NICE National Institute for Health and Care Excellence

Medical Technologies Advisory Committee (MTAC) Thursday 16

January 2025

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

This product class was selected for late stage assessment in 2023.

Clinical and economic evidence has been submitted to NICE by the companies in RFIs, and an external assessment group report has been completed by the EAG. Alongside this, a user preference report has been produced by NICE.

This pack presents the information required for the MTAC to make draft recommendations on this topic.

Guidance lead team

Technical analyst:	• Jakob Falloon
Technical adviser:	• Evan Campbell
Committee lead:	• Jennie Walker
Lead Specialist Committee member:	• Kathryn Morgan
EAG Leads	• Hayden Holmes (YHEC) • Lavinia Ferrante di Ruffano (YHEC)
Specialist Committee Members:	• Priti Bhatt, Tissue Viability Lead Community Services, Guy's and St Thomas' NHS Foundation Trust • Sam Lane, Tissue Viability Nurse, Royal Surrey County Hospital • Sarah Marquis, Matron District Nursing, Lancashire & South Cumbria NHS Foundation Trust • Stacey Evans-Charles, Tissue Viability Nurse Lead, NHS Highland • Lindsay Banks, Medicines Optimisation Pharmacist and Non-Medical Prescribing Lead, Bridgewater Community Healthcare NHS Trust

	• Jane Todhunter, Advanced Vascular Nurse Practitioner, North Cumbria Integrated Care Trust • Jo Dumville, Professor of Applied Health Research, Division of Nursing, Midwifery & Social Work, University of Manchester
Lay Specialist Committee Members:	• Kate Hawley • Elizabeth McCall
Professional Experts:	• Kate Williams, Senior Lecturer, Tissue Viability, Leeds Community Healthcare Trust • Mikyung Bailey, Tissue Viability Nurse , Berkshire Healthcare NHS Foundation Trust , Ayesha Marshall, Nurse Consultant Tissue Viability , South Tyneside & Sunderland NHS Foundation Trust • Clare Greenwood, Clinical Academic Researcher in Tissue Viability., St James University Hospital, Leeds • Lucy Cook, Nurse Practitioner, Guys and St Thomas's Foundation Trust • Keira Bradley, Senior Clinical Nurse Specialist, Leeds Teaching Hospitals NHS Trust • Lisa Hill, Lead Nurse Tissue Viability , Leeds Teaching Hospitals NHS Trust • Keith Moore, Tissue Viability Clinical Nurse Specialist, Bridgewater Community Healthcare NHS Foundation Trust • Emma Mallinson, Tissue Viability Nurse Specialist, Leeds Community Healthcare

Papers included in pack:

1. Front sheet
2. Final scope
3. External Assessment Report (EAR)

3a. Addendum to the EAR

4. Assessment Report Overview (ARO)
5. EAR collated comments
6. User preference report
7. User preference report collated comments
8. Register of Interests

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

5 Authors

Evan Campbell	Helen Gallo	Samantha Baskerville
Topic Adviser	Topic lead	Senior HTA Analyst
Dionne Bowie	Elizabeth Islam	Ella Van Berger
Scientific Adviser	Project manager	Project Administrator

July 2024

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 g

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

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Late-stage assessment

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

Addendum

Produced by: York Health Economics Consortium (YHEC)

Authors:

Hayden Holmes, Associate Director, YHEC

Lavinia Ferrante di Ruffano, Project Director, YHEC

Laura Kelly, Senior Research Consultant, YHEC

Mary Edwards, Senior Research Consultant, YHEC

Angel Varghese, Senior Research Consultant, YHEC

Sarah Medland, Senior Research Consultant, YHEC

Mick Arber, Senior Information Specialist, YHEC

Emma Carr, Research Consultant, YHEC

Ben Hyde, Research Assistant, YHEC

Monica Garrett, Research Assistant, YHEC

Sam Woods, Research Assistant, YHEC

Correspondence to: Hayden Holmes, York Health Economics Consortium, Enterprise House, University of York, YORK, YO10 5NQ.

Date completed: 02/12/24

Contains confidential information: Yes

Number of attached appendices: 0

1 Silver with antibiofilm mechanisms

Following submission of the external assessment report (EAR) on topical antimicrobial dressings for infected leg ulcers in people aged 16 and over, the EAG has developed this addendum to provide additional information using evidence which did not meet the evaluation scope but was raised by Convatec as relevant. We have taken a pragmatic approach to run this additional analysis in this instance because it may be beneficial to provide further context in light of the lack of appropriate data to inform the base case model for the silver sub-agent with antibiofilm mechanisms.

1.1 *EAG comment on suitability*

1.1.1 Harding et al (2016)

The clinical SR used data from Harding et al (2016) (Harding et al. 2016) to inform the the silver sub-agent with antibiofilm mechanisms. However, the EAG did not consider this appropriate evidence to use in the model. Harding et al (2016) conducted a prospective single-arm study of 42 people with venous leg ulcers enrolled at 6 study centers in the UK and Poland. Of these, a subset of 10 people had clinically infected venous leg ulcers.

People received treatment for 8 weeks, during which participants received treatment with 2 types of silver dressings. In the first 4 weeks, participants were prescribed Aquacel Ag+ dressings, which contains the sub-agent silver with antibiofilm mechanisms. In the subsequent 4 weeks, participants were prescribed Aquacel Ag+ dressings, which contains the sub-agent ‘silver salts and compounds’ without antibiofilm. The study reported the number of participants healed at 8 weeks.

The study’s sub-group of participants with infected venous leg ulcers adheres to the decision problem and is within scope. However, the key outcome (number healed) was reported at 8 weeks. Without outcome data at 4 weeks, the data is not reflective of ‘silver with antibiofilm mechanisms’, rather the healing rate when 2 different silver sub-agents are applied.

1.1.2 Convatec Clinical study report (CSR)

This open label RCT (ConvaTec Inc. 2024) compared Aquacel Ag+ Extra (agent subtype: ionic silver with antibiofilm agents, dressing category: alginate, gelling fibre, absorbent fibre) to Cutimed Sorbact (agent subtype: DACC, dressing category: wound contact layer) for 2 to 4 weeks in patients with chronic (>2 month) VLUs, followed by standard care wound management up to 12 weeks. Wound infection was not an inclusion criterion and only [redacted] patients (all in the Aquacel® Ag+ Extra arm) had infected wounds at baseline. For these reasons, the study was not considered eligible for including in the clinical review.

The trial was conducted across 20 study centers in Germany, Colombia and the UK in mixed care settings. Dressings were applied either by study staff or clinical providers on- or off-investigation site, or by subjects at home depending on the standard of care at each centre. The sample size calculations required [redacted] wounds to test for non-inferiority which was achieved in the full analysis population up to week 12 (Aquacel Ag+ Extra [redacted], Cutimed Sorbact [redacted]). Study authors reported a baseline [redacted]

The study reported [redacted]

The study population was [redacted] compared with the Harding et al (2016) study (n=10). Participants were treated with Aquacel Ag+ Extra exclusively, therefore, results will not be biased by the use of multiple silver sub-agents. However, the main concern with this study is that the population did not have a locally infected leg ulcer at study entry, ([redacted] did develop a local infection during the course of the study). Therefore, the population fell outside the scope for this research and the outcomes, if used in the model, may overestimate the benefits. In the colour-coding system used in the main report this study would therefore fall under the "orange" category that included studies of patients with non-infected wounds or wounds with an unclear infection status.

1.2 *Data to inform economic model*

1.2.1 Clinical efficacy data

In order to run a silver sub-agent analysis, clinical data was extracted from each study. These data are presented in Table 1.1 and Table 1.2.

Table 1.1 Data from Harding et al (2016)

Clinical parameter	Model input	EAG comment
Rate of infection resolution (per week)	0.069	This was not reported in the study, Therefore, this was derived using methods outlined in the EAR.
Healing rate from 0 to 4 weeks (per week)	0.018	At 8 weeks, 1 of 10 people had healed. Using multipliers derived from Guest et al (see EAR for methods), this was converted into a 4 week probability of healing of 7%. This was converted into a per week healing rate of 0.018 applicable for the first 4 weeks
Percentage discontinued	0%	Harding et al (2016) reported that one participant discontinued because of adverse events not related to the dressing. It was not stated whether the participant was in the clinically infected subgroup. Therefore, this was assumed to be 0.
Percentage with reoccurring infection	0%	Harding et al (2016) did not report the percentage with a reoccurring infection, therefore, this was assumed to be 0.

Table 1.2 Data from the Convatec RCT

Clinical parameter	Model input	EAG comment
Rate of infection resolution (per week)	[redacted]	This was not reported in the study, Therefore, this was derived using methods outlined in the EAR.
Healing rate from 0 to 4 weeks (per week)	[redacted]	At week 12, [redacted] of participants had healed leg ulcers. This gives a per week rate of [redacted]. Using multipliers derived from Guest et al (see EAR for methods), this was converted into a per week healing rate of [redacted] applicable for the first 4 weeks.
Percentage discontinued	[redacted]	[redacted] were discontinued prior to the end of study defined as all study wounds healed or attending Week 12 visit
Percentage with reoccurring infection	[redacted]	Table 50 (Summary of Adverse Events) in the Convatec CSR stated that [redacted] participants in the Aquacel Ag+ Extra group developed a wound infection.

1.2.2 Resource use and cost data

Harding et al (2016) did not report the frequency of dressing changes per week. The Convatec RCT reported an interquartile range of dressing changes every [redacted]. Therefore, it was assumed that in the 'infected unhealed wound' health state, [redacted] dressings were required per week, and in the 'non-infected unhealed wound' health state, [redacted] dressings were required per week.

1.3 *As per the EAR, the cost for silver with anti-biofilm mechanisms was £7.83. Silver sub-agent analysis*

This section summarises the results of the cost-effectiveness analysis of silver sub-agents. The data from the Convatec RCT and Harding et al (2016) for silver with anti-biofilm mechanisms, were compared with silver salts and compounds and elemental silver using data from the EAR. As per the principal results, PSA and DSA were run. Given that there a fully incremental analysis was done.

1.3.1 Convatec RCT

In the deterministic and average probabilistic results, silver with anti-biofilm mechanisms was cost-effective compared with both elemental silver and silver salts and compounds. This was indicated by the positive NMB (see Table 1.3 and Table 1.4).

Table 1.3: Deterministic pairwise analysis of silver sub-agents

	Silver with anti-biofilm mechanisms (Convatec)	Elemental silver	Silver salts and compounds
Total LYs	0.97	0.97	0.97
Total QALYs	[redacted]	0.69	0.69
Total cost GBP (£)	[redacted]	£7,385	£7,290
Incremental LYs	-	0.00	0.00
Incremental QALYs	-	[redacted]	[redacted]
Incremental costs	-	[redacted]	[redacted]
ICER	-	[redacted]	[redacted]
NMB	-	[redacted]	[redacted]

Abbreviations: GBP – Great British Pound; ICER – Incremental cost-effectiveness ratio; LY – Life years; NMB – Net monetary benefit; QALY – Quality-adjusted life year.

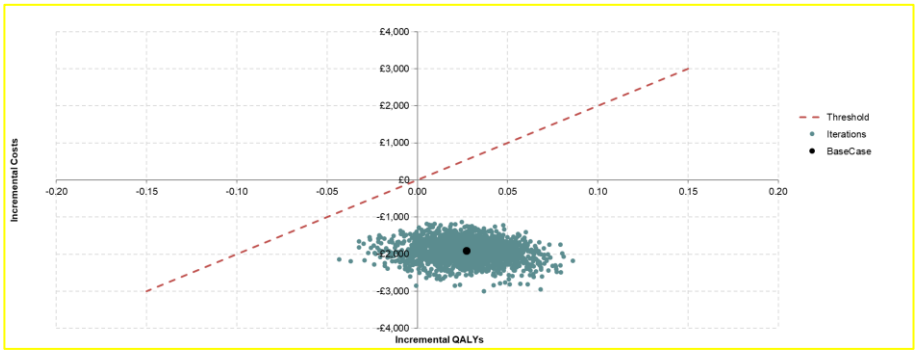
Table 1.4: Probabilistic pairwise analysis of silver sub-agents, mean (95% CI)

	Silver with anti-biofilm mechanisms (Convatec)	Elemental silver	Silver salts and compounds
Total LYs	0.97 (95% CI: 0.97 to 0.97)	0.97 (95% CI: 0.97 to 0.97)	0.97 (95% CI: 0.97 to 0.97)
Total QALYs	[redacted]	0.69 (95% CI: 0.63 to 0.76)	0.69 (95% CI: 0.63 to 0.76)
Total cost GBP (£)	[redacted]	£7,391 (95% CI: £6,623 to £8,159)	£7,326 (95% CI: £6,428 to £8,224)
Incremental QALYs	-	[redacted]	[redacted]
Incremental costs	-	[redacted]	[redacted]
ICER	-	[redacted]	[redacted]
Probability of cost-effectiveness		[redacted]	[redacted]
NMB	-	[redacted]	[redacted]

Abbreviations: CI – Confidence interval; GBP – Great British Pound; ICER – Incremental cost-effectiveness ratio; LY – Life years; NMB – Net monetary benefit; QALY – Quality-adjusted life year.

The cost-effectiveness planes (Figure 1.1) and Table 1.4 shows that the conclusions for the cost-effectiveness model are consistent for 100% of probabilistic runs. The vertical spread of costs is relatively small, compared with the spread of QALYs, suggesting there is less uncertainty in the costs. Furthermore, the costs never cross the x-axis, suggesting that, with the data reported in the Convatec RCT, silver with anti-biofilm mechanisms was cost saving compared with both elemental silver and silver salts and compounds. However, there is a wide horizonal spread, indicating uncertainty in the QALYs. A key outcome from the EAR was that the faster the cohort can progress to the healed health state the more likely it is that the outcome will be cost-effective because of a lower AMD cost, lower health state costs, and higher QALYs. Given that the available percent healed data for silver with anti-biofilm mechanisms from the Convatec RCT was from a population outside the scope, the per-week healing rate was numerically larger compared with elemental silver and silver salts and compounds. This indicates that the cohort progress to the healed health state quicker.

Figure 1.1: Cost-effectiveness plane for silver with anti-biofilm mechanisms (informed by the Convatec RCT) compared with elemental silver (left) and salts and compound (right)



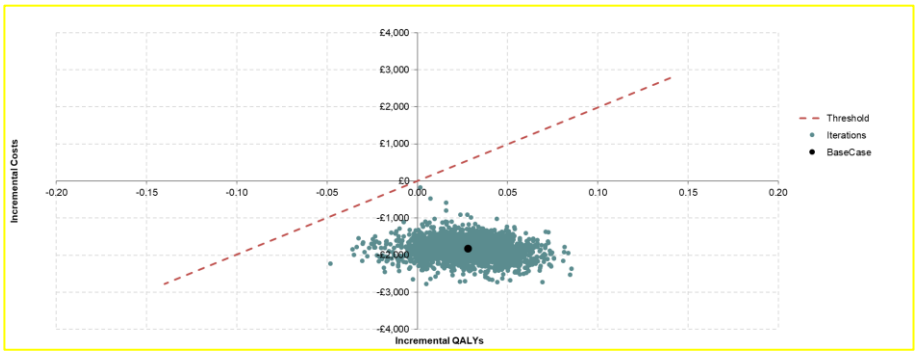
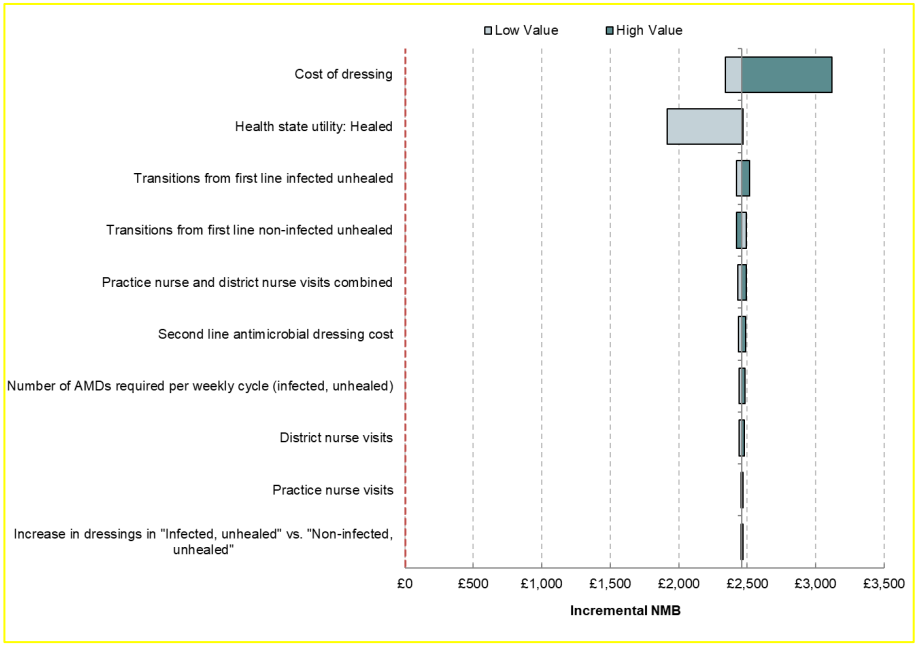
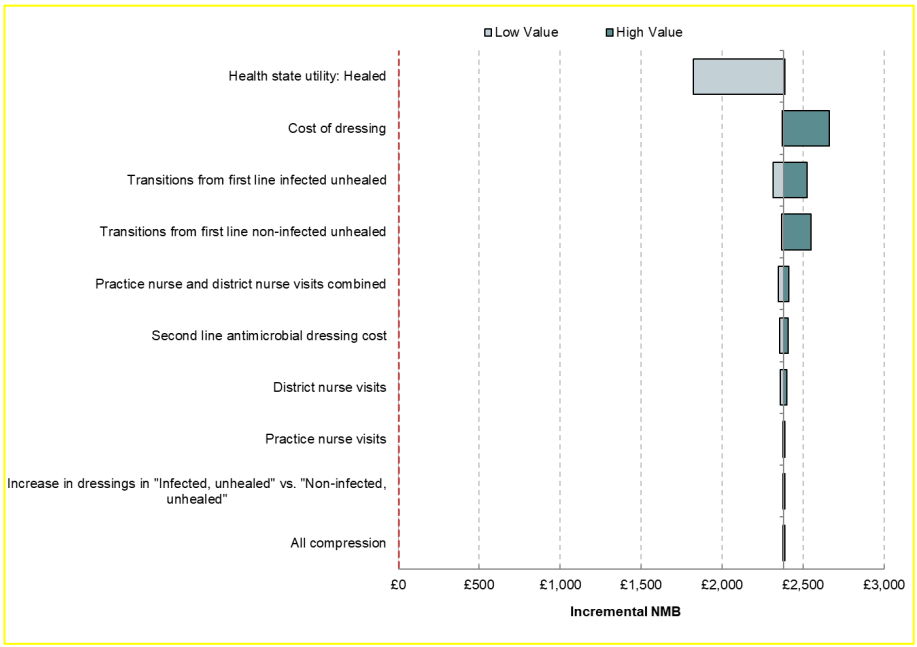


Figure 1.2: DSA tornado plot for silver with anti-biofilm mechanisms (informed by the Convatec RCT) compared with elemental silver (left) and salts and compound (right)




Low Value
High Value
Health state utility: Healed
Cost of dressing
Transitions from first line infected unhealed
Transitions from first line non-infected unhealed
Practice nurse and district nurse visits combined
Second line antimicrobial dressing cost
District nurse visits
Practice nurse visits
Increase in dressings in "Infected, unhealed" vs. "Non-infected, unhealed"
All compression
£0
£500
£1,000
£1,500
£2,000
£2,500
£3,000
Incremental NMB

Changes to the utility value of this health state had a substantial impact on the model. The findings from the cost-effectiveness plane are highlighted further in the DSA. Indeed, health state utilities were identified as one of the key drivers of cost-effectiveness, alongside use of extreme costs for AMDs and the efficacy data from first line infected, unhealed and first line non-infected, unhealed. No DSA scenarios changed the cost-effectiveness conclusion as observed by the bars in the tornado plot never crossing zero (Figure 1.2).

1.3.2 Harding et al (2016)

In contrast to Section 1.3.1, the average PSA and the deterministic results show that silver with anti-biofilm mechanisms was dominated by both elemental silver and silver salts and compounds, meaning it is less costly and less effective. This was indicated by the negative NMB (see Table 1.5 and Table 1.6).

Table 1.5: Deterministic pairwise analysis of silver sub-agents

	Silver with anti-biofilm mechanisms (Harding et al, 2016)	Elemental silver	Silver salts and compounds
Total LYs	0.97	0.97	0.97
Total QALYs	0.69	0.69	0.69
Total cost GBP (£)	£7,702	£7,385	£7,290
Incremental LYs	-	0.00	0.00
Incremental QALYs	-	-0.01	-0.01
Incremental costs	-	£317	£411
ICER	-	-£48,841	-£70,718
NMB	-	-£446	-£527

Abbreviations: GBP – Great British Pound; ICER – Incremental cost-effectiveness ratio; LY – Life years; NMB – Net monetary benefit; QALY – Quality-adjusted life year.

