assessment will not be including evidence on leg ulcers at risk of infection because outcome measures would be different.

3.1 Potential equality issues or considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

There are a number of individual and environmental factors which are associated with an increased risk of infected leg ulcers, these may include:

- Leg ulcers are more common in people who are seriously ill, have a neurological condition, impaired mobility, impaired nutrition, or obesity.
- The prevalence of venous leg ulcers increases with age.
- People with diabetes have an increased risk of infection. People with certain family origins (South Asian, Chinese, black African and African-Caribbean family origins) have an increased risk of diabetes.
- People with conditions such as anaemia, cardiac disease, respiratory disease, peripheral arterial disease, renal impairment or rheumatoid arthritis have an increased risk of wound infection due to possible poor tissue perfusion.
- Leg ulcers are a chronic complication for people living with haemoglobinopathies such as sickle cell disease and thalassaemia.
- Leg ulcers and some signs of infection may be less visible on darker skin tones.
- People undergoing chemotherapy or taking medications such as immunosuppressants, anticoagulants or non-steroidal anti-inflammatory drugs may be more prone to infection.
- Some dressings may not be appropriate for people having radiotherapy.
- Wounds in people who smoke, people who are dependent on alcohol, people who use drugs and people with nutritional deficiencies may be less likely to heal.
- People within unsanitary environments may be at higher risk of developing infection in a wound.
- It may be more difficult for people with no fixed address to access care for frequent dressing changes.

- People with a mental health condition and people with a learning disability, if it may impair compliance with their treatment plan, may be more likely to develop a wound infection.

- The scope includes a range of antimicrobial agents with individual instructions for use. There will be groups, such as women who are pregnant or breastfeeding or people with thyroid dysfunction who are contraindicated for use of some agents and these will need to be considered in line with current practice (British National Formulary; Public Health England 2016; NICE Clinical Knowledge Summaries).

- Some antimicrobial agents do not have an active agent and are suitable for pregnant or breastfeeding women. Some antimicrobial agents within the scope do not contain animal products and can be used by people in faith groups.

- Leg ulcers occur in people from all socioeconomic groups, but ulcers take longer to heal and recurrence rates are higher in people from lower socioeconomic groups

Age, disability, gender, religion, race and pregnancy are all protected characteristics under the Equality Act 2010.

4 Stakeholders

4.1 Healthcare professional organisations

The following healthcare professional organisations have been identified as stakeholders for this evaluation:

- All Wales Tissue Viability Nurses Forum
- British Association of Dermatologists
- British Burn Association
- British Geriatrics Society
- British Infection Association
- Circulation Foundation

- Clinical Pharmacy Association, Pharmacy Infection network
- Infection Prevention Society
- DH Advisory committee on antimicrobial resistance and HCAI
- European Wound Management Association
- European Pressure Ulcer Advisory Panel
- Legs matter
- National Wound Care strategy programme
- Royal College of Nursing (RCN)
- Royal College of Surgeons of England
- Royal College of General Practitioners (RCGP)
- Royal College of Physicians (RCP)
- Royal College of Pathologists
- Royal Pharmaceutical Society
- Society of Vascular Nurses
- Society of Tissue Viability
- The Welsh Wound Innovation Centre
- Vascular Society of Great Britain and Ireland
- Welsh Wound Network
- Wounds UK
- Wounds research network

4.2 Patient and carer organisations

NICE's Public Involvement Programme contacted / have identified the following patient and carer organisations for advice:

- Leg Ulcer Forum
- Age UK
- Wound Care Alliance
- Woundcare 4 heroes
- Lymphoedema support network
- British Skin Foundation
- Lindsay Leg Club Foundation
- Skin Deep Behind the Mask

4.3 Additional non-clinical professional organisations

The following non-clinical professional organisations have been identified as stakeholders for this evaluation:

- Association of British Healthcare Industries (ABHI)
- British National Formulary (BNF)
- Business Services Authority (BSA)
- British Healthcare Trades Association (BHTA)
- Surgical Dressing Manufacturers Association (SDMA)
- NHS Supply Chain

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Appendix A Related Guidance

- **Related Medical Technologies Guidance:**

  UrgoStart for treating diabetic foot ulcers and leg ulcers (2019 updated 2023) NICE medical technologies guidance 42

  Prontosan for treating acute and chronic wounds (2022) NICE medical technologies guidance 67

  The VAC Veraflo Therapy system for acute infected or chronic wounds that are failing to heal (2021) NICE medical technologies guidance 54

  PICO negative pressure wound dressings for closed surgical incisions (2019) NICE medical technologies guidance 43

  The Debrisoft monofilament debridement pad for use in acute or chronic wounds (2014 updated 2019) NICE medical technologies guidance 17

  The MIST Therapy system for the promotion of wound healing (2011) NICE medical technologies guidance 5

- **Related Guidelines:**

  Surgical site infections: prevention and treatment (2019 updated 2020) NICE guideline NG125

  Leg ulcer infection: antimicrobial prescribing (2020) NICE guideline NG152

  Diabetic foot problems: prevention and management (2015 updated 2019) NICE guideline NG19

  Major trauma: assessment and initial management (2016) NICE guideline NG39

  Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (2015) NICE guideline NG15

  Pressure ulcers: prevention and management (2014) NICE guideline CG179

- **Related Quality Standards:**

  Antimicrobial stewardship (2016) NICE quality standard 121

  Infection prevention and control (2014) NICE quality standard 61

  Surgical site infection (2013) NICE quality standard 49

Appendix D Abbreviations

CMC	Carboxymethylcellulose
CPRD	Clinical Practice Research Datalink
DACC	Dialkylcarboamoyl chloride
HCAI	Healthcare associated infections
IWII	International Wound Infection Institute
LSA	Late-stage assessment
NWCSP	National wound care strategy programme
PHMB	Polyhexamethylene biguanide
TVN	Tissue viability nurse