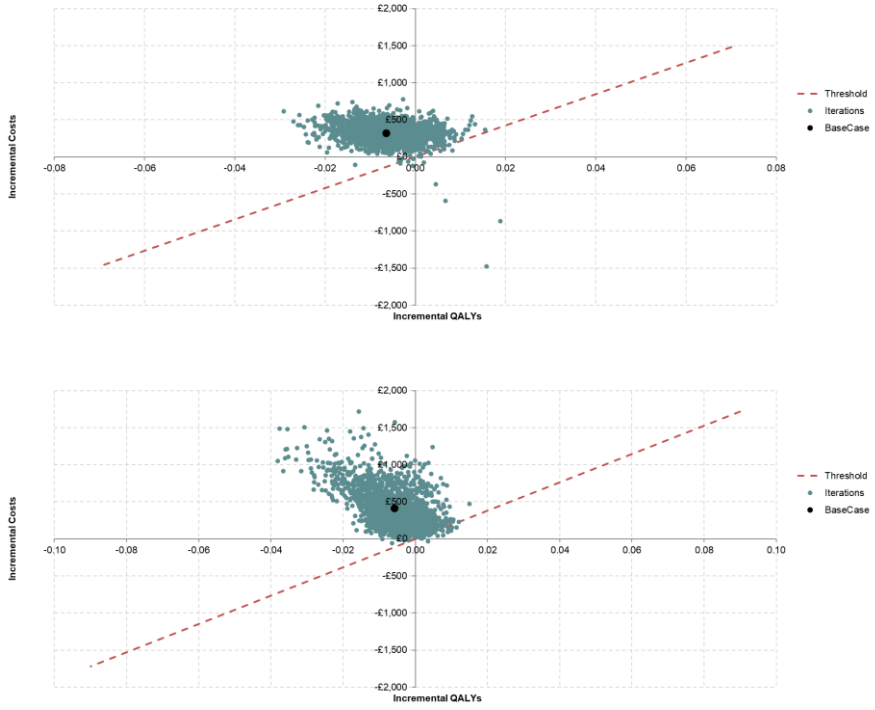
Table 1.6: Probabilistic pairwise analysis of silver sub-agents, mean (95% CI)

	Silver with anti-biofilm mechanisms (Harding et al, 2016)	Elemental silver	Silver salts and compounds
Total LYs	0.97 (95% CI: 0.97 to 0.97)	0.97 (95% CI: 0.97 to 0.97)	0.97 (95% CI: 0.97 to 0.97)
Total QALYs	0.69 (95% CI: 0.63 to 0.75)	0.69 (95% CI: 0.63 to 0.76)	0.69 (95% CI: 0.63 to 0.76)
Total cost GBP (£)	£7,712 (95% CI: £6,947 to £8,477)	£7,391 (95% CI: £6,623 to £8,159)	£7,326 (95% CI: £6,428 to £8,224)
Incremental QALYs	-	-0.01 (95% CI: -0.02 to 0.00)	-0.01 (95% CI: -0.02 to 0.00)
Incremental costs	-	£321 (95% CI: £139 to £503)	£386 (95% CI: £22 to £749)
ICER	-	-£49,629	-£71,423
Probability of cost-effectiveness		0.8%	1.2%
NMB	-	-£450 (95% CI: -£725 to -£176)	-£494 (95% CI: -£994 to £7)

Abbreviations: CI – Confidence interval; GBP – Great British Pound; ICER – Incremental cost-effectiveness ratio; LY – Life years; NMB – Net monetary benefit; QALY – Quality-adjusted life year.

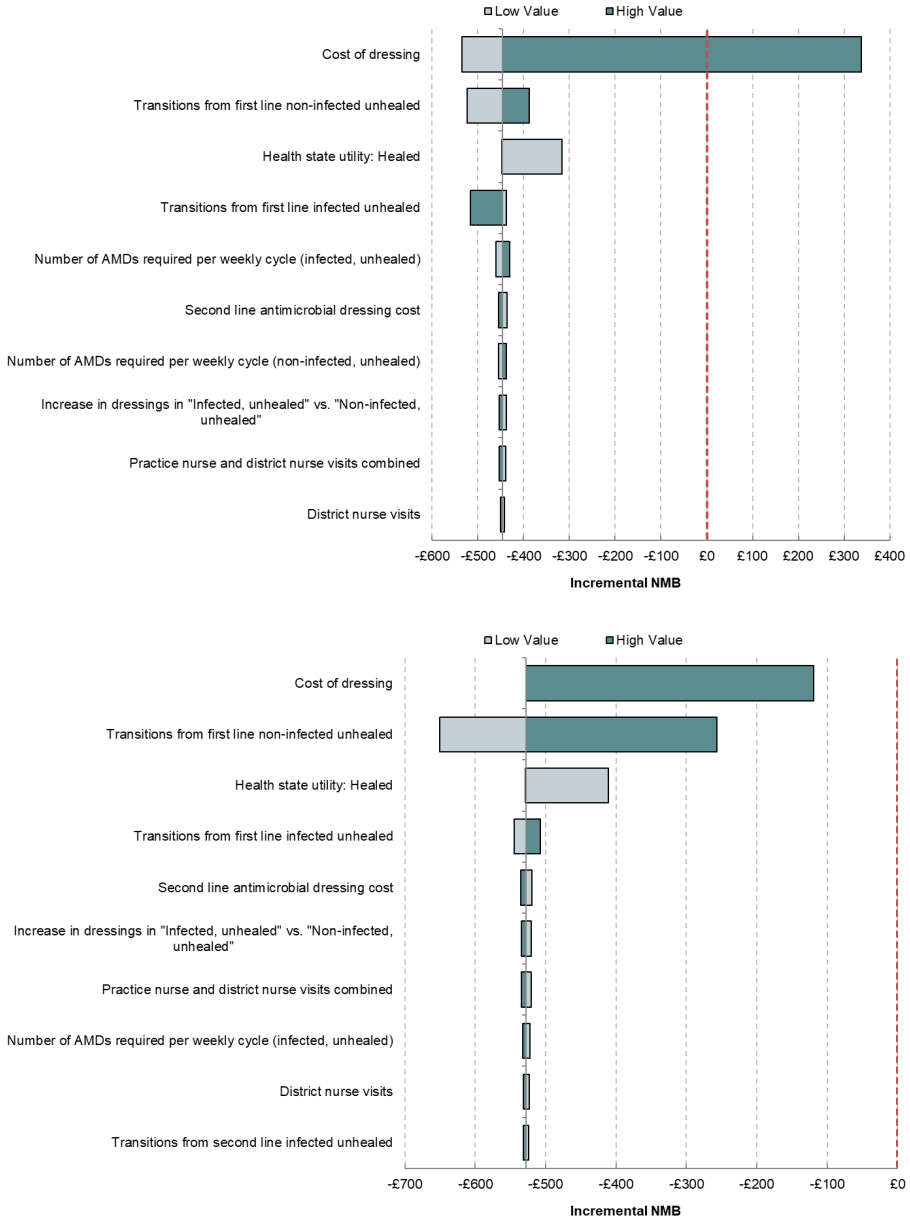
The cost-effectiveness planes (Figure 1.3) shows that there is only a 0.8% and 1.2% likelihood of silver with antibiofilm mechanisms being cost-effective at a threshold of £20,000 per QALY gained, compared with both elemental silver and silver salts and compounds, respectively. This is likely because the efficacy data from Harding et al (2016) was numerically lower than the efficacy data available to inform the other silver sub-agents. The points in the cost-effectiveness planes have a negative trajectory suggesting that as the intervention accrues more QALYs and that there is a decrease in costs. As per Section 1.3.1, the faster the cohort can progress to the healed health state, the more likely it is that the agent will be cost-effective.

Figure 1.3. Cost-effectiveness plane for silver with anti-biofilm mechanisms (informed by Harding et al, 2016) compared with elemental silver (left) and salts and compound (right)



The outcomes are more sensitive to changes in the cost of AMDs, compared with Section 1.3.1. Indeed, the cost of the AMD a key driver of cost effectiveness, above efficacy data and health state utility of the healed health state (Figure 1.4). When compared with elemental silver, which has a larger cost and resource use requirements, a use of the maximum AMD costs caused the conclusion to change.

Figure 1.4: DSA tornado plot for silver with anti-biofilm mechanisms (informed by Harding et al, 2016) compared with elemental silver (left) and salts and compound (right)



1.4 *Summary*

The conclusions from the two silver-sub analyses were contradictory. Indeed, when the Convatec RCT informed the model, silver with antibiofilm mechanisms was the dominant sub-agent compared with other silver subagents. Conversely, when the data from Harding et al (2016) informed the model, silver with antibiofilm mechanisms was dominated by the other silver subagents. Model outcomes with Harding et al (2016) predicted silver with antibiofilm mechanisms would cost [redacted] than when the Convatec RCT informed the model as well as accruing [redacted] QALYs.

Neither the Convatec RCT, nor the data from Harding et al (2016), was considered to be appropriate for use in the economic model to inform the EAR. This is because the participants of the Convatec RCT population did not adhere to the population specified in the scope, namely, people with leg ulcers with local infections. Furthermore, sub-agents used in Harding et al (2016) was a combination of silver salts and compounds and silver with antibiofilm mechanisms. The EAG acknowledge that there are key areas of uncertainty in the data and assumptions informing the economic model. However, data from Harding et al (2016) and the Convatec CSR were, and continue to be, inappropriate for use in the model. These results should not replace the existing silver sub-agent analysis, and they do not change the outcome from the principal analysis.

However, outcomes from both silver sub-agent analyses support those of the EAR, highlighting that, where there was a greater difference in efficacy, the cost savings and QALY gains associated with moving to the healed health state faster offset the additional AMD costs.

2 References

ConvaTec Inc. (2024) Clinical Sudy Report: a clinical study to compare the performance of Aquacel® Ag+ Extra™ and Cutimed® Sorbact® Dressing in the management of patients with venous leg ulcers over a 12-week period. London: Inc., C.

Harding KG, Szczepkowski M, Mikosinski J, et al. (2016) Safety and performance evaluation of a next-generation antimicrobial dressing in patients with chronic venous leg ulcers. International Wound Journal 13(4)**:** 442-8

NICE National Institute for Health and Care Excellence

Late-stage assessment

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

Assessment report overview

This overview summarises key information from the assessment and sets out points for discussion in the committee meeting. It should be read together with the final scope, the external assessment report and the user preference report. List of abbreviations used in this overview is in Appendix A.

The technology

The technologies identified for this assessment are topical antimicrobial dressings (AMDs) for treating infected leg ulcers available for use in the NHS. Topical AMDs are dressings that contain or deliver an antimicrobial agent directly to the wound or wound bed to provide sustained antimicrobial effects.

There are various forms of wound care dressing each with different intended clinical benefits, including gauze, film, hydrocolloid, hydrogel, foam and alginate. Some will be more appropriate for a particular type of wound presentation. For example, wounds with heavy exudate may need a more absorbent dressing. For this assessment, dressing types were categorised according to clinical indication, using information from the British National Formulary, the Surgical Dressing Manufacturers Association and clinical experts (Table 1).

Table 1 Categories and types of dressing included in the assessment

Category of dressing (based on clinical indication)	**Dressing types included**
Dressings for exuding wounds, to absorb whilst maintaining a moist environment	Alginate, gelling fibre, absorbent fibre
Dressings for moderate to high exuding wounds	Foams, absorbent pads
Dressings for superficial or partial thickness wounds	Wound contact layers, e.g. gauze
Dressings for deeper wounds and wounds requiring debridement of thick slough	Ointments, hydrogels, gels or pastes containing the antimicrobial agent, or ribbons made from one of the materials from another category
Dressings to aid debridement of devitalised tissue	Hydrocolloid

As well as different types of dressing, there are different antimicrobial agents available. Chemically or pharmacologically active antimicrobial agents used in dressings 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).

Some agents are available in different forms (described as sub-agents in the assessment):

- Honey: Manuka, monofloral, polyfloral
- Iodine: cadexomer iodine, povidone iodine
- Silver: ionic silver with antibiofilm agents, ionic silver, nanoparticulate silver, silver sulphate, silver sulphadiazine, metallic or elemental silver, silver oxysalts, ionic silver complex
- Copper: cupric oxide

For this assessment, the 8 sub-agents of silver were further categorised into 3 groups, as described by the International Wound Infection Institute (IWII 2022):

- silver salts and compounds: ionic silver, silver sulphate, silver sulphadiazine, silver oxysalts, ionic silver complex
- elemental silver: metallic or elemental silver and nanoparticulate silver
- silver with antibiofilm mechanisms: ionic silver with antibiofilm agents

There are many AMDs available to the NHS. This assessment focuses on AMDs listed in Part IX of the Drug Tariff. A full list of dressings included in the assessment is included in Table 2-3 of the External Assessment Report (EAR). Some of the included evidence may have used dressings that are no longer available on the Drug Tariff but are similar to dressings which are available.

Different clinical presentations require different dressings. This assessment is not meant to replace clinical reasoning of which dressing type to select. Instead, it is intended to evaluate if the price variation between the different antimicrobial agents can be justified by differences in performance or value to the NHS.

The condition and setting

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. 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). 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).

Most infected leg ulcers are treated in the community. This assessment aimed to focus on evidence from primary and community care settings in the UK.

Current practice

In addition to AMDs, care of infected leg ulcers includes other considerations aimed at reducing the microbial burden of the wound (IWII 2022). These considerations include where clinically indicated the use of compression products and systemic antimicrobial therapy (NICE 2020). A simplified care pathway is shown in Figure 3-1 of the EAR. The choice of dressing is informed by the wound presentation and individual patient needs. As such, dressing choice often changes throughout the duration of a wound. At the time of this assessment, there is no national guidance on the use of topical AMDs to treat leg ulcer infections. This has led to development of local guidance by local formularies (where these exist), and a wide variation in practice across the NHS.

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope.

Clinical effectiveness

The External Assessment Group (EAG) did systematic literature searches to identify relevant published clinical evidence and considered submitted evidence from companies. The search and selection methods are in section 4.1 of the EAR.

Where no evidence on infected leg ulcers was found for an agent, or the evidence was limited, the population criteria were broadened in stages, as follows until evidence for that agent was identified: infected wounds of the foot; infected wounds elsewhere on the body; non-infected or unknown infection status lower leg ulcers. Screening was done at an individual ‘agent’ level (such as honey or silver) rather than at sub-agent level (such as monofloral honey or metallic silver). Studies were considered to fully meet the

scope where they reported that participants had infected leg ulcers, whether the criteria for infection were reported or not.

Overview of key studies

The clinical review included 45 documents describing 38 studies (34 complete and 4 ongoing). Results were extracted and synthesised for the 34 completed studies, 21 fully met the scope and 13 met the broader population criteria as described above (Table 2).

- Studies which fully aligned with the decision problem: 18 studies on silver (4 RCTs comparing silver and no-agent, 1 pilot RCT comparing silver with DACC, 1 prospective cohort study comparing different silver dressings, 1 RCT comparing silver and iodine, 1 non-randomised study comparing silver with honey that was reported as a conference abstract only, 7 single arm trials and 3 prospective case series), 1 RCT on iodine (compared with no agent), 1 non-randomised comparative study on octenidine (comparing octenillin gel used with different types of secondary dressings against foam or alginate with or without silver, or hydrogel, used with secondary dressings), and 1 single arm trial on honey (results only available in a conference poster).
- Studies which partially met the decision problem in people with infected wounds of other types: 1 case series on DACC, 1 single arm trial and 1 prospective case series on honey, 3 studies on enzyme alginogel, 1 RCT and 1 single arm trial on chitosan.
- Studies which partially met the decision problem in people with non-infected lower leg ulcers: 1 RCT and 1 prospective case series on PHMB, 1 single arm trial and 2 prospective case series on copper.

No eligible studies were identified on chlorhexidine.

Generalisability of the evidence

The EAG had several concerns about the generalisability of the included studies in using AMDs to treat infected leg ulcers in the NHS. Included studies

were conducted across a range of countries and varied in setting. Of the 34 completed studies, only 8 were conducted at least partially in the UK. The evidence base included studies assessing care provided in inpatient, outpatient, home and community care settings across a range of countries. The variety of settings made it difficult to generalise to primary and community care settings in the UK. In some studies, signs of infection were reported but the wounds were not reported to be clinically assessed as 'infected' and in other studies the criteria for defining infection were often unreported. The reporting of concomitant care was inconsistent and wound bed preparation and secondary dressing treatment protocols varied. Further details on generalisability of the evidence base are described in section 5.3 of the EAR.

Risk of bias

Of the 21 studies that fully aligned with the decision problem, 17 were judged to have moderate or high risk of bias by the EAG. No formal risk of bias assessment was done for the studies that met the broader population criteria. More details on risk of bias are in section 5.2 of the EAR.

Table 2. Alignment of the evidence base with the decision problem (3 comparative studies are included under 2 different agents)

Alignment with decision problem	Chitosan	Copper	DACC	Enzyme Alginogel	Honey	Iodine	Octenidine	PHMB	Silver
Infected lower leg ulcers (aligned fully with the decision problem)	-	-	1 study n=40 **Green**	-	2 studies n=20, n=50 **Green**	2 studies n=93, n=281 **Green**	1 study n=16 **Green**	-	18 studies n ranged from 14 to 794 **Green**
Infected wounds on the lower limb (foot or mixed leg/foot)	-	-	-	-	1 study n=30 **Yellow**	-	-	-	-
Infected wounds elsewhere on body (including mixed lower limb/elsewhere)	2 studies n=90, n=20 **Yellow**	-	1 study n=13 **Yellow**	3 studies n=23, n=356, n=1,657 **Yellow**	1 study n=121 **Yellow**	-	-	-	-
Lower leg ulcers but non-infected / infection status unclear	-	-	-	-	-	-	-	2 studies n=50, n=67 **Orange**	-
Non-infected (or unclear infection status) wounds on the foot or elsewhere (or mixed lower-leg with foot/elsewhere ulcers).	-	3 studies n=12, n=13, n=25 **Orange**	-	-	-	-	-	-	-

Green indicates studies that aligned fully met the decision problem. Yellow indicates studies partially met the decision problem but still included infected wounds, while orange indicates studies partially met the decision problem but with uninfected wounds or queries over infection status

Evidence for sub-agents

There was evidence for 2 of the 3 sub-agents of honey (Manuka and monofloral), 1 of the 2 sub-agents of iodine (cadexomer iodine), 7 of the 8 sub-agents of silver (ionic silver with antibiofilm agents, ionic silver, silver sulphate, silver sulphadiazine, metallic or elemental silver, silver oxysalts, and ionic silver complex) and the sub-agent of copper (cupric oxide).

No evidence was available for polyfloral honey, povidone iodine or nanoparticulate silver.

Data on population subgroups

A number of population subgroups were identified in the scope, including type and location of ulcer and wound presentation (evidence to be assessed by the dressing type in Table 1), but there was insufficient evidence for any of these to be considered in the analysis.

Outcomes of interest

Most outcomes of interest were not well reported or were measured using different tools across the studies, making it difficult to draw conclusions from the data. Outcomes with the most available evidence were wound infection status, complete and partial healing of wound, and change in size or area of the ulcer or wound. Minimal data were found relating to patients' quality of life. The EAG concluded that no statistical pooling or quantitative analysis was appropriate because of the heterogeneity in study designs, populations, interventions and outcomes. More details are provided in Appendix D of the EAR.

The EAG concluded that the evidence was inadequate to draw conclusions on the relative efficacy of AMDs when used to treat infected leg ulcers. Results for key outcomes are described below. More details are provided in section 5.4 of the EAR.

As the aim of this late-stage assessment is to assess whether price variations between AMDs using different agents are justified by their incremental differences, the summaries below focus on studies that compare AMDs using different agents rather than those that compare AMDs with non-antimicrobial dressings.

Infection

Infection outcomes were reported in 3 comparative studies and 6 single-arm studies that fully met the decision problem, but definitions varied between studies. Two comparative studies favoured ionic silver over ionic silver complex, and Manuka honey over an unspecified silver agent. Single-arm data reported that the percentage of participants with an infection was lower for ionic silver compared with silver sulphadiazine. One study of silver sulphate also reported a reduction in signs of infection. One study comparing Octenidine gel combined with a wound contact layer showed a faster and greater improvement than Octenidine gel combined with a foam or alginate dressing.

Clinical signs of infection

No comparative studies assessed the performance of more than one agent in reducing covert or overt signs of infection.

Two single-arm silver studies reported the proportion of patients with friable granulation (covert sign of infection) at 7 to 8 weeks was 0% (baseline rate not reported) and 17% (rate at 1 to 2 weeks was also 17%) respectively. Six single-arm silver studies reported overt signs of infection. With the use of a silver sulphadiazine dressing, overt signs of infection reduced between 1 and 8 weeks, except malodour which remained at 35 to 38%. Studies of ionic silver and silver sulphate both reported a lower proportion of patients with malodour (0% and 1% at between 3 and 8 weeks), while a study of silver oxysalts reported that 64% of patients experienced a statistically significant reduction in wound odour at 3 to 4 weeks.

Complete or partial healing

Complete healing was reported as an outcome in 7 comparative studies and 14 single-arm studies, of which 5 and 7 respectively fully met the decision problem. Of the 5 comparative studies that fully met the decision problem, only 3 compared AMDs using different agents. The evidence favoured silver when compared to honey but statistical significance between treatment arms was not reported. The difference in number of completely healed wounds between silver and iodine was not statistically significant. Comparisons between silver sub-agents showed inconsistent results.

All single-arm studies of silver sub-agents showed that the number of healed wounds increased with time. Data for chitosan showed a similar pattern but with a dip rather than a peak at 4 weeks. Data for PHMB showed consistent increases in complete healing over time, as did studies of enzyme alginogel and copper.

There were no studies comparing AMDs to each other that measured partial healing. Four non-comparative studies of silver sub-agents reported partial healing of between 69% and 90% at different timepoints between 3 to 8 weeks. Data for enzyme alginogel, chitosan, monofloral and Manuka honeys, and DACC also reported an improvement in partial healing from baseline.

Change in wound size

One comparative study found no difference in wound size between cadexomer iodine and ionic silver. Two single-arm studies of ionic silver reported a consistent reduction in wound size up to 98% at week 8, with 2 further studies reporting a similar trend for silver sulphadiazine. One study of enzyme alginogel also showed a consistent reduction over time, while a lack of comparable data points across time means that it is hard to observe trends for other agents.

Pain and discomfort

One comparative study of AMDs with different agents reported no statistically significant difference between DACC and ionic silver complex for reducing pain and discomfort. Single-arm studies of silver sulphadiazine and ionic silver with antibiofilm reported that pain reduced consistently with time measured at either 4 or 8 weeks. A study of silver sulphate found that by 3 weeks, pain had halved from baseline, while studies of enzyme alginogel and Manuka honey also found a reduction in pain from baseline with time reported.

Frequency of dressing changes

One comparative study reported that more dressing changes were recorded in the ionic silver complex dressing arm compared to ionic silver at 8 weeks' follow up, but statistical significance was not reported and it was unclear what factors might be driving the difference. Two single-arm studies reported a mean wear time of 6.4 days at 4 weeks for ionic silver and 19 days at 8 weeks for silver oxysalts.

Recurrence of wound or infection

One single-arm study using silver sulphadiazine that fully met the decision problem reported that 45% (5/11) of patients had a reopening of a previously healed wound at 12 weeks. In 1 study using monofloral honey that partly met the decision problem, the rate of reopening and reclosing after a wound had closed was 13% (4/30) at 2 months and 27% (8/30) at 3 months. However, input from clinical experts indicates that recurrence is not linked to either infection, or the AMD used.

Safety outcomes

In terms of safety, the studies indicate that none of the assessed AMDs are associated with serious treatment related adverse events. However, most of the studies had small sample sizes. The most common treatment related adverse events were pain or irritation on application or removal.

The EAG noted that in June 2024 a Medical Device Review led the British National Formulary (BNF) to update caution notices for povidone iodine fabric dressings (Inadine) to contraindications for patients with various conditions including kidney and thyroid diseases.

Cost effectiveness

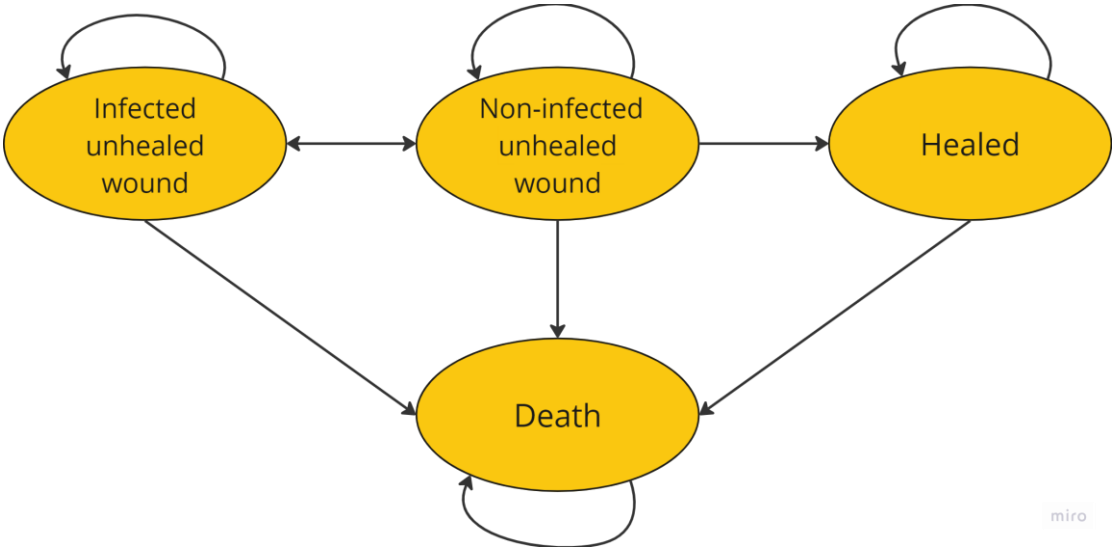
The EAG did a review to identify suitable health economic models. The same set of systematic literature searches was used to identify these studies. They found 6 economic evaluations of AMD agents and 8 peer-reviewed model structures. An overview of these models is in sections 6.2 and 7.1 of the EAR.

Health economic model

The EAG developed a Markov model (Figure 1) that included 4 health states:

- Infected, unhealed
- Non-infected, unhealed
- Healed
- Death.

Figure 1. Model structure



The model estimated cost-effectiveness of agents and sub-agents of dressings. A person would begin in the ‘infected, unhealed’ health state and commence treatment with an AMD, then either remain in this health state or transition to the ‘non-infected, unhealed’ health state. The person in the ‘non-infected, unhealed’ health state would either return to the ‘infected, unhealed’ state or heal completely. It was assumed for this model that, once healed, a leg ulcer could not reoccur. Therefore, once a person moved into the ‘healed’ health state, they remained in this health state until death or the end of the time horizon. The person could move to the death state from all health states. A time horizon of 1 year was used with 1 week cycles.

Once a person begins on an AMD, after a period of time (determined either by the agent in the dressing or their healing) they will move on to a second line ‘weighted basket’ of dressings. This weighted basket is informed by published literature and the efficacy of it was assumed to be equivalent regardless of the initial AMD used. This basket is discussed in more detail in the sub-section titled Discontinuation below.

Further details of the economic modelling are in section 7 of the EAR.

Population

The population focused on people with leg ulcers with local infections. The model population is informed by a retrospective cohort study (n=505) of venous leg ulcer management in the NHS. This is described in more detail in section 7.2.2 of the EAR.

Comparator

There was a low number of studies which compared different agents to each other.

The principal analysis compared all agents to each other in a fully incremental analysis and a pairwise analysis between agents. This compared the relative efficacy of each agent to each other. Sub-analyses were carried out using the same methods to compare the relevant sub-agents to each other.

The results of the principal and sub-agent analyses are presented here as the total costs and associated QALYs. Further detailed results of the incremental health effects and costs, incremental cost-effectiveness ratios (ICER) and incremental net monetary benefit (NMB) can be found in section 7 of the EAR.

Model inputs

Due to the limited nature of evidence, as well as the heterogeneity, the EAG had to make a number of assumptions to inform their model. More details on these are described in section 7.2.1 of the EAR.

Clinical parameters

Healing rate

The healing rate of ulcers is not linear over time. In the studies identified by the EAG, there was heterogeneity in the timepoints used to measure complete healing. The most common timepoints used were 4 and 12 weeks (used in 22 studies). The EAG developed a formula to allow the conversion of a percentage of wounds completely healed at 4 weeks to be converted to 12 weeks and vice versa because evidence suggested healing trend is non-linear.

The EAG then used the percentage healed to estimate a per-week rate of healing for each agent and sub-agent. Depending on the maximum number of weeks a particular agent was prescribed, as determined by clinical guidelines and evidence, the estimated per-week healing rate was used to inform the transition from the ‘non-infected, unhealed’ to the ‘healed’ health states. For example, agents that are prescribed for 12 weeks, such as honey, had a 12-week rate of healing applied. Agents that are prescribed for 4 weeks, such as silver, had a 4-week rate of healing applied. This per-week rate informed the model until discontinuation to the second line mixed basket.

Time to infection resolution

While 11 studies in the clinical review reported the percentage of ulcers which had been cleared of infection at a certain timepoint, there was a paucity of

evidence to inform the average time to infection resolution (Section 7.2.3.2 of the EAR). One study reported the weeks to infection resolution as 2.52, 3.80 and 3.88 for 3 types of silver dressings. The EAG took an average to estimate a mean time to infection resolution of 3.4 weeks (approximately 24 days). Using a conversion ratio, the EAG then calculated the rate of infection resolution per week for each agent and sub-agent in the model.

Due to a lack of evidence on the rate of infection resolution, it was necessary to assume the rate of infection resolution was proportional to the rate of healing. An alternative option, considered by the EAG, was to assume clinical equivalence between the agents. This option was deemed less appropriate as it was not supported by literature or clinical opinion and would not provide an answer in line with the objectives of this assessment. However, the EAG conducted a scenario analysis in which clinical equivalence across all efficacy measures was assumed (i.e. a simple cost comparison).

Recurrence of infection

In the absence of data to inform this parameter, it was assumed that there is no recurrence of infection. However, the EAG conducted a scenario analysis which modelled different rates of recurrence of infection.

Discontinuation

Clinical experts advised the EAG that they would expect a typical person with a leg ulcer to progress rapidly through a sequence of AMDs and other dressings. To adhere to what is observed in clinical practice, the model was designed to allow for discontinuation from the AMD applied as a first line treatment. However, there are no data to suggest the order of the sequence, nor the efficacy of specific AMDs when used in different treatment schedules.

Therefore, it was assumed that, after discontinuation from the first line AMD, the cohort would move onto a ‘basket’ of treatments as their second line. The efficacy of the mixed basket was informed by a published, peer-reviewed paper of 505 people identified from the UK-specific THIN database. The

efficacy data associated with the second line treatment was assumed to be equivalent regardless of the AMD applied at first line.

The model considered 2 types of discontinuations.

1. A per cycle rate of discontinuation due to personal preference or treatment related adverse events.

2. Discontinuation after a certain number of weeks as clinically indicated.

There were 3 studies that reported a proportion discontinuing, 4% for PHMB, 7% for silver and 12% for copper. Discontinuation was assumed to be 0% in those studies that had a 4 or 12-week healing rate but didn't report a discontinuation rate. See table 7-6 of the EAR for more information.

The second type of discontinuation was the maximum amount of time people could remain on the agent (the maximum prescription time), as indicated by clinical guidelines, guidance from the BNF, or the manufacturer's instructions. In the absence of these three options the length of the clinical trial was used to inform this endpoint. See Table 7-4 of the EAR for maximum time spent on each agent.

Costs

Technology costs

AMD costs were sourced from Part IX of the Drug Tariff. To appropriately assess the cost differences of dressings associated with each agent and sub-agent, a weighted average cost of all dressings containing the agent or sub-agent of interest was calculated. The weighted average cost, standard errors, and the minimum and maximum costs associated with each agent and sub-agent is presented in Table 7-7 of the EAR. The costs for all dressings in Part IX of the Drug Tariff and the Clinical Practice Research Datalink (CPRD) market share is presented in Appendix H of the EAR.

Frequency of dressing changes

It was assumed that a person in the 'infected, unhealed' health state would experience more dressing changes than those in the 'non-infected, unhealed' health state. The values used in the base case of the model are summarised in Table 7-8 of the EAR. It was also assumed that the same resource use applied to both the 'infected, unhealed' and the 'non-infected, unhealed' health state. However, variation of resource use between health states was explored in a scenario analysis. Resource use parameters and unit costs of resources are summarised in Table 7-9 and 7-10 of the EAR.

Unhealed ulcer resource use

The resource use and associated costs in Table 7-9 and Table 7-10 of the EAR were used to derive the health state costs for the 'infected, unhealed' and 'non-infected, unhealed' health states. The EAG calculated from the literature that the resource use for an unhealed ulcer was 4.5 times more than that of a healed ulcer and adjusted the resource use accordingly if a person was in the 'healed' state or not.

There were limitations to the data that the EAG used to calculate their costs:

- the database referenced focussed on care delivered via GP practices so may not fully represent costs from community delivered care,
- the data did not differentiate between a person with or without an infected ulcer (the difference between two of the health states in the model),
- the data was pre COVID-19 pandemic and the delivery of care around GP appointments and virtual wards may not be reflected in the data.

To ameliorate these limitations the EAG conducted scenario analyses to investigate higher health state costs for the 'infected unhealed' health state than the 'non-infected unhealed' health state, and using data from 2021.

Registry data

Although it had limitations, the EAG used CPRD data to assume market share of different AMDs. The CPRD data reported market share of 303 different

types and sizes of AMDs, 231 of which aligned with the AMDs included in the model. AMD costs were sourced from Part IX of the Drug Tariff. Further information can be found in Appendix H of the EAR.

Health-related quality of life

Health state utility data was identified for leg ulcers, the EAG selected what they felt was the most appropriate study (Cheng et al. 2019) and assigned EQ-5D-3L utility values of 0.78 for a healed wound and 0.64 for an unhealed wound for inclusion in the model. There was however a paucity of data for utility values for infected leg ulcers. The EAG therefore assumed that the utility associated with an infected leg ulcer is equal to the utility associated with a non-infected leg ulcer. This may have resulted in an underestimation of the QALY benefits of resolving an infection. The EAG explored if this had an impact on the cost effectiveness by varying the utility values for the infected non-healed and non-infected unhealed ulcers in a scenario analysis. For more details and results please see sections 7.2.5. 7.2.8.1, 7.2.8.2 and 7.3.4 of the EAR.

Model results

Appropriate efficacy data was available for 6 of the 10 agents to inform the principal analysis: chitosan, copper, honey, iodine, PHMB and silver.

There was no efficacy data available for chlorhexidine, enzyme alginogel, octenidine and DACC. Therefore these 4 agents were not included in the model.

Base case

Probabilistic base case

The base case cost-effectiveness results were derived from a probabilistic sensitivity analysis. The ranges used to inform many of the inputs were not robust, and the addition of estimated ranges would have introduced uncertainty. The EAG were unable to conclude if one agent is more efficacious than another and advised caution when interpreting the ICERs as

representing cost-effectiveness. The EAG recommended caution when interpreting the outcome of the fully incremental analysis which ranked iodine as the referent agent and dominated all other agents as cost-effective. This was due to iodine generating the smallest costs per person, costing £6,494 (95% CI: £5,579 to £7,408), and being the most effective accruing 0.70 (95% CI: 0.64 to 0.77) QALYs over 1 year of treatment. However, the size of the ICERs, and the cost-effectiveness of iodine are largely driven by the very small incremental QALYs. Furthermore, the uncertainty of these ICERs was driven by uncertainty of the costs which generated large confidence intervals (Figure 2). The very small incremental QALYs and the overlapping of the confidence intervals indicate that there were no significant differences between the QALYs of any agents (Figure 3). Further details on the probabilistic base case results are in Table 7-15 in section 7.3 of the EAR.

Figure 2. Total cost associated with each agent and 95% confidence intervals

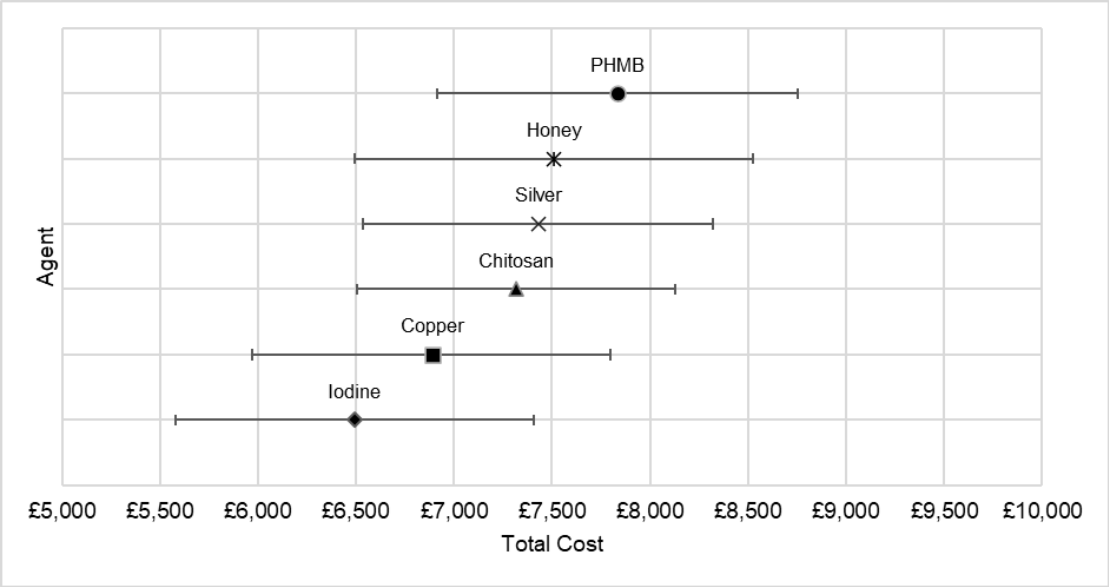
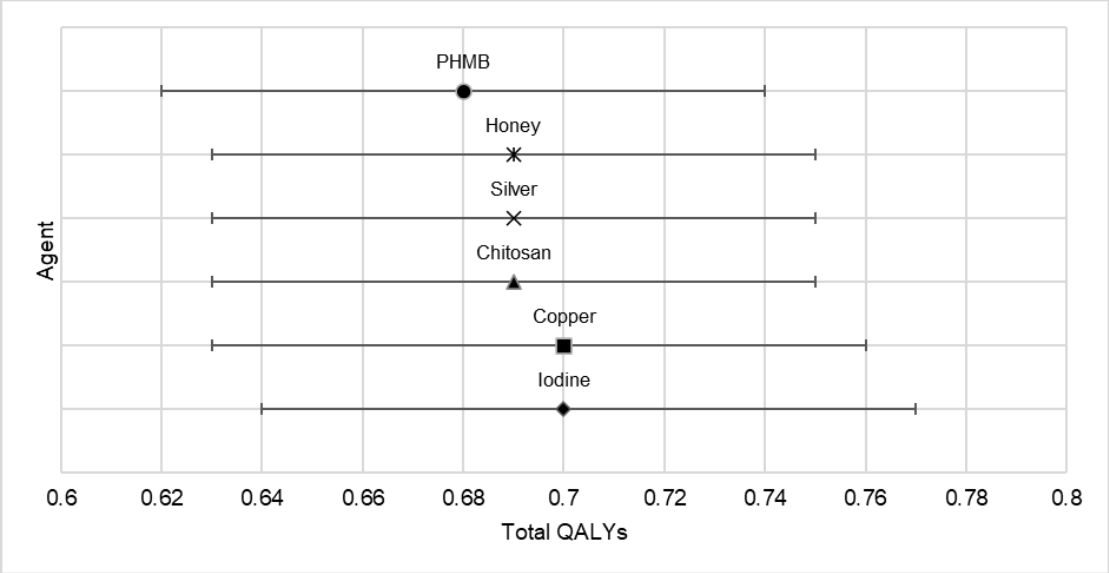


Figure 3. Total QALYs associated with each agent and 95% confidence intervals



Deterministic base case and sensitivity analysis

The results from the deterministic base case were in alignment with the probabilistic base case.

Additionally, the EAG found that:

- Agents that healed ulcers faster were likely to generate the smallest costs and the highest QALYs as people will spend less time in the two more costly 'infected unhealed' and 'non-infected unhealed' health states and more time in the less costly 'healed' 'health state'.
- The largest proportion of total costs were attributable to the 'non-infected unhealed' health state (range 62 to 71%) due to people spending longer in this health state, compared to the 'infected unhealed' health state (range 8 to 22%), and 'healed' health state (11 to 19%). Cost of the AMD provided the smallest contribution to total costs (3 to 6%).
- The rate at which infection is cleared is a key driver of cost-effectiveness. Only 1 study in the assessment included this as an endpoint so the data is largely based on assumptions which were in turn based on time to overall healing. More robust data is needed to make robust conclusions on the cost-effectiveness.

- Agents with large maximum costs of dressings compared with the weighted average, namely, silver and copper, show the use of the maximum cost as a large driver of cost-effectiveness. In agents where there is less variation across the cost of different products and brands, the cost of the AMD has less of an impact.
- Decreasing the health state utility for the 'healed' health state had a large impact on results. The incremental QALYs observed in the base case were extremely small, therefore changing the utility value associated with the 'healed' health state will have a large impact on cost-effectiveness outcomes.
- There is very little impact when the utility of the 'healed' health state is increased, because it is bound above by the population norms.

Further details on the deterministic base case results are in Table 7-17 in section 7.3 of the EAR.

Scenario analyses

The EAG conducted several scenario analyses to assess the impact of assumptions used to inform some model parameters including:

AMD cost

- Maximum and minimum cost of dressing containing agent.
- Variation of frequency of dressing changes: 1 per week regardless of health state; 3 per week in infected health state and 1 per week in non-infected health state; 3 per week in infected health state and 1 per week in non-infected health state using minimum and maximum cost.
- Iodine cost to align with cadaxomer iodine (base case used povidone iodine cost and cadaxomer iodine efficacy)

Resource use parameters

- Using peri-pandemic resource use data; varying the costs in the 'infected unhealed wound' health state by 25% and 250% larger than the 'non-infected unhealed wound' health state.
- The cost of the healed health state set to £0
- The cost of the infected unhealed health state 3.2 times more than that of an uninfected wound, and the cost of the infected unhealed health state 3.2 times more than that of an uninfected wound and the "healed" health state set to £0.

Best practice scenarios

- People discontinue AMDs in the 'non-infected unhealed wound' health state and the treatment effect of AMDs remains (no AMD cost); people discontinue AMDs in the 'non-infected unhealed wound' health state and automatically move onto second line basket.

Efficacy parameters and prescription time

- Assumption of equivalent efficacy data with no edits to time of prescription; all agents are prescribed for 4 weeks; and all agents are prescribed for 12 weeks.
- Efficacy data is not changed but all agents are prescribed for 4 weeks; and 12 weeks.

Reoccurrence of local infection parameters

- Assumption ulcer infections reoccur at a per-week rate of 0.1 and 0.5.
- Assumption that a per-week rate of 0.1 ulcer infections reoccur for first line, and a per-week rate of 0.5 ulcer infections reoccur for second line.

Utility parameters

- Alternative health state utilities used from Walzer et al (2018).
- Health state utilities assuming 'infected unhealed wound' health state has utility 10% lower than 'non-infected unhealed' wound.

For many of the assumptions investigated by the EAG, the conclusion of cost-effectiveness did not change. This was driven mainly by the lack of impact on QALYs. This conclusion was consistent across the use of maximum and minimum cost scenarios; variations in the frequency of dressing changes; resource use sources and health state cost assumptions; reoccurrence of local infection; variation in health state utilities; and discontinuation of AMDs in the unhealed non-infected wound health state.

An assumption of equivalence between the utilities of the ‘infected unhealed wound’ and the ‘non-infected unhealed wound’ was needed because of a paucity of data specific to the ‘infected unhealed wound’ health state. The scenario analysis around this input found that lowering the utilities and increasing the health state costs of the ‘infected unhealed’ health state made no significant changes to the cost-effectiveness conclusions.

Further detail on the results from the scenario analyses are in section 7.3.4 of the EAR.

Sub-agent analysis and other sub-group analysis

There was enough evidence to compare the three sub-agents groups within silver (elemental silver, silver salts and compounds, and silver with antibiofilm mechanisms) and two sub-agents within honey (manuka honey and monofloral honey). The results of both analyses were very uncertain driven by nearly equal QALYs between the sub-agents with overlapping confidence intervals. In addition, the results for the silver sub-agent analysis changed depending on which study was used to inform efficacy parameters. Further information on the results from the sub-agent analyses can be found in section 7.3.3 and the addendum of the EAR.

There was not enough evidence to conduct analysis of any of the other sub-groups, including type of leg ulcer, wound presentation, location of ulcer, and complexities that may impact treatment of leg ulcer infections.

Future work

Due to the heterogeneity and limitations of the current evidence base, the EAG were not able to draw conclusions on the cost-effectiveness of the different agents or sub-agents. The EAG made the following recommendations for future work:

- Studies should focus on UK NHS populations with infected leg ulcers, with clear reporting of infection status at baseline and clear definition of infection.
- Studies should focus on the use of AMDs in clinical practice and include details of the sequencing for secondary and tertiary products, along with frequency of and resource use for dressing changes.
- Outcomes gathered should focus on what is most valued by patients and health professionals including time to healing, infection clearing, pain, and discomfort. These should be gathered over a sufficiently long term to capture all instances of infection resolution, reinfection, and complete healing, as well as consequential risks of infection such as cellulitis, gangrene and amputation.
- For pragmatism, this could be accomplished using observational methodology using hospital data, but patients should be matched for key baseline characteristics likely to affect treatment outcomes.

User preferences

Fifteen healthcare professionals took part in the user preference assessment to determine the most important criteria when selecting an antimicrobial dressing for infected leg ulcers. They identified 5 main criteria that were related to clinical presentation: wound presentation; medical history and patient characteristics; previous dressing regimes and efficacy; mode of action of agent or dressing; and cytotoxicity of antimicrobial agent. In addition, 5 criteria that were considered to be independent of clinical presentation were identified. Ranked in order of importance, the 5 additional criteria were conformability, ease of removal, application directions, cost, and sustainability.

It is notable that none of these criteria are specific features of individual dressings, but instead quite generic and related to the performance of the dressing. Apart from cost and to a lesser extent, ease of removal, these preferences were not captured by the evidence.

Details on the identified user preferences are in section 4 of the user preference report.

Survey of people with lived experience

NICE conducted a survey of people with lived experience of using AMDs to treat infected leg ulcers. 19 people responded to the survey, of whom 12 had used an AMD for an infected leg ulcer. Most people (10/12) did not know what type of dressing they were prescribed and were not involved in the selection of the AMD. When asked if they knew what agent they were prescribed, 5 people said their dressing contained honey as an agent, 1 silver, 1 iodine, and 5 people did not know. When asked what factors would make them choose a dressing over another the results were as follows (people could select more than one answer):

- Comfort (n=9)
- Ease of removal of dressing (n=8)
- Effectiveness in reducing healing time of wound (n=7)
- Effectiveness in reducing healing time of infection (n=6)
- Dressing staying in place for as long as needed (n=5)
- Avoidance of reactions to the dressing (n=5)
- Ease of applying the dressing (n=5)
- How often the dressing needs to be changed (n=4)
- Odour control (n=3)
- Appearance (n=2)
- Cost (n=1)

Equality considerations

The final scope and the scoping equality impact assessment describe equality considerations for this assessment. The EAG did not identify additional equality issues.

Limitations and key issues

Clinical effectiveness

Limitations

- The EAG considered that the evidence base identified does not allow a clear assessment of the relative efficacy of different AMDs to treat infected leg ulcers.
- There was a lack of studies that compared different agents with each other.
- There was a lack of studies that fully met the decision problem.
- It was not feasible to do a meta-analysis because of heterogeneity in study designs, populations, interventions and outcomes.
- Key issues limiting the reliability of studies included the possibility of uncontrolled confounders, small sample sizes, and very limited reporting of methods. Outcome definitions and methods of measurement also differed across studies, were reported at varying timepoints and often did not assess the statistical significance of findings. Author reported definitions of “infection” may vary (particularly in older studies), so there is potential inconsistency in included populations.
- Single-arm studies often reported at only 1 timepoint, meaning that conclusions across studies could not be drawn.
- All but 4 of the 21 studies that fully met the decision problem were judged to have a moderate or high risk of bias.
- There was not enough evidence for sub-group analyses, so all dressing types were included in the model.

Key issues:

- What can the published studies tell us about the comparative effectiveness between the different antimicrobial agents used in AMDs?
- What additional data would be helpful to inform an assessment of the antimicrobial agents used in AMDs?

Cost effectiveness

Limitations:

- The EAG considered that results from the economic model do not provide enough certainty to allow robust conclusions on the cost-effectiveness of different agents in AMDs when used to treat infected leg ulcers. This was because the differences between QALYs were so small and the 95% confidence intervals all overlapped.
- There was a lack of comparative head-to-head randomised controlled trials and observational studies on NHS service delivery which could inform the model.
- The evidence base available to inform the model was disparate, heterogeneous, and at times in populations beyond the targeted scope.
- The EAG had to make several assumptions due to limited data but explored as many of these as possible in the scenario analyses.
- Data on time to infection resolution, which was a driver of cost-effectiveness, were sparse and assumptions had to be used.
- The model assumed that AMDs were used even after the infection had cleared which may not be representative of best practice. Doing so may increase the modelled resource use after the infection has been cleared. However, this is how the results were presented in the literature. This limitation was explored in a scenario analysis and found not to impact the cost-effectiveness but it means the model may not align with recommended use.

- Several key parameters were informed by studies of venous leg ulcer management and other types of leg ulcers may have different healing rates.
- Resource use estimates and market share data that was applied to the costs were based on primary care data. Leg ulcer treatment and care is provided in the community, so this may have underestimated total costs.
- There was limited data available on treatment-related adverse events.
- The location and aetiology of the wound varied amongst studies.
- Recurrence of leg ulcers was not modelled because of a lack of data.

Key issues:

- There is a large amount of uncertainty in the results from the model, and a lot of limitations to the model. Can the results be used to determine if the price variation between antimicrobial agents used in AMDs is justified?

User preferences

Limitations:

- It is possible that the small sample of healthcare professionals who volunteered to take part in the user preference assessment are not fully representative of the wider population of people who choose which antimicrobial dressings to use for infected leg ulcers. However, they came from a range of NHS trusts in England and Scotland and included experienced tissue viability nurses and those who work in community settings.

Key issues:

- Apart from cost, none of the criteria important to healthcare professionals selecting an AMD for use were captured well in the literature.

Appendix A Abbreviations

AMD	Antimicrobial dressing
CPRD	Clinical Practice Research Datalink
EAG	External assessment group
EAR	External assessment report
ICER	Incremental cost-effectiveness ratio
QALY	Quality-adjusted life year
RCT	Randomised controlled trial

Health Tech Programme

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

Section A: External Assessment Report – Factual accuracy comments:

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
1.	Individual stakeholder		General	This appears to be a well considered document and I cannot discern any factual inaccuracies.	Thank you.
2.	The Leg Club foundation			No comments from us, thank you	Thank you.
3.	Essity	65	5.1	**Simplifying Assumptions**: The economic model relied on several simplifying assumptions due to a lack of robust data. For example, the model assumed that the rate of infection resolution was proportional to the rate of healing. This assumption introduces uncertainty and may not accurately reflect clinical practice . For this reason how can this be deemed as an effective way of showing the economic impacts for the dressings	The EAG acknowledged the limitations in this assumption in the report. A relationship between infection resolution and healing rate was deemed appropriate by the EAG and clinical opinion. Additional scenarios have been performed to test this assumption further, see Table 7.26.
4.	Essity	9	Executive summary	Y**HEC have stated that the evidence was not appropriate for economic evaluation -** The evidence base identified does not allow a clear assessment of the relative efficacy of different AMDs to treat infected leg ulcers, and so does not provide conclusions on the validity of price variability. With the number of assumptions included how is this a valid way of reviewing the true impact of AMDs. This highlights that cost is a key driver without been able to	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				establish the true cost of each product and its true wider impact how is the LSA findings valid The use of this model in current evidence level will make decision making harder and could lead to more infections as NHS will be following inaccurate data	
5.	Essity	12	1.1	The LSA is relating to infected leg ulcers and evidence for the other wounds was considered for the agent. DACC was excluded when the DACC technology was highly evidenced for other wound types, and this was excluded from the economic model. With the use of evidence away from leg ulcer been included the scope of the LSA should change or other types of evidence included. This is not a fair and representative reflection of the evidence available for DACC if others are been included from studies not related to leg ulcers	Thank you for your comment. A pragmatic approach to study selection was taken whereby if no or limited evidence was available for an antimicrobial agent in the NICE scope population of infected leg ulcers, evidence in a wider population was sought in stages (first infected wounds of other types, then non-infected wounds if no evidence in the former population was found). The same approach was used for each agent. Evidence for DACC was included in the clinical review as a pilot RCT that fully met the scope was identified (Mosti et al 2015). Because this was a pilot RCT with a small population, wider evidence was sought. Evidence in a population with infected wounds of other types was identified and included in a case series study (Bruce et al 2012). The evidence for DACC was not reported in a way deemed appropriate for inclusion in the economic model. The EAG acknowledges the limitations of this method of widening the scope to other populations without conducting searches specific to these populations. This pragmatic decision

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					was made with NICE owing to the time and resource limitations of the LSA process.
6.	Essity	13	1.1	Dressing types do not include super absorber dressing?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
7.	Essity	184	7-11	Cost for utility for infection and non-infected wounds the same? no reference for this available how was this cost developed	There was a lack of data reporting the state-specific utility and resource use associated with infected unhealed and non-infected unhealed wounds. However, the EAG acknowledged the limitations of this approach and explored a set of scenario analyses in which the infected, unhealed wound health state had a lower utility and a higher cost. Please see section 7.3.4 for the outcomes. The resource use and associated costs in Table 7.8 and Table 7.9 were used to derive the health state costs for the infected, unhealed and non-infected, unhealed health states.
8.	Essity	148	7.2	AMDs do not heal wounds the EAG states this - The EAG chose to focus on short-term impacts because the primary benefit of AMDs is infection resolution, which is the point at which the wound becomes uninfected (BMJ Publishing Group Ltd and the Royal Pharmaceutical Society of Great Britain 2024).	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
9.	Essity	65	5.1	**Limited Comparative Evidence**: The document acknowledges that there was insufficient comparative evidence for many of the AMDs	Thank you for your comment, that is correct.
10.	Essity	65	5.1	The generalizability of the economic evidence to the treatment of patients with infected leg ulcers within a UK healthcare setting was poor. Only one of the six economic evaluations included in the review was conducted in the UK. This limitation affects the applicability of the findings to the NHS.	–Thank you for your comment, we would agree with this.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
11.	Essity	65	5.1	**variability in Clinical Practice**: The document notes significant variability in the use of AMDs across different healthcare settings. This throws doubt into the effectiveness of the LSA and the economic model	– Thank you for your comment, we agree that use of AMDs across included studies appears to have been variable, and the discussion has noted that this impacts on the generalisability of the evidence base (and results of the LSA).
12.	Essity	65	5.1	**Lack of Robust Data on Infection Resolution**: There was a lack of robust data on the rate of infection resolution for many of the AMDs. The model had to rely on assumptions and limited data, which introduces uncertainty into the analysis.	Comment is not a factual inaccuracy, no change to report has been made.
13.	Essity	65	5.1	**Economic Evidence Limitations**: The economic evidence review identified a limited number of economic evaluations (six studies) and noted that there was a lack of robust data to inform incidence rates and utility decrements for adverse events. This limitation affects the reliability of the economic modeling.	Comment is not a factual inaccuracy, no change to report has been made.
14.	Essity	65	5.1	**Overlap in Confidence Intervals**: The probabilistic analysis showed a large overlap between confidence intervals, which demonstrates that the available evidence cannot conclude whether there are clinically meaningful differences between the cost and quality-adjusted life years (QALYs) of the agents. This overlap indicates a high level of uncertainty in the results.	Comment is not a factual inaccuracy, no change to report has been made.
15.	Essity	65	5.1	**Inconsistent Reporting of Outcomes**: The document mentions that there were differences in the reporting of outcomes, with some studies not providing clear definitions or consistent measurement methods. This inconsistency can lead to difficulties in comparing results across studies and affects the reliability of the economic model	Thank you for your comment, we agree that this is a limitation of the review and this is noted in the discussion section.
16.	Essity	1	1	Removal of DACC technology creates unfair biased towards the other technology in this economic assessment. On prescription in the July 23- July 24 this was over 8% of the market. Understandably evidence is	Comment is not a factual inaccuracy, no change to report has been made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				required but with the number of assumptions made in the economic model the exclusion of DACC does not seem to create a fair basis for review for the product	
17.	Essity	11	3	Generalisability of the review evidence base for using AMDs to treat infected leg ulcers in a UK NHS setting was considered to be generally poor, with heterogeneity in the populations, outcomes and study designs of the studies further contributing to uncertainty. Results of the economic modelling demonstrated that the available evidence cannot conclude whether there are significant differences between the cost-effectiveness of the agents. With this statement how accurate or useful will this LSA be in its findings ?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage
18.	Essity	16	2.3	The use of the (Clinical Practice Research Datalink 2024) 24.21% Percentage UK population coverage: 16,227,262 of 67,026,300 (24.21 %) it states that iodine was the most used AMD. This was prior to the updated IFU and patient safety notice which was published in June 2024 The figure used for % used - The proportion of AMDs represented by DACC and PHMB dressings has fallen slightly (DACC: 11.0% in 2018 to 6.8% in 2023 – is this based on FP10 prescribing only ? if so this is not a fair representation of usage of DACC technology – [redacted]	The CPRD data set was released in June 2024. It collects data from GP practices in the UK, not in community or acute care. Although this source is imperfect it was deemed the most appropriate, as it is one of the largest UK healthcare datasets on prescribing. See page 170 of the report on how assumptions needed on market shares were made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				[redacted]	
19.	Essity	26	3	biofilm is outside the scope of this assessment – IS THE MODELING valid with the emission of biofilms when they are present in over half of wounds and prevent wound healing ? **Approximately 60%** of non-healing chronic wounds contain biofilms. A meta-analysis found that **78.2%** of chronic wounds had biofilms Another review suggested that **at least half** of all chronic non-healing wounds contain biofilms.	"The inclusion of biofilm in this assessment was discussed during the scoping period and it was decided that biofilms would not be included in this assessment, due to the difficulty in measuring performance of AMDs against it." Pg 26 of report.
20.	Essity	149	7.2.1	However, these assumptions have been applied to the model due to the lack of evidence available to inform an alternative approach and rate of infection resolution was not included as an outcome in the studies informing – What is the validity of the LSA if there isn't enough information included to have the right factors that impact wound healing ?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
21.	Essity	152	7.2.3.1	Healing rate – AMDs do not heal wounds - **Primary Function**: The primary function of AMDs is to reduce the microbial burden in infected wounds, which can help create a more favourable environment for healing. They are not primarily designed to heal wounds directly but to manage infection and prevent its spread – Why is the modelling based on wound healing when an AMD is not indicated for wound healing only supports a favourable environment	There was a lack of consistent clinical trial endpoints across studies reporting infection-related endpoints. Wound healing was reported consistently across clinical trials and studies in AMDs for infected leg ulcers. The model was designed to be flexible and includes a per-cycle rate of infection resolution. No change to the report has been made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
22.	Essity	26	3	biofilm is outside the scope of this assessment – IS THE MODELING valid with the emission of biofilms when they are present in over half of wounds and prevent wound healing ? **Approximately 60%** of non-healing chronic wounds contain biofilms. A meta-analysis found that **78.2%** of chronic wounds had biofilms Another review suggested that **at least half** of all chronic non-healing wounds contain biofilms.	"The inclusion of biofilm in this assessment was discussed during the scoping period and it was decided that biofilms would not be included in this assessment, due to the difficulty in measuring performance of AMDs against it." Pg 26 of report
23.	Essity	157	Table **Error! No text of specified style in documen t.**-1:	Studies selected to inform the time to per-week healing rate – it should not considered that all wounds have compression evidence from NWCSP first tranche highlights less the 50% have a diagnosis - – Hull-Case-Study-Final.pdf Only 48% of people with leg wounds had a comprehensive assessment, including the assessment of arterial supply.	This is not an assumption in the model.
24.	Essity	224	7.3.4	Iodine has contra indication and has stated in the IFU which would is not included within the costing model. The use of iodine would require test to be completed by the HCP before use. The economic has not factored this cost and therefore is not a fair representation of the cost of iodine to the NHS The model also states 4 or 12 week usage which is not reflected in iodine IFU As of the financial year ending March 2024, there were approximately **2.24 million people** aged 18 and over with	10 different iodine dressings are included to inform the costs, 2 of which are Inadine. Inadine is a "povidone iodine" dressing (a sub-agent of iodine). The clinical review did not identify evidence for povidone iodine that was appropriate for use in the model. The efficacy data is based upon Cadexomer iodine. The EAG is not aware of tests that must be completed prior to the use of an iodine-

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				a GP diagnosis of chronic kidney disease (CKD) in England. This represents about **4.4%** of the adult population . Additionally, it's estimated that around **7.2 million people** in the UK are living with CKD, which is more than 10% of the entire population **Contraindications:** Inadine® dressing should not be used: • Where there is a known iodine hypersensitivity (allergy) • Before and after use of radio-iodine (until permanent healing) • If you are being treated for kidney problems • In pregnant and breast-feeding women • In cases of Duhring's herpetiform dermatitis (a specific, rare skin disease) • In patients with any thyroid diseases as povidone iodine may be absorbed **Warnings / Precautions:** Inadine® dressing must be used under medical supervision: • In new-born babies and infants to the age of 6 months as povidone iodine may be absorbed through unbroken skin • To treat deep ulcerative wounds, burns or large injuries. Medical supervision should be sought if using Inadine® dressing for more than one week	containing dressing. Contraindications to iodine use, including pregnancy, breast-feeding, lithium use, thyroid disorders and severe renal disease are likely to be included in a person's medical history or known by the person. Therefore, in many cases, the HCP could exclude contraindications through discussion with the person and review of their medical history, rather than requiring tests. As such, a cost for tests to rule out contraindications prior to iodine use has not been included in the model. The 12-week usage of iodine dressings (which is used in the base case) was informed by the BNF, which stated that "max. duration [of iodine dressings was] up to 3 months in any single course of treatment". The EAG acknowledges that there are contraindications. Because of the nature of the indication, regular. nurse visits are included (as per section Table 7-8). The number of nurse visits was taken from an observational study of venous leg ulcers with a mixed basket of treatments. Therefore, the cohort would be under constant supervision. As per Section 3.2 (Figure 3.1) in the model protocol, it was assumed that the wounds of the cohort entering the model had already been assessed and an antimicrobial dressing chosen, considering the aetiology of the leg ulcer; the location; the wound presentation and complexities. Any assessments prior to initiation onto the AMD were outside of scope.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
25.	Convatec	NA	NA	It should be acknowledged up front that an accurate diagnostic test for local wound infection does not exist. Because the LSA has limited its scope to only infected venous leg ulcers, the lack of an accurate diagnostic test has a multitude of effects on the accuracy of the LSA. The only way to diagnose an infected leg ulcer is via clinical signs and symptoms which are *not* accurate (and in leg ulcers, signs of local infection are also very similar to manifestations of venous or arterial disease, e.g., excess exudation, inflammation, redness), and holistic patient assessment, both of which rely on the experience and skill of the clinician. Older studies identified in this LSA, including some from over 40 years ago, appear to reply on outdated microbiological culture methods and arbitrary qualitative microbial growth scales to describe 'infection', when today we would describe this as colonization.	Thank you for your comment. We have considered studies that report having included infected leg ulcers to meet the NICE scope. We acknowledge that studies that reported including "infected leg ulcers" without clear criteria for wound infection may have used definitions that vary, introducing variabilty into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
26.	Convatec	24-27	3	**"few are clinically infected"** is not supported by infection rates of 18% (leg ulcers) and 41% (VLU). Regardless, it begs the question of why the LSA scope would be narrowed down to so 'few' wounds in this subset. If **"80% to 100% of leg ulcers may be colonized with bacteria"**, then up to 100% of leg ulcers are *at-risk* of infection, and AMDs are indicated for wounds that are infected or at-risk of infection. Hence, manufacturers reasonably conduct clinical studies of infected *and* at-risk populations. Hence **"strategies to prevent infection and improve wound healing rates have been recommended (Guest et al. 2020)"**. **"Innovative features, while clinically relevant, are not considered in this assessment due to a paucity of data"** Yet Fig 3.1 states **"Consider desirable innovative features".**	Thank you for your comment on the rate of infection; we agree that it is not quite correct to say "few" are infected, rather that few**er** relative to the number bacteriologically colonised are infected. This has been amended. The further content of this comment queries the NICE scope and are not factual inaccuracies. Page 26 of the report states: "The inclusion of biofilm in this assessment was discussed during the scoping period and it was decided that biofilms would not be included in this assessment, due to the difficulty in measuring performance of AMDs against it." No changes to report were made. We will review other comments at consultation stage

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				"A biofilm is a structured community of microorganisms that produces unique infections" **"Unique infections"** is incorrect terminology. What is meant here? Challenging? Recurrent? Persistent? Recalcitrant? **"It is recognised that biofilms influence chronic wound healing, although their influence is not yet fully understood"** The literature strongly associates biofilm with wound chronicity, and implicates biofilm in contributing to local infection and delayed wound healing. **"…it was decided that biofilms would not be included in this assessment, due to the difficulty in measuring performance of AMDs against it"** This argument is flawed, since it is also difficult to measure performance of AMDs against planktonic microorganisms in clinical studies due to challenges with wound sampling methods, comprehensiveness of standard microbiological culture, lack of validated molecular methods, etc. The only valid way to measure the effect of AMDs against biofilm is using standard and/or validated *in vitro* biofilm test methods, of which there are numerous that regulatory authorities recognise. **"consideration of biofilm is outside the scope of this assessment"** It might be simpler to ignore biofilm, but biofilm has emerged and is now recognised as a key local barrier to wound healing. Ignoring biofilm weakens the entire initiative, especially when use of antibiofilm protocols and antibiofilm dressings is known to result in positive clinical outcomes (Torkington-Stokes et al, 2024) and with those, associated cost savings (the purpose of this initiative).	
27.	Convatec	81	Table 5-2	**"ConvaTec Inc. Aquacel ag+ extra™ and cutimed™ sorbact dressing in the management of venous leg ulcers over a 12-week period. Identifier: NCT05892341.**	In this trial 6/204 (3%) of participants had infected wounds at baseline, therefore this was not eligible for inclusion in the review. Because

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
		315	Appendix B	**In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2022. Available from https://clinicaltrials.gov/study/NCT05892341. * ConvaTec submitted a clinical study report with results during the RFI process, but this was not added to the review as the trial population did not meet the decision problem and evidence for the sub-agents assessed was already included in the review"** Trial population was hard-to-heal venous leg ulcers that were infected or at risk of infection. This study is publicly posted on clinicaltrials.gov, has been published in poster form (Beraldo et al. Superior healing outcomes with an advanced wound care dressing vs. standard of care in hard-to-heal venous leg ulcers: results from a multinational randomized controlled trial. Wounds UK conference, 11-13 November 2024), and is in advanced stages of peer review publication process. This RCT is more clinically significant than the included Harding 2016 study.	evidence meeting the NICE scope was identified for silver AMDs overall, we did not then include further evidence for silver dressings that met a broader scope.
28.	Convatec	334	Appendix B	**"Torkington-Stokes R, Moran K, Martinez DS, Granara DC, Metcalf DG. Improving outcomes for patients with hard-to-heal wounds following adoption of the wound hygiene protocol: real-world evidence. J Wound Care. 2024.33(5):304-10 – Ineligible population"** This study included *272 leg ulcers who were switched from SoC to Aquacel Ag+ Extra*; of all 693 wounds, 43% were considered to be locally infected at baseline, and this reduced to 3% at final assessment. A leg ulcer-specific analysis was provided to the LSA authors: *261 leg ulcers (excluding arterial ulcers: 183 venous, 50 mixed, and 28 unknown leg ulcers; including 83 from Italy, 74 Spain and 72 UK) were included in the Wound Hygiene clinical evaluation. Of these, 98 (38%) leg ulcers were diagnosed as locally infected. In a median of 31 days, infected leg ulcers reduced from 38% to 3.0%, mean leg ulcer volume was reduced by*	The EAG considered that the leg ulcer specific document submitted as part of this LSA did not provide sufficient information to allow an adequate assessment of the reliability of evidence (specifically lacking in details on the baseline data for this subgroup, descriptions of the study's design and outcome event numerators as key outcomes reported as proportions only). Therefore, this study was not included.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				80%, and 23% of leg ulcers completely healed. For the infected leg ulcer population, there was a mean leg ulcer volume reduction of 81%, and 27% of infected leg ulcers completely healed. These outcomes for 98 infected leg ulcers were essentially identical to the broader 261 leg ulcer population, which were in turn similar to the entire 693 hard-to-heal wound population. This mirrors the population of Harding et al., 2016 (a study that was included): all leg ulcer patients, with reported outcomes for the infected leg ulcer sub-population. Excluding this large and relevant real-world study that was supplemented with LSA-specific information, while including some small and low-quality studies on other dressings (Table 4-1), does not seem reasonable. Note: the fact that over 400 studies were excluded and only 34 were included suggests that the scope of the LSA is too narrow for the reality of wound care.	
29.	Convatec	85	5.3	**"The breadth of dates across which the studies were conducted may limit the applicability of their findings to current care, particularly for the 3 studies published in the 1980s"** Methods of infection diagnosis 40 years ago were different to those used in modern wound care. The authors describe **"bacterial infection of ulcers"** when they likely meant colonization; they also discuss *S. aureus* and *P. aeruginosa* 'infection' from swab samples, when growth or colonization would now be more appropriate	Thank you for your comment. We have considered studies that report having included infected leg ulcers to meet the NICE scope. We acknowledge that studies that reported including "infected leg ulcers" without clear criteria for wound infection may have used definitions that vary, introducing variability into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
30.	Convatec	40 65	Table 4-1 5.1	**"Yang et al 2015 - GREEN"** – Small size (n=20), **"chronically infected"** may not mean clinically infected (chronically infected is terminology more associated with biofilm), and not peer reviewed (poster only), yet this study was deemed to fully meet criteria. Contrast with peer reviewed publications excluded, e.g., Torkington-Stokes et al 2024, which was excluded due to ineligible population,	Thank you for your comment. We have applied a consistent approach to selecting evidence: We have excluded studies reporting hard to heal ulcers or chronic wounds where infection is not stated. We have included studies where all ulcers were stated to be infected (author-reported definitions); OR for agents with

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				despite it including 98 locally infected leg ulcers and had outcomes on wound size, healing status and infection status.	insufficient evidence we also included studies where ulcers or wounds were not infected. There was considerable evidence for silver agents that met the NICE scope fully, thus silver studies that might have met a broader PICO such as Torkington Stokes 2024 (due to reporting a mixed infection-status population) were not included. As noted above, the supplementary document reporting limited subgroup data was not included as the EAG could not independently verify its reliability. However, we acknowledge that studies that reported including “infected leg ulcers” without clear criteria for wound infection may have used definitions that vary, introducing variabilty into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
31.	Convatec	174-176	7.2.4.2 Table 7-8	**The assumptions in Table 7-8 create an unrealistic and inaccurate cost-in-use for silver dressings.** It assumes all silver dressings will be changed 5 times per week for infected, unhealed ulcers. This is based on findings from Meaume et al, 2005, a study examining the impact of Silvercel dressings (an elemental silver, alginate dressing). Alginate dressings are a heritage technology that require changing more frequently than modern gelling fibre dressings (Harding et al., 2001). Furthermore, elemental silver dressings account for only approximately 7% of all silver dressing used. To assume that all silver dressings must be changed with the same frequency of Silvercel vastly overstates the number of	The EAG acknowledge that the resource use estimates associated with silver AMDs were high relative to other AMDs. The model base case results have been updated to align with Forlee et al (silver salts and compounds).

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				silver dressings that would be used in practice (and therefore understates the cost-effectiveness of silver as an antimicrobial agent). It would be more appropriate to assume dressing change frequency for silver as a weighted average between sub-agents (this would be consistent with the approach used to calculate the average cost per dressing for each agent detailed in Table 7-7). This would more accurately reflect the number of dressing changes required in practice and give a more accurate representation of the cost-effectiveness of silver dressings. At present, the assumptions made in Table 7-8 create an inaccurate analysis of the cost-effectiveness of silver as an antimicrobial agent for infected VLUs. This is also inconsistent with the approach taken for other antimicrobial agents in the same table. Some assumptions are taken from literature, some are taken from NHS guidance docs. This will significantly bias the health economic analysis. Most AMDs have *up to* 7 days wear time (and NHS guidance documents reflect this). The authors have then used the 'up to 7 days' figure for the 'uninfected healed' state for PHMB and honey. In the absence of evidence, they have also assumed 5 days wear time for the 'infected, unhealed' state for PHMB. This biases the health economic analysis in favour of antimicrobial agents with incomplete literature on wear time. This inconsistent approach, and the subsequent flawed assumptions made here, have a significant effect on the outcomes of the health economics analysis (as acknowledged by the report's authors). Table 7-26 (page 229) acknowledges that if the model assumes dressings	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				are changed once per week, or 3 times per week, all agents became more cost-effective compared with iodine (apart from PHBM in the later assumption). Whilst we welcome this acknowledgement from the authors, it is not given appropriate emphasis compared with the primary analysis (which concludes, erroneously, that iodine is the most cost-effective agent for AMDs). The assumptions made in terms of dressing change frequency for the primary analysis should be reconsidered. We suggest a weighted average for each agent based on sub-agent wear time.	
32.	Convatec	65	5.1	**"No evidence that partly met the decision problem was included for silver, as sufficient evidence that fully met the decision problem had already been identified for studies of this AMD"** (and earlier on p27: **"Where no evidence was found for an agent, or the evidence was limited (for example consisting of conference abstracts or studies with small sample sizes), the population criteria were broadened in stages until evidence for that agent was identified")** This approach risks leading to results that are biased in favour of AMDs that lack evidence. By including less relevant studies for only some AMD types, a larger base of 'partly meeting' studies for other AMD types (e.g., iodine, silver) are ignored. E.g., ignoring Torkington-Stokes et al 2024, which was excluded due to ineligible population, despite it including 98 locally infected leg ulcers and had outcomes on wound size, healing status and infection status, seems unreasonable.	This comment queries the NICE scope and is not a factual inaccuracy. We will review other comments at consultation stage. On Torkington Stokes 2024, the EAG considered that the additional document summarising subgroup data did not provide sufficient information to allow an adequate assessment of the reliability of evidence (specifically lacking in details on the baseline data for this subgroup, descriptions of the study's design and outcome event numerators as key outcomes reported as proportions only). Therefore, this study was not included.
33.	Convatec	174	7.2.4.2 Table 7-8	Frequency of assumed dressing change within Table 7-8 does not represent face validity nor real life practice in a community setting. Utilisation of 5 dressings per week	The frequency of dressing changes was explored in scenario analysis due to the uncertainty. See page 227 of report. Scenarios were run for dressing changes to be set the

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				would suggest 5 x DN visits which the NHS does not have capacity to support. This flawed assumption has significant impact on the health economic analysis and should be reconsidered.	same for all comparators e.g. once a week (regardless of infection status). Iodine remained the referent agent in all dressing change scenarios.
34.	Convatec	15	2.2.1	Table 2-1 attempts to categorise types of dressing based on their clinical indications but it makes a factual error in the indications for gelling fibres. claims that **"alginate, gelling fibre, absorbent fibre"** dressings are for **"low exuding wounds, to absorb whilst maintaining a moist environment."** Gelling fibre dressings are also indicated as a primary dressing for moderate and highly exuding wounds. Foams are generally for moderate to zero exuding wounds, not moderate to high as stated. Combing ointments, hydrogels, gels and pastes with ribbon dressings is not appropriate. Table 2-2 states **"Silver with anti-biofilm mechanisms (this group includes silver with additional anti-biofilm mechanisms)"** – this repetitive statement should correctly read 'ionic silver with anti-biofilm sub-agents' (according to verbiage before table).	Thank you for alerting us to this, this has been corrected.
35.	Convatec	198	7.2.4.3	The values itemised with the table 7-10 are inconsistent with those published by NHS England within NHS Procurement, Value and Savings methodology 2024.	These values were derived using the methods outlined in the tables above and sensitivity analysis and scenarios were performed around them to assess validity.
36.	Convatec	160-161	Table 7-4	**"Maximum time agents are prescribed (as indicated by clinical guidelines)"** This is factually inaccurate for all silver dressings. Table 7-4 claims this is 4 weeks based on guidance from NHS Hertfordshire and West Essex Integrated Care Board. There are two problems with this: 1. This is local policy from a single ICB, not evidence-based guidance on a national level.	The source of Brassington and Crotty was used as an independent resource that could be found on silver dressing duration, published by NHS pharmacists. We acknowledge the real-world use of silver dressings may exceed 4 weeks, dependent on the hospital or even pharmacist. Therefore, the

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				2. The authors of the HWE ICB guidance only cite one source for their 2-4 week recommendation. Their cited source is an industry-sponsored op-ed that recommends a "two-week challenge" upon which to reassess, with no defined end point for the silver prescription. This sentiment is echoed in the Wounds International Consensus paper "Appropriate Use of Silver in Wounds" which recommends to *reassess* every two weeks. If the wound shows signs of improvement, but signs of infection are not resolved, the recommendation is to *continue silver use*. There is no evidence-based guidance to recommend silver dressings are discontinued after 4 weeks. Further detail is given in comment 41.	EAG performed a scenario analysis in which the silver dressings were continued for 12 weeks. Two further sources are identified. Croydon CCG in 2020 states that Silver dressing should be stopped after 2 weeks. https://swlimo.southwestlondon.icb.nhs.uk/wp-content/uploads/2021/06/Prescribing-Top-Tips-for-Prescribing-Dressings-inc-Silver-Dressings.pdf In addition, a source from Powys Teaching Health Board, recommends maximum use of 4 weeks. "over usage of silver dressings can cause bacterial resistance, toxicity, side effects and potentially delay wound healing" https://pthb.nhs.wales/services/pharmacy-and-medicines-management/professionals/prescribing-guidelines/files/silver-dressings-guidance/#:~:text=The%20right%20dressing%20for%20the%20right%20patient%20at%20the%20right%20time&text=This%20means%20silver%20dressings%20should,as%20the%20infection%20is%20controlled.
37.	Convatec	173	7.2.4.2	**"People with leg ulcers require regular dressing changes, particularly if their leg ulcer has a local infection"** Fluid handling is often a bigger driver of dressing change. This is why the format of the dressing (gelling fibre vs. alginate vs foam, etc.) is so critical to the health economic analyses. The LSA does not account for this, reducing the validity of the findings.	In the final protocol, it was planned that subgroups would be explored indirectly using categories of dressing, for example hydrocolloid compared with foams and absorbent pads. However, following publication of the protocol, the EAG was made aware that the agents could not be grouped (i.e. silver and honey foams grouped together). Therefore, the EAG revised

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					their approach with sub-agents aligning with the International Wound Infection Institute (IWII) principals of best practice (2022) (International Wound Infection Institute (IWII) 2022). There was a paucity of evidence to allow for further disaggregation of the sub-agents into the categories defined in the scope without introducing additional uncertainty into the analysis.
38.	Convatec	132	5.5.1.9	**"Two single-arm studies reported that with a silver sulphadiazine dressing, 7% of patients had positive swab cultures (after previously having had a negative swab)"** Positive swab cultures do not equate to infection. Positive swab cultures do not equate to re-infection and should not be reported as such.	Thank you for alerting us to this. On reviewing this data we agree with your comment, this has been removed.
39.	Convatec	95	5.4.3.1	**"1 study (n=50) (Molle et al. 2023) favoured honey over silver in the number of ulcers with negative bacterial swab tests at day 15"** Negative swabs cannot be considered absence of clinical infection, just as positive swabs cannot be considered diagnostic of infection. This statement should be removed.	Thank you for your comment. Though bacterial presence is not a sufficient condition for diagnosing wound infection, reduction in microbial burden is noted as a component of wound infection management in the IWII 2022 consensus document. The wording is clear that this refers to the swab results and does not report this as the absence of infection. Therefore this has not been removed. We have amended the pertinent section of the detailed outcome summary for clarity around this.
40.	Convatec	95	5.4.3.1	**"6 silver studies that fully met the decision problem reported local infection… silver sulphadiazine (Degreef and Michiels 1984, Melotte et al. 1985)"** As discussed above, the definition of infection used in these older studies may not be applicable today.	We acknowledge that studies that reported including "infected leg ulcers" without a clear criteria for wound infection may have a definition that is not consistent with the modern definition requiring clinical signs of infection. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
41.	Convatec	89	5.4.1.1	**"1 study compared 2 ionic silver dressings (Acticoat and Aquacel Ag) and 1 ionic silver complex dressing (Comfeel/Biatain Ag) (n=25 in each arm) (Gago et al. 2008), finding statistically faster complete healing with Acticoat ionic silver compared to ionic silver Aquacel"** Acticoat is not an ionic silver dressing, it is nanoparticulate silver / metallic/elemental silver; "ionic silver Aquacel" should be *Aquacel Ag*. Note: It should be made clear that Aquacel Ag dressing is no longer available and has been superseded by Aquacel Ag+ Extra.	Thank you for your comment, we have edited throughout to ensure that "Aquacel Ag" is written in full. *Though Aquacel Ag is no longer available it was among the list of eligible dressing types provided by the NICE scope. We have added a note in the Discussion that the included AMDs may include some dressings that are no longer available. Acticoat has been labelled an ionic silver dressing based on advice from the SDMA, who noted that "Acticoat also contains ionic silver which is the primary agent providing the antimicrobial activity." This has therefore not been changed.
42.	Convatec	89	5.4.1.2	**"At 8 weeks, these results appeared reversed with the highest proportion reported for ionic silver, and lower rates for silver sulphadiazine. Ionic silver plus antibiofilm reported the lowest rate at this timepoint"** 8 weeks is incorrect; it was 4 weeks with Aquacel Ag+ followed by 4 weeks with Aquacel.	Thank you for alerting us to this, this has been corrected.
43.	Convatec	86	5.3	**"Wounds were not always reported to be clinically assessed as "infected", with some studies instead describing the presence of a range of signs of infection. Where wounds were explicitly reported to be infected, the criteria used by assessors for making this judgement were often unreported"** Agreed. Misunderstanding of what infection is (it's not just the presence of bacteria in a wound) is a fundamental challenge of this LSA approach of only considering 'infected' leg ulcers. There is no accurate way of diagnosing infection in wounds. AMDs usually have approved indications for wounds that are infected *and at-risk of infection*, since the intention of AMDs is not just to	We acknowledge that studies that reported including "infected leg ulcers" without a clear criteria for wound infection may have a definition that is not consistent with the modern definition requiring clinical signs of infection. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation. The remainder of this comment queries the NICE scope and is not a factual inaccuracy. We will review other comments at consultation stage

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				treat established local infection, but *to prevent local infection from occurring* in the first place. At present, the inconsistency in the definition of "infected" between studies is likely to bias clinical and health economic outcomes of the LSA in favour of those agents where supporting studies take a less selective definition of "infection." LSA authors should either: 1. Remove all studies where infection status is unclear or outdated (e.g. Melotte et al 1985; Green et al, 1984; Skog et al, 1983; Miller et al, 2010). 2. Broaden te scope of the LSA to include studies examining VLUs that are infected or *at-risk of infection*. This would more accurately reflect how AMDs are used in real-world practice.	
44.	Convatec	202	7.3.1.2	**"The results show that iodine is the least costly and most effective agent."** There are several flawed assumptions made in the health economic model that make this statement misleading and inaccurate to real-world practice. To summarise: table 7-4 takes efficacy data for iodine as an agent from only cadexomer iodine (as healing data for povidone iodine was not included). However, there is no evidence of parity between these sub-agents (and, in practice, these sub-agents deliver iodine to the wound in radically different ways). Table 7-7 then details that the assumed cost-per use for iodine a weighted average of all iodine subagents based on usage frequency. Povidone iodine is an order of magnitude less expensive than cadexomer iodine (£0.39 vs £8.69) and is overwhelmingly the subagent of iodine used in practice (~95% of all iodine dressings used are povidone iodine). This skews the assumed cost of iodine heavily towards povidone iodine (£1.45).	The section this refers to describes the results of the analysis using the listed inputs and acknowledged assumptions. The interpretation of the results state "it is essential to exercise caution when interpreting the model results." Multiple scenario analyses were conducted around the assumptions used, including the maximum dressing costs. An additional scenario in which the cost for iodine aligns with the cost for Cadexomer iodine has been performed.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				How this effects the model: the agent-level model assumes that all iodine dressings will have the efficacy of cadexomer iodine (£8.69 avg. cost per dressing) but a cost more similar to povidone iodine (assumed cost £1.45). Without credible evidence of parity between these two radically different dressing types, the model is likely to vastly overstate the cost-effectiveness of iodine as an agent: reporting the efficacy of an expensive cadexomer iodine dressing, but calculating the cost largely influenced by the cheap povidone iodine. We understand the assumptions made in table 7-4 are intended to give a conservative estimate for each agent. However, in practice, these assumptions give an unrealistically favourable picture of the cost-effectiveness of iodine. This makes the outputs of the model misleading and inaccurate to real world practice: there is no dressing available that will provide cadexomer iodine's efficacy at a cost similar to povidone iodine.	
45.	Convatec	202	Figure 7.8	As per comment 20.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
46.	Convatec	204	Table 7-17	As per comment 20.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
47.	Convatec	205	Table 7-18	As per comment 20.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
48.	Convatec	208	Table 7-21	As per comment 20.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
49.	Convatec	172	Table 7-7	Weighted average on iodine row not appropriate due to vast difference in cost of cadexomer iodine vs. povidone iodine (later is 22-times cheaper). All other AMD types are similar in weighted average (silvers, honeys, etc.).	See comment 44.
50.	Convatec	228-238	7.3.4, Table 7-26 and Table 7-27	**"Iodine was the least costly, at £0.29 per pack"**, **"Iodine accrued the lowest total cost for the year per person"**, **"Iodine was the referent agent"**, **"All other agents became more cost-effective compared with iodine"**, **"Iodine accrued the lowest total cost for the year per person"** etc. These all relate to povidone iodine only for cost, yet use cadexomer iodine data for effectiveness.	This is describing an exploratory scenario analysis whereby the minimum cost of the dressing was used.
51.	Convatec	161	Table 7-4	**"Assumed equivalent the sub-agent with the smallest percentage healed (conservative assumption"** This is considering the *outcomes from cadexomer iodine (expensive)* but the *cost from povidone iodine (low cost)*. This skews the cost-effectiveness. Because povidone iodine is so widely used, the weighted average cost of iodine as an agent seems incredibly low. But the only sub-agent reporting endpoints is cadexomer iodine (a much more expensive preparation). By grouping these it makes iodine appear to be far more cost-effective.	See comment 44.
52.	Convatec	239	7.3.5	**"The model does not capture this and, therefore, likely underestimates the benefit to the patient experience if 1 dressing could be prescribed for longer periods"** Both cadexomer iodine dressings and povidone iodine dressings 'white out' (antimicrobial is used up) quickly in clinical use.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
53.	Convatec	174	7.2.4.2 Table 7-8	Cadexomer iodine (and povidine iodine) dressings are known to 'white out', that is, become exhausted of active molecular iodine (I_2) quickly in clinical use. This manifested in a clinical study where cadexomer iodine dressings were changed more than daily on an average: *8 times/week (range 5–16 times/week)* (Schwartz et al. A prospective,	Thank you for your comment. The number of dressing changes was explored in sensitivity and scenario analysis.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				non-comparative, multicenter study to investigate the effect of cadexomer iodine on bioburden load and other wound characteristics in diabetic foot ulcers. Int Wound J 2013; 10: 193-199). Whilst this is not a study specific to infected VLUs, it is likely to be more reflective of real-world practice than the "up to 3 days" maximum wear time assumed by the LSA authors in the absence of evidence. This is another example where the inconsistent approach to dressing change frequency has biased the health economic outcomes (as detailed in comments 7 and 12). These biases regarding dressing change frequency have a material effect on the outcome of the health economic analysis, as acknowledged by the LSA authors in table 7-26.	
54.	Convatec	194-201	7.3.1.1, Table 7-15, Table 7-16 and Figures 7.3-7.8	**"The fully incremental analysis ranked Iodine as the agent that would generate the smallest costs per person, costing £6,494 (95% CI: £5,579 to £7,408) to the England and Welsh NHS over 1 year of treatment. It was also the most effective, accruing 0.70 (95% CI: 0.64 to 0.77) QALYs and, therefore, was the referent agent and dominated all other agents"** and **"Iodine is the most cost-effective treatment" and "iodine was cost-effective in all cost-effectiveness thresholds"** These statements, Table 7-15, Table 7-16 and Figures 7.3-7.8 are all based on *povidone iodine's cost (low)* but *cadexomer iodine's (expensive) clinical outcomes*.	The cost of iodine was a weighted average of sub-agents, with weighting based on CPRD market share, as were all included agents. Minimum and maximum cost of dressings was explored in scenario analysis. Iodine remained the referent in both analyses, see page 253 of report.
55.	Convatec	201-207	7.3.1.2, Tables 7-17 to 7-21	**"The results show that iodine is the least costly and most effective agent"**, **"iodine is cost-effective compared to all other agents"**, **"It follows that those treated with iodine have the smallest costs and the largest QALYs"** Flawed, as detailed above in comment 30.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
56.	Convatec	202	Figure 7.8	Cost-effectiveness plane comparing silver and iodine is inaccurate for two reasons: 1. Flawed assumptions made that overstate the efficacy and effectiveness of iodine, as detailed in comments 20 and 33. 2. Flawed assumptions made in the frequency of dressing changes for silver, as detailed in comment 7	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
57.	Convatec	157	7.2.3.2 Table 7-3	Assuming conservative equivalence (that cadexomer iodine covers all iodine-containing dressings, i.e., also povidone iodine) is not appropriate. The starch (cadexomer) beads have additional physical properties which likely make cadexomer iodine more effective than povidone iodine as a dressing.	See comment 44.
58.	Convatec	159	Table 7-3	Table 7-3 makes a factual error in its selection of study to support healing rates for copper dressings. It describes the patient population of Treadwell 2022 as "hard to heal leg ulcers." This is incorrect. Treadwell 2022 examines a population of "hard to heal acute and chronic wounds." This is a mix of aetiologies AND locations. The authors do not specify that all dressings be located on the lower limb. Likewise the caution statement in table 7-3 warns that patients "may have a less-severe *leg ulcer*." This is incorrect, whilst it is likely that the wounds included in this study are less severe, not all included wounds are ulcers, nor are they located on the leg. This study should be excluded due to ineligible population.	The report has been reworded to state wounds rather than pressure ulcers.
59.	Convatec	163	Table 7-4	Table 7-4 makes a factual error in reporting the healing rates of infected VLUs for copper dressings.	Section 5.2 reports that, because no studies that fully met the decision problem were identified for

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				The reported rate of healing is 32% at 4 weeks based on Treadwell 2022, this conference poster abstract does not specify the wound(s) included are: A) Clinically infected B) Venous aetiology C) Located in on the lower limb This is a study of non-infected wounds of various aetiology and location. The study does not meet the decision problem, due to ineligible population, and should not be included in the health economics analysis. The healing rate for this study is very high compared with other included studies that do fully meet the decision problem. This is unsurprising, given that infected wounds generally heal slower and venous leg ulcers typically take longer to heal than other wound types. This error overstates the healing rate of copper dressings and, subsequently, vastly overstates the cost-effectiveness of copper dressings in the following sections.	copper. Where no data were available to fit the decision problem, the PICO needed to be widened.
60.	Convatec	196	Table 7-15	Total cost and QALYs for copper are inaccurate due to use of study with ineligible population to estimate healing rate (as detailed in comments 34 & 35).	See responses to comments 34 & 35
61.	Convatec	197	Figure 7.3	As per comment 36, the total cost and QALYs for copper are inaccurate due to use of study with ineligible population to estimate healing rate (as detailed in comments 34 & 35).	See responses to comments 34 & 35
62.	Convatec	198	Table 7-16	All given values for copper are inaccurate due to use of study with ineligible population to estimate healing rate (as detailed in comments 34 & 35).	See responses to comments 34 & 35

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
63.	Convatec	247	8.2	**"A key driver of cost-effectiveness was the efficacy data"** A key driver was clearly *cost*, since *cost from povidone iodine was used*, while *efficacy from cadexomer iodine was used*. Assumptions made on frequency of dressings of dressing changes is also a key driver of cost-effectiveness and changing these has a profound impact on the cost-effectiveness of different AMDs (acknowledged by the authors in table 7-26).	Comment is not a factual inaccuracy, no change to report has been made. Cost is highlighted as a key driver throughout section 7.
64.	Convatec	200	Figure 7.5	Cost-effectiveness plane comparing copper and iodine is inaccurate for two reasons: 1. Flawed assumptions made that overstate the efficacy and effectiveness of iodine, as detailed in comment 20 Erroneous use of a poster presentation with ineligible population to assume healing rates for copper, as detailed in comments 34 & 35	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
65.	Convatec	242	7.3.6	**"An example of this is Forlee et al, whose participants remained on silver dressings for 8 weeks (Forlee et al. 2014), yet, guidance from the NHS recommends silver dressings should be used for a maximum of 4 weeks to avoid silver toxicity (Brassington and Crotty 2024)."** Based on a misleading interpretation without evidence. This statement shows a lack of academic rigour on the part of the LSA authors: 1. Brassington and Crotty (2024) is not a peer reviewed reference and should not be reported like one. 2. Brassington and Crotty, in turn, do not provide adequate substantiation for their claim that "silver dressing is potentially harmful" or "2-4 weeks treatment at a maximum is recommended." a. Brassington and Cross cite an industry sponsored op-ed piece (Wounds UK	The source of Brassington and Crotty was used as an independent resource that could be found on silver dressing duration, published by NHS pharmacists. We acknowledge the real-world use of silver dressings may exceed 4 weeks, dependent on the hospital or even pharmacist. Another source from a Croydon CCG in 2020 states that Silver dressing should be stopped after 2 weeks. https://swlimo.southwestlondon.icb.nhs.uk/wp-content/uploads/2021/06/Prescribing-Top-Tips-for-Prescribing-Dressings-inc-Silver-Dressings.pdf In addition, a source from Powys Teaching Health Board, recommends maximum use of 4

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				"Adopting the 2-week challenge in practice: making the case for silver dressings"). This document makes no reference to a maximum treatment time (it merely suggests undertaking a "two-week challenge" as part of a promotional campaign for Acticoat nano-crystalline silver dressings) b. The Wounds UK document makes no reference to "harm," "toxicity" or "adverse events." 3. Brassington and Crotty (2024) does not substantiate the LSA's claim that "NHS recommend silver dressings should be used for a maximum of 4 weeks to avoid toxicity." a. This document appears to be the work of only two pharmacists, it does not represent the view of the NHS b. It is unclear who else, if anyone, has reviewed and approved this document c. The widest possible scope for this document is a single Integrated Care Board The LSA authors are here reiterating a myth without evidence or a supporting primary source. If the LSA authors cannot find a credible primary source to support their claim, this statement should be removed.	weeks. "over usage of silver dressings can cause bacterial resistance, toxicity, side effects and potentially delay wound healing" https://pthb.nhs.wales/services/pharmacy-and-medicines-management/professionals/prescribing-guidelines/files/silver-dressings-guidance/#:~:text=The%20right%20dressing%20for%20the%20right%20patient%20at%20the%20right%20time&text=This%20means%20silver%20dressings%20should,as%20the%20infection%20is%20controlled.
66.	Convatec	244	8.1	**"The clinical evidence review did not identify evidence adequate to draw conclusions on the relative efficacy of AMDs when used to treat infected leg ulcers"** and **"The EAG therefore considers the evidence base to be uncertain"** Because the scope was too narrow. NICE were advised of this beforehand.	This comment queries the NICE scope and does not pertain to factual inaccuracies, thus no further change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
67.	Convatec	246	8.1	**"The EAG considers the generalisability of the evidence base to be poor due to the small number of UK studies (7 of 34 included studies)"** Generalisability in this case means using non-UK data that is *generally similar* to UK (e.g., European, Canadian), not that it *is* UK data	Thank you for your comment. We have considered generalisablity to the UK NHS context, so while healthcare systems in some european countries may be more similar to the UK NHS the generalisabliity of their findings is uncertain – there are likely to be differences in the identification of infection and treatment approaches aside from which AMDs are used. Therefore this evidence is unlikely to be as applicable to the UK NHS as those of studies conducted in the UK. We acknowledge that there is uncertainty and have added this to the discussion.
68.	Convatec	249	9	**"The current evidence base does not allow a clear assessment of the relative merits of different AMDs in UK patients with infected leg ulcers, so no conclusions on the relative efficacy on the range of AMDs can be drawn"** Because the scope was too narrow, as NICE were advised beforehand.	The remainder of this comment queries the NICE scope and is not a factual inaccuracy. We will review other comments at consultation stage
69.	Convatec	28		"…**no evidence was included for some sub-agents because sufficient evidence that fully met the decision problem had already been included for other sub-agents within that agent grouping**. Further evidence from broader populations was not sought for missing sub-agents as this was not feasible within the scope and resource available to complete the LSA." Please clarify which sub-agents did not require evidence due to the existence of evidence of other sub-agents.	Thank you for your comment, this has been added.
70.	Convatec	42 65 66	Table 4-1 5.1 5.1	**"Skog et al 1983 - GREEN"** What clinical signs and symptoms of local wound infection were used to diagnose infection? This study was many years before any clinical signs & symptoms were standardised as best practice. Study was over 40 years ago, and on obtaining the article, it is apparent that an	Thank you for your comment. We have considered studies that report having included infected leg ulcers to meet the NICE scope. We acknowledge that studies that reported including "infected leg ulcers" without clear criteria for wound infection may have used definitions that

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				understandably outdated qualitative bacterial growth-related '+++' scale was used to describe infection. The authors describe **"bacterial infection of ulcers"** when they likely meant colonization; they also discuss *S. aureus* and *P. aeruginosa* 'infection' from swab samples, when growth or colonization would now be more appropriate. Given that these patients would likely not meet the IWII definition of "local infection," the LSA authors should consider removing this study due to ineligible population (or broadening the scope to include studies of VLU patients "at risk" of infection for consistency).	vary, introducing variabilty into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
71.	Convatec	46 65 67 76	Table 4-1 5.1 5.1	**Degreef et al 1984 - GREEN"** What clinical signs and symptoms of local wound infection were used to diagnose infection? This study was many years before any clinical signs & symptoms were standardised as best practice. If these patients do not meet the IWII definition of "local infection," the LSA authors should consider inclusion of this study due to ineligible population (or broadening the scope to include studies of VLU patients "at risk" of infection for consistency).	Thank you for your comment. We have considered studies that report having included infected leg ulcers to meet the NICE scope. We acknowledge that studies that reported including "infected leg ulcers" without clear criteria for wound infection may have used definitions that vary, introducing variabilty into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
72.	Convatec	51 65 67 76	Table 4-1 5.1 5.1	**"Melotte 1985 - GREEN"** – **"bacteriological infection"** may not be relevant to local clinical infection we understand today. Could just mean culture-positive. If these patients do not meet the IWII definition of "local infection," the LSA authors should consider removing this study due to ineligible population (or broadening the scope to include studies of VLU patients "at risk" of infection for consistency).	Thank you for your comment. We have considered studies that report having included infected leg ulcers to meet the NICE scope. We acknowledge that studies that reported including "infected leg ulcers" without clear criteria for wound infection may have used definitions that vary, introducing variabilty into the evidence base. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
73.	Convatec	58 65 66	Table 4-1 5.1 5.1	**Miller et al, 2010 - GREEN"** 1 clinical sign of infection is not usually enough to diagnose local infection; because each individual sign in isolation may be due to other issues, so several clinical signs and symptoms are required concurrently to diagnose local infection with more confidence. Critical colonization term is no longer used, and it has never possible to detect critical colonization (an arbitrary cut-off based on bacterial colonization and biofilm development). **"…either infection or critical colonisation"** Critical colonization is not detectable.	We acknowledge that studies that reported including "infected leg ulcers" without a clear criteria for wound infection may have a definition that is not consistent with the modern definition requiring clinical signs of infection. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation. We also note that in the case of Miller et al 2010 patients were included if they presented with at least 1 clinical sign of infection or critical colonisation – though the latter term is no longer used, the list of signs in the study eligibility criteria (cellulitis, suppuration, sepsis) are clinical signs of infection.
74.	Convatec	73	5.1	Mosti et al. 2015 was a pilot study (**"comparative, randomised, single centre pilot study"**) rather than an randomised controlled trial (RCT); small patient populations (n=20 each arm).	Thank you for alerting us to this – Mosti 2015 is described as a pilot RCT in the study summary table but elsewhere has not been fully described as a pilot study. We have added this information throughout.
75.	Convatec	75	Interventions and comparators	**"2 evaluated ionic silver (both Aquacel Ag+ Hydrofibre dressings, dressing category: alginate, gelling fibre, absorbent fibre (Harding et al. 2016, Vanscheidt et al. 2003))."** Vanscheidt et al 2003 examined Aquacel Ag, not Aquacel Ag+ dressings. Aquacel Ag+ contains additional anti-biofilm active ingredients (EDTA and benzethonium chloride). "evaluated a silver AMD of uncertain subtype and dressing category " - Microlyte Ag contains both metallic silver and ionic silver in a polyvinyl alcohol, polyacrylic acid resorbable matrix (it's a synthetic skin sub).	Thank you for alerting us to this error, this has been corrected. Thank you for notifying us of the Microlyte Ag agent subtype, this has been noted throughout. The eligibility of this intervention was queried with specialist committee members, via NICE, during study selection, who confirmed that it should be included in the review due to it's similarity with other dressings available.
76.	Convatec	89	Table 5-4	Degreef and Michiels 1984 and Melotte et al. 1985 are around 40 years old. As described above, outdated terminlogy and methology in disgnosing infection casts doubt on inclusion of these old studies.	We acknowledge that studies that reported including "infected leg ulcers" without a clear criteria for wound infection may have a definition that is not consistent with the modern definition

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Table header should read *'Ionic silver with anti-biofilm sub-agents'* (and in all other tables when mentioned).	requiring clinical signs of infection. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation. The wording in the report ("Silver with anti-biofilm mechanisms") aligns with Table 2-2. For consistency with the determined sub-agent groups described in Table 2-2, no change has been made to the report.
77.	Convatec	90	Table 5-5	Table headings need superscripts. Flaminal and KytoCel (and p91 and elsewhere) spelling. Why are Flaminal, KytoCel and MedCu trade names included? Monofloral honey, manuka honey and PHMB are not reported with trade names.	Thank you for your comment. We have updated the report to remove all brand names for consistency and used the generic agents names instead.
78.	Convatec	92	5.4.2.2, Table 5-7	**"ionic silver with antibiofilm agent"** should read *'ionic silver with anti-biofilm sub-agents'.* Table header should read *'Ionic silver with anti-biofilm sub-agents'.* **"an unclear silver sub-agent dressing (Manning et al. 2020)"** Microlyte Ag contains both metallic silver and ionic silver in a polyvinyl alcohol, polyacrylic acid resorbable matrix (it's a resorbable synthetic skin sub, rather than a dressing).	The wording in the report ("Silver with anti-biofilm mechanisms") aligns with Table 2-2. For consistency with the determined sub-agent groups described in Table 2-2, no change has been made to the report. Thank you for notifying us of the Microlyte Ag agent subtype, this has been noted throughout. The eligibility of this intervention was queried with specialist committee members, via NICE, during study selection, who confirmed that it should be included in the review due it's similarity with other dressings available.
79.	Convatec	10	Exec sum	**"…evidence base identified does not allow a clear assessment of the relative efficacy of different AMDs to treat infected leg ulcers, and so does not provide conclusions on the validity of price variability"** As we highlighted beforehand due to the "subset of subset" approach taken. Added to the fact that comparative studies have never been required, with the exception of isolated	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				markets (e.g., France), so companies are unlikely to invest millions and years in such studies of niche patient populations.	
80.	Convatec	10	Exec sum	**"Further evidence should be collected to compare the performance of different agents and sub-agents within AMDs"** Realistically this can only be done properly (removing myriad confounding clinical factors) and exhaustively *in vitro.*	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
81.	Convatec	12	1. Table 1-1	**"nanoparticulate silver"** and **"metallic/elemental silver"** could be combined. PHMB dressings do not need exemplifying, since iodine- and silver-containing dressings are not exemplified above. **"Comparator(s) – An antimicrobial dressing that is considered current standard of care in the NHS"** What dressing is this?	Thank you for your comment, we have edited the PHMB sub-agents to constitute differences in dressings (not sub-agents). For the silver dressings, the subagent categorisations used in the report are those developed by IWII and recommended by NICE and the specialist committee members. This comparator criteria specifies that *any* AMD used as standard of care in the NHS would be an eligible comparator.
82.	Convatec	10	Exec sum	**"Observational designs using hospital data may provide pragmatic means of evaluation. These should focus on UK NHS patient populations with infected leg ulcers and clearly report the infection status of leg ulcers at baseline as well as how this was determined. Where possible, patients should be matched for key baseline characteristics that are likely to affect treatment outcomes including healing"** Agreed, though this requires data of sufficient quality and standardization to be collected, which is not generally the case in UK healthcare systems.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
83.	Convatec	14	2.1 Table 2-2	Please insert: "dressings that contain *an antimicrobial agent* or deliver an antimicrobial agent directly to the skin"	Thank you for your comment, this sentence has been edited accordingly.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				PHMB sub-agents are just dressing materials (foam, biocellulose, gauze), not formulations (as with the honey, iodine and silver sub-agents).	On the dressing vs formulation comment, these are the subagent categorisations decided by discussion between NICE, the Surgical Dressings Manufacturers Association, stakeholder input and input from professional experts.
84.	Convatec	22	Table 2-3	Aquacel Ag+ Extra should read 'Ionic silver with anti-biofilm sub-agents' according to verbiage before table 2-1).	The wording in the report ("Silver with anti-biofilm mechanisms") aligns with Table 2-2. For consistency with the determined sub-agent groups described in Table 2-2, no change has been made to the report.
85.	Convatec	30 68 76	4.1 5.1 5.1	**"PHMB PuraPly"** (PuraPly AM) is an animal-derived (porcine small intestine submucosa) extracellular matrix (skin substitute/xenograft), rather than a wound dressing. This does not appear to be similar to other AMDs on the tariff. Koullias et al. 2022 was included. **"unclear agent subtype and dressing categorization"** – see above description.	Thank you for your comment, Koullias 2017 was checked with the specialist committee members, via NICE, during the review who confirmed it's relevance due to similarity with other PHMB dressings available. Thank you for notifying us of the Microlyte Ag agent subtype, this has been noted throughout. The eligibility of this intervention was queried with the specialist committee members, via NICE, during study selection, who confirmed that it should be included in the review due to it's similarity to other dressings available.
86.	Convatec	95	5.4.3.2, Table 5-10	References to swab cultures from (c) and (d) are not relevant to clinical infection. Positive culture does not mean clinical infection, nor does negative culture mean clinical non-infection. This should be removed.	Thank you for your comment. Though bacterial presence is not a sufficient condition for diagnosing wound infection, reduction in microbial burden is noted as a component of wound infection management in the IWII 2022 consensus document. The wording is clear that this refers to the swab results and does not report this as the absence of infection. Therefore this has not been removed. We have amended

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					the pertinent section of the detailed outcome summary for clarity around this.
87.	Convatec	119	5.4.9.2	(And througout) text should read *'ionic silver with anti-biofilm sub-agents'.*	Please see the response to comment 84.
88.	Convatec	129	5.5.1.1	**"while data for silver sulphadiazine also showed linear (but slower) improvement except for a peak at 4 weeks. This 4-week data point was informed by one small study only."** This study should be referenced and, if Melotte et al (1985), acknowledged to be outdated.	Thank you for your comment, this is a summary section providing a brief overview of results in which study references are not included. The detailed data and reference pertaining to this sentence can be found in the preceding sections. We acknowledge that studies that reported including "infected leg ulcers" without a clear criteria for wound infection may have a definition that is not consistent with the modern definition requiring clinical signs of infection. We have added a sentence to the study selection summary and discussion sections to clearly note this limitation.
89.	Convatec	132	5.5.1.9	Positive swab cultures do not equate to infection. This statement should be removed.	Thank you for alerting us to this. On reviewing this data we agree with your comment that this does not reflect re-infection. This has been removed.
90.	Convatec	133	5.5.2	**"Generalisability of the evidence base for using AMDs to treat infected leg ulcers in a UK NHS setting was considered to be generally poor, as only 7 of the 34 studies were conducted in the UK"** Generalisability in this case means using non-UK data that is *generally similar* to UK (e.g., European, Canadian), not that it *is* UK data.	Please see response to comment 57.
91.	Convatec	136	6.2	Type of silver (ionic silver complex) should be mentioned when discussing Jemec et al (2014).	Table 6.1 gives information on the type of silver, as phrased in the publication.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
92.	Convatec	155	7.2.3.2	Discussion of infection resolution using the 1985 references may not be appropriate	This study was not used to inform the model.
93.	Convatec	202	7.3.1.2	**"It is important to note that we have assumed that AMDs are still used in the non-infected, unhealed health state, which is not reflective of 'best practice'"** This statement regarding 'best practice' is misguided. Most AMDs are indicated (this means *approved by Regulatory authorities*) for wounds that are infected *and at risk of infection*. AMDs are designed to *prevent local infection*, as well as treat it. Do the LSA authors have evidence to substantiate the claim made here? If not, they should remove it.	This was communicated to the EAG by stakeholders based on clinical practice.
94.	Convatec	240	7.3.5	**"One clinical expert noted that they believed a copper dressing could be worn for a longer period than the 4 weeks used in the base case model"** Not relevant.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
95.	Convatec	316	Appendix B	**"Dissemond J, Aare K, Ozer K, Gandhi D, Ryan JL, DeKoven M. Aquacel ag advantage/ag+ extra and cutimed sorbact in the management of hard-to-heal wounds: a cohort study. J Wound Care. 2023.32(10):624-33 - Ineligible study design"** This study used the approach recommended by the LSA authors, namely **"Observational designs using hospital data [to] provide pragmatic means of evaluation"**.	Thank you for your comment – on reviewing this study we agree that "ineligible study design" is not an accurate exclusion reason. This study was excluded as "No separate results for eligible population subgroup" as results for patients with infected leg ulcers are not reported separately.
96.	Convatec	338	Appendix C, Table 11-1	Amber and green colours not explained for wound cleansing and secondary dressing.	Thank you for your comment, colour ratings were not used for secondary wound preparation/dressing characteristics. These colour codings refer to the degree to which the study population met the NICE scope, as in Tables 4.1 and 5.1. As this information is already summarised in these earlier tables we have removed the colour coding from Table 11.1.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
97.	Convatec	N/A		Iodine dressings are more frequently being reported as a restricted item for children, pregnant/lactating women, people with thyroid disorders or renal impairment (Formulary) And under medical supervision for deep ulcerative wounds, burns and large injuries (CHFT News - Inadine products have been upgraded to contraindications)	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
98.	Convatec	10	Exec sum	**"Further evidence should be collected to compare the performance of different agents and sub-agents within AMDs"** Realistically this can only be done properly (removing myriad confounding clinical factors) and exhaustively *in vitro.*	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
99.	Convatec	10	Exec sum	**"current evidence base does not allow a clear assessment of the relative merits of different types of AMDs in UK patients with infected leg ulcers"** Not realistic to expect this to change, with such a narrow scope (subset of infection status in a subset of wounds in a geographical subset).	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
100.	Convatec	9	Exec sum	**"Non-comparative, small sample sizes, did not often report statistical significance, were largely considered at high risk of bias"** This is due to the nature of clinical studies required by the authorities that companies must conduct.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
101.	Convatec	9	Exec sum	**"EAG therefore considers the evidence base to be uncertain"** As we highlighted beforehand due to the subset of infection status in a subset of wounds approach taken. If the scope had been infected or at risk chronic wounds, the outcome would have been different *and more useful*.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
102.	Convatec	10	Exec sum	**"Generalisability to the UK NHS setting was poor, with only 7 of the 34 studies being conducted in the UK"** Generalisability in this case means using non-UK data that is *generally similar* to UK (e.g., European, US?), not that it *is* UK data.	Please see response to comment 57

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Again, largely due to the nature of clinical studies required by *European* authorities for CE Marking. Companies who market products globally cannot be expected to conduct country-specific studies.	
103.	Convatec	253	10	Jemec et al 2014 reference duplicated	Thank you for alerting us to this, this has been corrected.
104.	Convatec	8	Exec Sum	The scope of this analysis was leg ulcers of any aetiology and not just venous leg ulcers. This ambiguity needs correcting. Also, different leg ulcers with different aetiologies develop as a result of different underlying diseases and respond differently to different treatments, heal at different rates and this impacts on their probability of developing infection, probability of infection amelioration, probability of re-infection and probability of ulcer recurrence following healing. Ideally, there should be a different model for each wound type as a conflation of the results for all leg ulcers cannot inform clinical decision making for a patient with a specific wound type.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
105.	Convatec	8	Exec Sum	Uninfected unhealed is not an appropriate state as it's conflated two states: uninfected static and uninfected improved. This can lead to inaccurate or misleading results	Comment is not a factual inaccuracy, no change to report has been made.
106.	Convatec	11	Future evidence	"Observational designs using hospital data may provide pragmatic means of evaluation" This is unlikely as most ulcers are managed in the community and not in a hospital setting	Comment is not a factual inaccuracy, no change to report has been made. The example of hospital data was used as this is the largest healthcare dataset that is readily available for research.
107.	Convatec	12	Future Evidence	"Outcome data should be gathered over a sufficiently long term (informed by clinical input) to capture all instances of infection resolution, reinfection, and complete healing" And	Thank you for your comment, we have added this to the report as further useful evidence that could be gathered over the longer term.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				consequential risks of infection including developing cellulitis, gangrene or undergoing an amputation	
108.	Convatec	12	Table 1.1	Diabetic foot ulcers and venous leg ulcers manifest from different aetiologies and outcomes associated with an intervention for one ulcers type cannot be applied to the other type	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
109.	Convatec		7.1	"The EAG leveraged existing model structures and adapted them to include 4 health states: 'infected, unhealed'; 'non-infected, unhealed'; 'healed', and 'death' to align with the decision problem" ideally this should be separated into non-infected static and non-infected improved	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
110.	Convatec		Fig 7.1	**Model Structure** What is the start point of the model? Is it infected venous leg uclers? Combining non-infected static and improved ulcers into one health state represents an intrinsic flaw in the model. Ulcers in these two different states consume different levels of healthcare resources and associated costs and their outcomes are different	As stated in section 7.2, the cohort will begin in the 'infected, unhealed wound' health state.
111.	Convatec		Table 7.2	Model Assumptions: "It was assumed that a wound (and/or infection of that wound) cannot reoccur during the time horizon." Infection can frequently reoccur if the ulcer does not heal, so this is not a valid assumption. EAG should have modelled infection reoccurrence	The EAG did include the functionality to allow for infection reoccurrence from the non-infected, unhealed health state. This assumption was referring to the 'healed wound' health state (i.e. once the wound had

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					completely healed, the ulcer could not reoccur in the one-year time horizon in the model)
112.	Convatec		Table 7.2	Model Assumptions: Once a percentage of the cohort transitions to the 'healed' health state, they automatically discontinue their AMD and transition to the second line treatment." Once healed an ulcer would no longer require any further treatment except possibly prophylactic compression hosiery, so this doesn't reflect clinical practice	The decrease in resource use costs (presented in section 7.2.4.3) between the healed and unhealed health states was designed to capture this decrease in resources.
113.	Convatec		Table 7.2	Model Assumptions "The per-week rate of infection resolution was assumed to be proportional to the per-week healing rate at 4 weeks" I have never seen any evidence to support this, so in my view its not a valid model assumption	The EAG acknowledged the limitations in this assumption in the report. A relationship between infection resolution and healing rate was deemed appropriate by the EAG and clinical opinion. Additional scenarios have been performed to test this assumption further, see Table 7.24.
114.	Convatec		Table 7.2	Model Assumptions: "When a proportion of the cohort discontinues an AMD, they move onto a weighted basket of AMDs." An AMD or all AMDs? This is ambiguous	They discontinued the first line AMD (for example, silver) and moved onto a weighted average basket containing all types of AMD.
115.	Convatec		Table 7.2	Model Assumption: "There was also a lack of robust data available to inform incidence rates and utility decrements. All clinical experts agreed that, in the absence of robust data to inform the model, it was appropriate to use hospitalisation rates as a proxy." Hospitalisation rates for what?	Hospital admissions associated with venous leg ulcer management, as per Guest and Fuller (2023)
116.	Convatec		Table 7.2	Model Assumptions "Where there was no data to inform the number of dressings per health state, a ratio of 2:1 was applied to the number of dressings in the 'non-infected,	A reliable source has not been identified therefore an assumption was used. No changes to the report were made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				unhealed' health state to derive the number of dressings in the 'infected, unhealed' health state " This is not valid as the number of dressings and frequency of dressing change in the non-infected static state will be around 50-75% more than non-infected improved state and dressing	
117.	Convatec		Table 7.2	Model Assumption "Guest et al (2023) did not disaggregate leg ulcer resource use by infection or healing status (Guest and Fuller 2023). Therefore, it was assumed that the resource use data was a combined cohort of people with unhealed infected and unhealed non-infected leg ulcers. It was noted by clinical experts that those with infected wounds would incur more resources and therefore higher costs. This was assessed in scenario analysis." See Table 5 in Guest JF, Fuller GW, Vowden P. Venous leg ulcer management in clinical practice in the UK: costs and outcomes. Int Wound J 2017; doi: 10.1111/iwj.12814	Table 5 in Guest et al (2018) does not provide up-to date cost / resource use data for specific resources for each health state. Furthermore, resource requirements have shifted since 2015/16, when these data were collected. Additional scenario analysis were performed, looking into the outcome if the cost of the infected, unhealed wound health state was larger and there were no differences to the overall results.
118.	Convatec		Table 7.2	Model Assumption: Guest et al (2023) did not disaggregate leg ulcer resource use by infection or healing status (Guest and Fuller 2023). However, it was highlighted in Guest et al (2018) that there was an associated cost. Indeed, over a year, Guest et al observed that that the cost of managing a healed venous leg ulcer was 4.5 times less than that of managing an unhealed venous leg ulcer over a year (Guest et al. 2018).	There was a lack of evidence to inform specific, up-to-date resource used for the healed health state. Given the possibility of an ulcer reoccurrence, it is expected that those in the healed health state would accrue costs in the months following their ulcer healing. An assumption was required to inform this. Additional scenario analysis has been performed

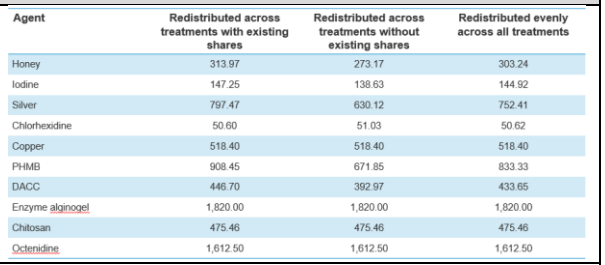
Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				The EAG have misinterpreted the study. Guest et al observed that that the cost of managing A VLU THAT GOES ON TO HEAL was 4.5 times less than that of managing an unhealed venous leg ulcer over a year. Once healed the VLU incurred no resources and was zero cost.	and found no difference to the overall results other than a decrease in costs.
119.	Convatec		Figure 7.2 Equation 7.1	. Therefore, **Error! Reference source not found.** was used to inform the percentage of leg ulcers healed at 4- and 12-weeks with standard of care. A ratio of these percentages allowed for the percentage of the population healed at 12 weeks to be estimated from the population healed at 4 weeks and vice versa. This healing curve relates to all VLUs and not solely infected VLUs. It cannot be applied to solely infected ulcers See Figure 4 and Table 5 in Guest JF, Fuller GW, Vowden P. Venous leg ulcer management in clinical practice in the UK: costs and outcomes. Int Wound J 2017; doi: 10.1111/iwj.12814 . For example, agents that are prescribed for 12 weeks, such as honey, had a 12-week rate of healing applied. Agents that are prescribed for 4 weeks, such as silver, had a 4-week rate of healing applied. Has the EAG allowed for infected unhealed ulcers to transition to non-infected unhealed ulcers? The time it takes for this transition should be subtracted from the healing curve. Using this transition time, the EAG should have generated a new healing curve specifically for ulcers that are initially infectedSee Figure 4 and Table 5 Guest	Upon review of Figure 4, it was observed that the ratio of the hazards for infected and non-infected leg ulcers remained constant over time. Therefore, the conversion ratio between 4 and 12 weeks was not expected to differ. An additional scenario analysis was performed in which the intercept was halved to align with the infected time-to-healed curve (i.e. 11% healed at 4 weeks)

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				JF, Fuller G, Vowden P. Venous leg ulcer management in clinical practice in the UK: costs and outcomes. Int Wound J 2017; doi: 10.1111/iwj.12814	
120.	Convatec		7.2.3.2 Time to infection resolution	"To allow for rate of infection resolution to differ by agent, it was necessary to assume the rate of infection resolution was proportional to the rate of healing, because of the lack of evidence" I don't think this is a rational assumption and I'm not aware of any evidence to support this	The EAG acknowledged the limitations in this assumption in the report. A relationship between infection resolution and healing rate was deemed appropriate by the EAG and clinical opinion. Additional scenarios have been performed to test this assumption further, see Table 7.26.
121.	Convatec		7.2.3.2 Time to infection resolution	"Gago et al (2008) reported that 36% of the population had completely healed at 8 weeks (Gago et al. 2008). Using a conversion ratio (derived as per the methods in Section **Error! Reference source not found.**), the EAG estimated that 26% of the population had completely healed at 4 weeks. This estimate was used to derive a per-week healing rate from 0 to 4 weeks. " At 4 weeks I would expect around 10% of infected ulcers to have healed. For an indication, see see Figure 4 Guest JF, Fuller GW, Vowden P. Venous leg ulcer management in clinical practice in the UK: costs and outcomes. Int Wound J 2017; doi: 10.1111/iwj.12814	The Guest et al (2018) paper did not report the time to infection resolution, which was required for the calculation. There was a lack of evidence informing the time to infection resolution and the per-week healing rate.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
122.	Convatec		7.2.3.2 Time to infection resolution	"The ratio of the per-week infection resolution and per-week healing rates from 0 to 4 weeks was subsequently calculated as 3.85 using the aforementioned estimates from Gago et al (2008) (Gago et al. 2008)." This is not a valid ratio for reasons already covered	See earlier responses to comments.
123.	Convatec		Table 7.3	"Miller reported the healing rate at 4 and 12 weeks in a large, UK RCT. It is expected that the healing rate at 12 weeks is smaller than 4 weeks. This trend was not observed in Miller et al (with an increased healing rate at 12 weeks). Therefore, the 4 week input was used in the model. " The Miller article is confusing. However, while ANCOVA found no significant difference between the treatment groups in the overall wound healing rate the healing rate for the silver group was significantly higher than the healing rate for the iodine group in the first two weeks. This indicates that overall time to healing was shorter in the silver group. Did EAG consider this?	For consistency with other available evidence, the 4- and 12-week healing rates were used.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
124.	Convatec		Table 7.3	"Treadwell et al did not explicitly state whether this population of hard to heal leg ulcers were infected and the percentage healed at 4 weeks was larger than other studies for other agents. " The study comprised 25 patients with acute and chronic hard to heal wounds which included non-healing postoperative wounds, chronic traumatic wounds, venous leg ulcers, and diabetic foot ulcers. Results are not granular and its questionable how EAG could have used this data	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
125.	Convatec		7.2.3.3 Recurrence of infection	"In the absence of data to inform this parameter, it was assumed that there is no recurrence of infection." Not a valid assumption. Infection reoccurs in static ulcers	There was no data to inform this, however, multiple scenario analyses were performed in which reoccurrence of infection was assumed.
126.	Convatec		Table 7.5	(Guest et al. 2018) These healing rates do not pertain to infected wounds. Need to see Figure 5	See comment 119.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
127.	Convatec		Table 7.5	"The percentage of the cohort discontinuing for personal preference or treatment-related adverse events was informed, where data was available, by the clinical trials from which the efficacy data was sourced. However, only 3 trials reported the percentage of the population who discontinued, therefore, where this data was missing, it was assumed that per-week discontinuation for adverse events was assumed to be 0. This data is presented in **Error! Reference source not found.**." The effect of changing this assumption should be tested in sensitivity analysis.	And additional scenario analysis investigating discontinuation was performed.
128.	Convatec		Table 7.6	These studies should have been used to plot a line of best fit for the rate of discontinuation over 12 months	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
129.	Convatec		7.2.4.1	Cost of AMDs: "Option 3 was considered most appropriate because it allowed for even distribution of the market share across AMDs and ensured that AMDs with data will always have a larger weight than those without data, as, if these did not appear in the CPRD data, it is reasonable to assume they are used less frequently Was sensitivity analysis performed using options 1 and 2?	No, scenario analysis was conducted using the minimum and maximum costs. However, the weighted average cost using each method was derived. These costs are presented in the screenshot below (in pence). The third option was a midpoint of the three methods. The largest difference observed was for PHMB, which was not modelled because of a lack of appropriate evidence for the economic model.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					
130.	Convatec		7.2.4.2 Table 7.8	Frequency of dressing application: “It was assumed that the cohort in the “infected, unhealed” health state would experience more dressing changes than those in the “non-infected, unhealed” health state.” The cohort in the non-infected static state would experience more dressings than those in the non-infected improved health state The values used in the base case of the model are summarised in **Error! Reference source not found.**. The Meaume article is a prophylactic study not a therapeutic study and 28% of the patients had a category 3 or 4 pressure ulcer not a VLU - so not an appropriate study to have used. None of the wounds were infected at baseline.	Number of dressing changes is explored in sensitivity analysis. Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
131.	Convatec		7.2.4.3 Unhealed pressure	Given that these data consisted of a mixed population, it was assumed that the same resource use was applicable	A scenario analysis was done which considered a larger cost for the ‘infected, unhealed wound’ health state.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			ulcer resource	to both the infected, unhealed and the non-infected, unhealed health state Not a valid assumption	
132.	Convatec		Table 7.9	£12.81for all compression This cost seems rather low	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
133.	Convatec			Guest et al (2018) reported that those with an unhealed ulcer cost 4.5 times more than those with a healed ulcer (Guest et al. 2018). Therefore, data from Guest et al (2023) was used for the model to derive a health state cost for people with an unhealed ulcer (Guest and Fuller 2023). A multiplier of (1/4.5) was applied to derive the cost for a “healed” leg ulcer. Once an ulcer heals it is zero cost	Thank you for your comment. A scenario has been performed assuming £0 for the healed wound health state.
134.	Convatec		Table 7.11	Health state costs Infected unhealed wound £205.68 Non infected unhealed wound Healed £45.71 The cost for these two unhealed states should not be the same. Infected wounds cost more to manage	Thank you for your comment. A scenario analysis has been conducted with a healed health state cost of £0

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Healed would should be zero cost	
135.	Convatec		7.3.1.1 base case	**Error! Reference source not found.**. All results were discounted at 3.5% annually for costs and QALYs as per the NICE reference case. “ Results should be presented with and without discounting	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
136.	Convatec		Table 7.15	Results are confounded by using data pertaining to non-infected wounds	This is acknowledged by the EAG in the limitations section.
137.	Convatec		Table 7.16	**Mean (95% confidence interval) pairwise analysis (compared to iodine)** Where are the time to infection resolution and time to heal results for each dressing?	Please see Table 7.18
138.	Convatec		7.3.1.2 Deterministic base case	“The model assumes time to infection resolution is proportional to the healing rate. Therefore, dressings containing agents with a slower healing rate spend more time in the ‘infected, unhealed’ health state and, therefore, have higher costs than other agents. The agents associated with the highest cost were honey and PHMB. This suggests time spent in the infection health state is a key driver of costs.” Invalid assumption as mentioned earlier. The effect of changing this assumption should be shown in sensitivity analysis “**Error! Reference source not found.** displays the discounted, patient-level, deterministic costs over 1 year, for each health state and agent. The largest proportion of total costs were attributable to the ‘non-infected unhealed wound’ health state, which contributed to between 62%	Additional scenarios have been added to explore this assumption further, see Table 7.26.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				(for PHMB) to 71% (copper) of the total costs. Comparatively, the 'infected unhealed wound' health state contributed to between 8% (copper) and 22% (PHMB) and the 'healed wound' health state to between 11% (PHMB) and 19% (iodine) of the total costs. AMD costs provided the smallest contribution to total costs, of between 3% (iodine) and 6% (silver). As mentioned earlier this is a conflation of two states Healed state should be zero cost	
139.	Convatec		Table 7.17	**Discounted, patient-level, deterministic fully incremental analysis over 1 year** Time to heal and time to infection resolution should be presented in an outcomes table	This is presented Table 7.18
140.	Convatec		Table 7.19	**Discounted, patient-level, deterministic life years over 1 year** Why is there any difference in life years since the background mortality rate has been assumed to be unaffected by a wound	This is the time spent in each health state. The sum of a row will add up to the total life years.
141.	Convatec		Table 7.23	**Probabilistic pairwise analysis of silver sub-agents, mean (95% CI)** If there is no difference in QALYs then how was an ICER generated? Surely this is just cost minimisation	QALYs were reported to 2 decimal places.
142.	Convatec		7.3.4	Scenario Analysis: "When the prescription times became equivalent, copper became the referent treatment. This is because copper is a relatively low costing agent, and the healing rate is higher compared with the other healing rates informing the model from clinical data available to inform the model. It is important to note that clinical experts	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				raised a question over whether copper could be prescribed for longer than the 4-week period used in the model. “ What is meant by this term in the context of wound care?	
143.	Convatec		7.3.4	“ Up-to-date resource use studies reflecting post-pandemic care are required to improve the accuracy of cost estimations. It is particularly important for this data to be disaggregated by health state to allow for a more detailed and accurate cost analysis.” Anecdotal evidence suggests that post-pandemic dressings are being changed less frequently in clinics and there is an increase in self-care or care provided by family members or other informal carers What is the effect of this in a scenario analysis?	Scenario analysis around the number of dressing changes was conducted. Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
144.	Convatec		7.3.5	**Summary and interpretation of the economic evidence** The probabilistic base case analysis shows a large overlap between confidence intervals in the utilities and the costs (Section **Error! Reference source not found.**). Could this be because the structure of the model is intrinsically flawed by combining two distinct health states? The model showed that a longer prescription time allowed for a prolonged treatment effect of the AMD. Therefore, the cohort was able to progress to the healed health state faster Any ulcer has to transition to an improved health state before transitioning to a healed health state	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
145.	Convatec		7.3.5	"Therefore, this parameter that may be important to consider when assessing the merits of AMDs." This is a paradoxical statement. If an infected wound has not resolved in a timely fashion, it is best to switch to a different AMD and not continue with the same dressing for a longer period.	Clinicians highlighted that people often experience a sequence of AMDs. The EAG acknowledged the limitations of including sequencing in the limitations.
146.	Convatec		7.3.5	One clinical expert noted that they believed a copper dressing could be worn for a longer period than the 4 weeks used in the base case model. Is there any evidence for this? See my earlier comment about switching AMDs	Clinical expert opinion is used to inform parameters when published studies are not available.
147.	Convatec		7.3.6	**Limitations "**. One clinical expert highlighted that healing is slower for arterial leg ulcers and mixed arterial and venous leg ulcers than pure venous leg ulcers. Healing rates definitely differ between different wound types	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
148.	Convatec		7.3.6	**Limitations:** Subgroup analysis on the size, location and length of time the ulcer had persisted were not consistently available in literature. Cannot apply efficacy data on diabetic foot ulcers to venous leg ulcers and vice versa for reasons explained previously	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
149.	Convatec		8.2	**Discussion** "The modelling demonstrated that the largest proportion of costs incurred in the management of leg ulcers in this population was attributable to the 'infected unhealed wound' and the 'non-infected unhealed wound' health state (**Error! Reference source not found.**). Therefore, interventions and technologies that can reduce	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				the amount of time spent in the 'infected unhealed wound' and provide a sustained treatment effect in the non-infected unhealed wound' health state (if best practice is assumed) may have substantial scope to reduce their total cost of treatment" This paragraph does not reflect the ulcer pathway. Infected ulcers once ameliorated would transition to either a static unhealed state or an improved unhealed state. A large proportion of ulcers in the static state will remain there indefinitely. Many ulcers in the improved state will heal	
150.	Convatec		9	**Conclusion:** The results from the model are misleading because (1) the model is structurally flawed, (2) outcomes form non-infected ulcers were applied to infected ulcers, (3) data from ulcers types not included in the model was utilised and (4) different ulcer types were combined into one model which is unable to inform clinical decision making. Ultimately, the decision problem does not reflect the challenges of clinical practice	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
151.	BBraun	19	Table 2-3	Prontosan Gel and Prontosan Gel X should not be included as they are not an antimicrobial dressing. Prontosan Gels are not within the scope of this LSA, i.e. not an intervention listed in table 1-1. Prontosan Gel & Gel X are betaine surfactant **wound cleansing gels** with PHMB (0.1%, lower concentration than PHMB antimicrobial dressings) and indicated for non-infected and infected wounds (see IFUs section 1 & 2). The primary purpose of Prontosan Gel is for wound bed preparation (section 3), not treatment of wound infection. Several clinical experts listed on the panel have direct experience of Prontosan and are aware it is not a treatment for infection; the absence of a Betaine and PHMB gel category in table 2.2 confirms this. (Please also refer to page 312 clinical evidence, Prontosan Gel and Gel X clinical trial recruitment is for non-infected ulcers)	Prontosan wound Gel X is listed as a hydrogel dressing on part IXa of the drug tariff. Hydrogel dressings containing PHMB are in scope. No further change to report has been made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
152.	BBraun	600	11.8 Appendix H	Acknowledging the issues with inaccurate records in CPRD (20% of market share missing), this has produced a market share of 0.01% for Calgitrol Paste 100g, this is inaccurate as this product has not been supplied to any NHS routes to enable it to appear within CPRD data during this date range and should be taken out of the cost weighting for silvers as a high volume (multi-use) primary dressing.	No change has been made to the report because no evidence has been provided to substantiate this comment.
153.	BBraun	172	Table 7-7	These costs are not weighted appropriately to reflect clinical use. The weighted average has not taken into consideration the multi-use element of some antimicrobials. For example, honey ointments and gels are multiuse, silver-alginate paste can be recapped and reused over several dressing changes. PHMB appears to be affected by Prontosan Gels being incorrectly included (also not accounting for the 8-week opening time and multiuse). A paste or gel (primary dressing) can be used over several dressing changes, meaning a tube will have a 'per dressing-change cost' specific to each patient. The '**per dressing-change cost**' is more accurate than a 'per dressing cost' when comparing to individual single-use (secondary) dressings; for example, a paste may cost £6 and be used twice, a secondary dressing may cost £4 and can only be used once; yet across 2 dressing changes the total cost is £6 for the (primary dressing) paste and £8 for the (secondary, single-use) dressing. We believe this may also be impacting the market share, with 11.8 appendix H showing lower market share than anticipated for multi-use dressings, gels and ointments etc. (share of prescriptions/requisitions being reported on rather than share of **use during dressing changes**, which is difficult to determine from CPRD data as a product may only be included in the notes when it is ordered, not every time it is used).	The EAG acknowledged the limitations of the CPRD data to inform market share. However, it was thought to be more appropriate and a simple, non-weighted average. The scenario analysis considered maximum and minimum cost.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
154.	BBraun	172	Table 7-7	For PHMB: Please note that the higher limit of £34.13 is the price for a 250g product, intended for larger wounds with an 8-week product shelf life after opening; Cooper et al (doi: 10.1016/j.jtv.2023.03.001) estimates a monthly use which is much lower than calculated in the economic model, clinical case studies indicate around £2.08 per use in VLUs 15x15cm. The weighted average is therefore inaccurately skewed for PHMB as a result of this lack of accounting for multi-use, higher volume primary dressings.	A scenario with the minimum cost of dressing containing agent has been conducted.
155.	BBraun	171	7.2.4.1, paragraph 2	CPRD data not capturing community data is problematic. Some geographical areas use off-prescription dispensing models which will not capture prescriptions, and therefore market share will not be accurately represented with this method of antimicrobial dressing supply not being accounted for. For example, one region may use 90% of their dressings through an off-prescription model and therefore only 10% are prescribed and captured in CPRD data; another region may only use prescription routes of supply which would be better represented within the CPRD data, introducing a geographical bias and not capturing the market share accurately when regional formularies are taken into account. The majority of dressing changes are handled within community (Guest 2020), it is imperative that this data is used to inform the market share for use in the economic modelling – it will also inform accurately the use of multi-use primary dressings (i.e. how many dressing-changes a multi-use antimicrobial has been used for). Data we have available to us suggests that up to **63%** of the wound care products we supply are being dispensed through **non-prescription routes in community**, this is highly likely to be reflective of the market as a whole and therefore we question whether a database missing more than half of the usage of antimicrobials is fit for purpose.	CPRD was used as this is a large dataset which was readily available for the analysis. No change to report has been made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
156.	BBraun	173	7.2.4.2, paragraph 3	Use of the study 'Meaume 2005' to derive a multiplier for infected wound dressing wear time is not wholly appropriate. This study includes Pressure Ulcers, which were an exclusion criterion for clinical evidence. This is outside of the scope and should not inform leg ulcer dressing change within the economic model.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
157.	BBraun	174	Table 7-8	The wear time assumptions are not accurate and based on weak sources of information, clinical and manufacturer input should have been sought here. For example, iodine has a manufacturer-suggested usage of up to two dressings per day, making 4.17 dressing changes per week too low. The CPRD data should have been analysed to determine this.	Wear time assumptions were tested in the scenario analysis.
158.	BBraun	184	Table 7-11	Infected unhealed wounds and non-infected unhealed wounds do not cost the same to manage; an infected VLU can cost £10,285 compared to an uninfected VLU which is reported as costing £3,328 (table 5 Guest, Fuller, Vowden 2017 doi: 10.1111/iwj.12814). Harding, Posnett and Vowden also break down resource use by health state of ulcers which could be informative here (doi: 10.1111/iwj.12006).	It is important to note that an assumption around this was tested in the scenario analysis. There were no differences to the overall results when the resource use requirements in the infected, unhealed health state were larger.
159.	BBraun	195	Table 7-15	Considering all issues raised with market share, clinical relevance, clinical-use weightings and health state errors this table should be omitted or redacted until accurate information is input into the economic model. The EAG state that there is no conclusion over one agent being more beneficial over another due to the evidence available, however 7-15 gives the impression that a conclusion has been drawn and may be misinterpreted as conclusive or informative if available to the public.	Clarification has been added at the start of the report in the results section.
160.	Urgo	10	Quality & relevance of the economic evidence	Healing as a primary end point is not representative of best practice. The purpose of an antimicrobial is to treat local infection. Efficacy and cost effectiveness cannot be correctly measured if the dressings are assumed to be	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				used inappropriately, this inappropriate use will result in higher cost.	
161.	Urgo	10	Quality & relevance of the economic evidence	The final scope shows the intermediate outcomes as 'reduction in signs of local infection'. Evidence submitted by Urgo Limited demonstrates this however, the evidence submitted has been excluded.	See response to comment 163 and 164.
162.	Urgo	13	Outcome s	Healing (wound healing and **infection resolution**). The Modelling used and evidence base focusses on wound healing. Infection resolution is the most appropriate modelling for an AMD.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
163.	Urgo	30	4.2 Included and excluded studies	RCT (JWC_21_2_96_102_Lazareth) submitted by Urgo Limited was excluded. This RCT met the population requirements (venous leg ulcers), the intermediate outcomes (reduction in signs of local infection, change to wound bed condition) and demonstrated time to healing and complete wound healing.	Thank you for your comment. This RCT was excluded because the study participant criteria excluded patients with clinically infected wounds and was thus outside the NICE scope.
164.	Urgo	32-64		Urgo Medical submitted several clinical studies including an RCT and an extremely large observational study. None of this evidence is included and it is unclear how this clinical evidence did not meet requirements.	We believe this comment may refer to the following studies: Lazareth et al 2008 (RCT) Dalac et al 2016 (observational study) Meaume et al 2014 (EARTH trial, RCT) Meaume et al 2012 (TLC-NOSF trial, RCT) And/or the following studies: Lutzkendorf et al 2022 (observational study) Dissemond et al 2020 (observational study) The former were excluded because they excluded participants with clinically infected wounds or only a minority of patients had infected wounds at baseline. The latter were excluded because they included mixed wound

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					types and did not report results separately for the relevant leg ulcer subgroup.
165.	Urgo	26		Biofilm is recognised to have significant impact on wounds with local infection. While it can be difficult to measure in a clinical rather than lab setting, there is an overwhelming number of clinical publications in favour of biofilm-based woundcare so this should perhaps be noted in a more significant way in the report.	Thank you for your comment. As noted in the report, biofilm was out of scope.
166.	Urgo	132	5.5.1.12	'Based on the available data, all the assessment AMD's appear to be safe.'' Following a Medical Device Regulation (MDR), changes to the indications and contra-indications for Inadine have been updated. **Contraindications:** Inadine dressing should not be used: • where there is a known iodine hypersensitivity (allergy) • before and after the use of radio-iodine (until permanent heal • if you are being treated for kidney problems • in pregnant and breast-feeding women • in cases of Duhring's herpetiform dermatitis (a specific, rare s • in patients with any thyroid diseases as povidone iodine may **Warnings / Precautions:** Inadine dressing must be used under medical supervision • in new-born babies and infants to the age of 6 months as pov through unbroken skin • to treat deep ulcerative wounds, burns or large injuries. Medical supervision should be sought if using Inadine dressing fo Do not reuse. Reuse may result in infection or cross contaminatio 11.3% of males and 1535% of females aged 65 – 74 are expected to have stage 3 – 5 CKD (chronic kidney disease), rising to 28.1% (males) and 35.9% (females) aged 75 and over (Public Health England, Chronic kidney disease prevalence model)	Thank you for your comment, this is useful information and we have added a note of it to the safety section and discussion.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				~50% of people 75 and over meet criteria for chronic kidney disease (*BMJ* 2016;352:h6559) Thyroid disease is more common in females and hypothyroidism is found in more than than 5% of people aged over 60 (NG145). Venous leg Ulcers account for 60 – 80% of leg ulcers with prevalence for all leg ulcers increasing with age. Risk factors for developing venous leg ulcers include increasing age and female sex (NICE, CKS, Leg Ulcer). With contraindications for Inadine including kidney disease and thyroid disorders, both of whiocvh have increased prevalence in increasing age and female sex, the 'assumed' safe statement is incorrect.	
167.	Urgo	194	7.3.1.1	''The fully incremental analysis ranked iodine as the agent that would generate the smallest costs per person''. Iodine has clear contra-indications that negate its use in people with renal or thyroid disease. Has this population cohort, been excluded and therefore taken into account in the cost?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
168.	Urgo	194	7.3.1.1	''The fully incremental analysis…''. Iodine requires secondary dressings and/or fixation to enable management of the infected wound (absorption) and to keep iodine in place. Have these additional incremental costs been included in the cost modelling?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
169.	Urgo	194	7.3.1.1	''The fully incremental analysis'' uses the weighted mean average to compare AMD's. AMD foams in particular have a large selection of sizes. The weighted mean average calculation, therefore, provides a higher cost for silver foams dressings. The most common used AMD foam size is 10 x 10cm. The weighted mean average should be	The weighted average uses CPRD data on market shares to weight the specific products, see Appendix H. As CPRD is the best available real world data on the usage of AMD products we consider this to be the most robust approach to costing the AMDs. The sizing of 10 x 10 being

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				based on a standard size with outliers removed to provide a more robust pricing comparison. Both above, if included, will reduce the costs per person for iodine making it more representative of the true costs per person and more robust comparison for other AMD products.	the most common is represented in the cost due to the weighting.
170.	Urgo	228	Table 7-26	Due to the vast range of sizes for silver dressings and based on the clinical need for AMD's to provide management of wound symptoms (exudate absorption etc.), the larger sizes available should be considered as outliers. Comparisons of pricing on the most commonly used sixes (10 c 10cm and equivalents) would provide a more accurate representation of pricing variances.	The weighted average uses CPRD data on market shares to weight the specific products, see Appendix H. As CPRD is the best available real world data on the usage of AMD products we consider this to be the most robust approach to costing the AMDs. The sizing of 10 x 10 being the most common is represented in the cost due to the weighting.
171.	Urgo	248	8.2	''Prescription time and efficacy were key parameters that could be considered''. Additional dressings used such as secondary dressings and/or retention dressings should be considered to determine the total cost.	Comment is not a factual inaccuracy, no change to report has been made.
172.	Urgo	All		There is no reference or methodology to include/exclude compression therapy within the scope of healing for infected leg ulcers. For mixed and venous, compression therapy increases healing ulcer rates. An AMD used without compression therapy in a mixed or venous aetiology leg ulcer, may not heal due to: 1. AMD's are not designed for wound healing but to resolve/remove a localised wound infection AMD use without compression therapy may not heal despite the AMD removing/resolving the localised wound infection	Comment is not a factual inaccuracy, no change to report has been made. Variation in secondary dressings has been noted in section 5.3.
173.	Coloplast	General Comment	All	We are committed to working with NICE on this late-stage assessment and we thank the EAG for its careful assessment of the evidence. Although we understand this is outside the scope of the current fact check step, we urge NICE to reconsider the value to clinicians, patients, and wider NHS policy of continuing with this LSA in its current	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				scope and methodology. NICE aims to be transforming its programmes to produce more usable guidance however, although none are yet complete, all LSA evidence assessments so far available are inconclusive, and so very unlikely to enable decision-making to develop practical guidance with beneficial impact. As we have consistently commented, Coloplast as a company would prefer to work with NICE and other stakeholders to further develop the methodology for late-stage assessment to enable more useful and usable outputs. We have previously argued in this and other LSAs that the categorisation of features is not a suitable or safe method for assessment of the evidence base developed by companies when introducing incremental innovations, because the performance of the given proprietary dressing should be evaluated as a whole, not by disaggregating individual features. In this assessment there is a particular issue with grouping of silver-based products and assuming that they are generalisable across sub-agents without consideration of their mode of action. There is difference impacting cost across agents therefore excluding type particularly around the need for a secondary dressing is not representative of products indication for use, clinical practice and introduces bias into the results.	
174.	Coloplast	General Comment	All	The Economic Model and Report have been reviewed by an independent health economist. Full details of the health economists' reflections can be found in our economic model comments table, however, to summarise the main areas of factual inaccuracies are: - Not all available evidence has been adequately used within the assumptions and modelling - Given the importance of assumptions about efficacy, none of the scenarios adequately tests these assumptions.	Additional efficacy scenarios have been explored.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				We look forward to receiving the EAGs feedback on the model specific comments.	
175.	Coloplast	11	Executive summary	We thank the EAG for its carefully developed considerations in the recommendations for future evidence covered in detail in section 9.1 and are committed to initiatives to improve the evidence base in this important clinical area. Companies would welcome input from NICE and propose a collaborative protocol development for future evidence generation.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
176.	Coloplast	13	Table 1-1	On p13, the EAG's comments/variation to the NICE decision problem states: "The comparator is the referent agent (the agent that is the most cost-effective compared to the others)." Although the report describes many comparative studies, we have found no further reference in the critiques to the dressing that the EAG considered to be current standard of care in the NHS (based on either clinical expert advice, clinical evidence, or cost-effectiveness). Please can this be clarified.	
177.	Coloplast	14	Table 1-1	The report states: 'The assessment will not include evidence on leg ulcers at risk of infection because the outcome measures would be different'. Can you please explain the rationale to therefore include studies of non-infected leg ulcers given this, as the outcome measures for this cohort of patients should also be considered different and so the 2 approaches are factually inconsistent. Non-infected wounds are likely to heal faster as the healing process is not stalled by the infection. Therefore, comparing outcomes between infected and non-infected leg ulcers introduces bias.	Thank you for your comment. As discussed in the methods section, broader evidence was sought where evidence that fully met the PICO was not available. This was decided on an agent-by-agent basis. The limitations in this approach have been noted in the discussion.
178.	Coloplast	14	2.1	Error in first sentence: Topical AMDs deliver antimicrobial agents to the wound/wound bed, not the 'skin. The active ingredient is released in response to wound exudate.	Thank you for alerting us to this, this has been corrected

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
179.	Coloplast	14	2.1	General comment regarding the sentence 'Therefore, AMDs can be considered in the treatment of local wound infections'. Please note that topical AMDs can also be considered in the treatment of wounds with confirmed or suspected biofilm, and for use in conjunction with systemic antibiotics as recommended by the IWII.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
180.	Coloplast	15	Table 2-1	Factual errors in categories and types of dressing overview. Please note: - Alginate and gelling fibre dressings are not recommended for low exuding wounds as outlined. They are indicated for wounds with moderate to high levels of exudate. These products are at risk of sticking to the wound bed if used in low exuding wounds, causing potential harm to the patient. - Foams are generally indicated for low-highly exuding wounds. - Hydrogels and ribbons (for example) require a secondary dressing to help keep the product in place, support with exudate management and to provide a bacteria and waterproof layer over the wound. - Some foams can conform to the wound bed up to 2cm in depth, meaning they are also suitable for use in 'deeper' wounds (depending on the definition of deeper wounds used). - Alginates and gelling fibers will also aid autolytic debridement and are often used for this treatment objective. This information can be found within manufacturer's instructions for use.	Re: "low" exuding wounds, thank you for noting this – this is an error and has been corrected. The dressing categories were developed by NICE based on clinical input, the BNF and a framework supplied to by the SDMA. The indications outlined in the first column of table 2.1 are generalisations and not intended to be exhaustive or prescriptive of the use of each type of dressing. No further changes to the report have been made.
181.	Coloplast	18	2.4	Please can the respective specialisms of the professional experts consulted to devise the sub-agent categorisation be published? This method is pivotal to the subsequent evidence assessment and so stakeholders require	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				assurance that there was suitable expertise on leg ulcer and antimicrobial use.	
182.	Coloplast	22	Table 2-3	Coloplast products are listed as 'silver salts and compounds' in the report but as 'silver with anti-biofilm mechanism' elsewhere in the report and model (data library tab). Please can the EAG confirm what constitutes anti-biofilm mechanisms so our products can be appropriately categorised. Please note many silver dressings have anti-biofilm mechanisms but do this by means other than a surfactant.	Thank you for your comment, the subagent categorisations used in the report are those developed by IWII and recommended by NICE and the specialist committee members.
183.	Coloplast	25	3	The last sentence on p25 states: "Innovative features, while clinically relevant, are not considered in this assessment due to a paucity of data." Please can the features defined as 'innovative' in this sentence be clarified? If they have clinical relevance, and the evidence identified for the features included in the decision problem is also sparse, then a paucity of data does not just seem to justify their exclusion. It would be helpful for stakeholders if evidence generation recommendations applied to all features with potential added value.	Features of AMD agents that were not listed in the scope were not modelled. The AMD agent is the scope of this analysis
184.	Coloplast	26	3	The report states 'It was decided that biofilms would not be included in this assessment'. Please note evidence suggests over 80% of chronic wounds have a biofilm, therefore it is reasonable to conclude that locally infected wounds often have a biofilm such as the wounds within the included studies. In evidence summary there is reference to silver dressings with anti-biofilm mechanism, can the EAG please therefore explain the relevance of this in relation to biofilm exclusion from the decision problem.	Thank you for your comment. You are correct that infected wounds also often present with biofilm. This sentence refers to the exclusion of wounds with biofilm alone, absent clinical signs of infection.
185.	Coloplast	28	4.1	On p28, the report states: "Information regarding which sub-agents were assessed by the included studies was identified later as part of the data extraction process, following a request from NICE after study selection had been completed. Included studies	Thank you for your comment. The EAG defined 'sufficient evidence' as having identified at least one study fully meeting the decision problem for each agent. Where no studies were found, or only conference abstracts

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				were categorised by sub-agent. No additional studies were included. This means that no evidence was included for some sub-agents because sufficient evidence that fully met the decision problem had already been included for other sub-agents within that agent grouping. Further evidence from broader populations was not sought for missing sub-agents as this was not feasible within the scope and resource available to complete the LSA." Please can the EAG explain how the judgement of 'sufficient evidence' was reached. It seems counter-intuitive to potentially exclude studies that partly meet the decision problem when the fully relevant evidence was inconclusive, and some studies that partly met the decision problem were included. Coloplast understands the rationale for the evidence identification and selection methods set out in sections 4.8 and 4.9 of the interim LSA process and methods statement but believes the post-protocol changes in the sub-agent categorisation may have resulted in non-systematic searching. Coloplast does not believe that the 'scope and resource available to complete the LSA' is an appropriate justification for this.	or posters were identified, or only pilot studies or studies with small sample sizes were found, this constituted insufficient evidence. This was decided on an agent by agent basis. Where no/insufficient studies were identified for a particular agent, the list of studies excluded at full text was reviewed to identify studies that partly met the decision problem, using the method explained in section 4.1: where no evidence in infected leg ulcers was available, evidence in infected wounds of other kinds was included; where this was unavailable, evidence of non-infected (or unclear infection status) lower leg ulcers was included. Following the finalisation of this process, 412 records remained excluded at full text. The research effort to review all 412 records to identify evidence for additional sub-agents would be substantial, and was not something that could be prioritised within the time available to complete this pragmatic review. The decision to proceed with this approach was a pragmatic one, to enable a summary of evidence at the sub-agent level to be presented to the committee, using the resources available in order to enable completion of the review. We have noted as a limitation that searches were not designed for these broader patient populations, and thus may not have identified more relevant studies in these populations.
186.	Coloplast	28	4.1	Inclusion approach query: The EAG broadened the study inclusion criteria to consider studies which only partly met the decision problem in terms	Thank you for your comment. The identification of studies conducted in broader populations was conducted systematically – the phrase 'in-

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				of eligible populations – such as those with infected ulcers other than between the knee and ankle, and those with non-infected ulcers. However, on p28, the report states: "Any studies in a broader population were identified from the search results 'in passing', and no additional search to reflect the broader population was conducted." Please clarify what additional checks were done to ensure that important, relevant evidence was not missed by the non-systematic 'in-passing' approach to identifying the partly met studies, especially in light of the inconclusive nature of the evidence which fully met the decision problem.	passing' did not refer to non-systematic checking, and we have edited the report for clarity. Our method was to search through all records deemed ineligible at full text phase, that had been identified by the EAG's literature search and the records submitted in company RFIs. As described, this search was designed to identify studies assessing the decision problem and so was not specifically designed to identify studies not meeting the decision problem, such as those evaluating non-infected leg ulcers or other wound types. Had the EAG limited evidence to studies addressing NICE's decision problem, then there would have been little evidence to present to this LSA's committee. The decision to search using existing records available (and not to conduct a new literature search aimed at identifying studies undertaken in broader populations) was a pragmatic one to enable the most relevant evidence to be presented to the committee, using the resources available. This approach was agreed between NICE and the EAG. We have noted as a limitation that searches were not designed for these broader patient populations, and thus may not have identified more relevant studies in these populations.
187.	Coloplast	29	4.1	Studies were evidenced in our RFI response that do not appear to have not been included in either the analysis or Appendix B with a rationale for their exclusion – Wang, Lazaro and Scanlon. Can you please confirm why these studies that partially meet the decision problem are not referenced at all in the report.	Thank you for your comment. As you note, these studies *partly* meet the decision problem (Wang and Lazaro included patients with diabetic foot ulcers, and Scanlon considered patients with delayed healing though not necessarily infected leg ulcers). As noted in the methods, wider evidence was sought when no evidence meeting

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					the decision problem had been identified for a particular agent. These studies evaluated silver AMDs, for which evidence meeting the decision problem had already been identified (including evidence for Biatain Ag), thus further studies that only partially met the scope were not sought for silver AMDs.
188.	Coloplast	29	4.1	Physiotulle Ag is a contact layer not a hydrocolloid.	Thank you for alerting us to this, this has been corrected
189.	Coloplast	30	4.2	Please can the report clarify whether investigators or companies were contacted to check when findings on the ongoing studies in Appendix E would be available, given that 3 of the 4 were registered or protocols published in 2017, 2019 and 2020?	The EAG did not check this, but no relevant published studies relating to these ongoing studies were identified from the EAG literature searches. .
190.	Coloplast	88	5.4.1	An AMD is designed to resolve infection, putting the wound on a positive healing trajectory, but are not solely responsible for healing outcomes in clinical practice. We therefore question the weighting given to healing outcomes within the model, without consideration for other non-AMD contributions towards healing. Infection resolution is a more clinically appropriate end point for measurement of efficacy. If the EAG maintains wound healing as the primary efficacy measure, please consider the following input: The report states “7 comparative studies reported healing outcomes, of which 5 fully met the decision problem (Dimakakos et al 2009, Miller et al. 2010, Meaume et al. 2005, Molle et al.2023, Gago et al. 2028”. Please explain why the results from larger, comparative studies were not considered in the assumptions on healing	See response to Comment 6

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				rates in the economic model. Instead, the results of a small single arm study including 14 patients was chosen as the only reference for the healing assumption for silver (Forlee et al. 2014). It is unclear why other comparative studies relevant for ionic silver complex such as e.g. Dimakakos et al 2009 were not considered. Given that this parameter has a significant impact on the model outcomes, a meta-analysis of the results of all the studies that met the decision problem on healing outcomes should have been considered for each agent group.	
191.	Coloplast	89	5.4.1	The report states '1 study compared 2 ionic silver dressings (Acticoat and Aquacel Ag) and 1 ionic silver complex dressing (Comfeel/Biatain Ag) (n=25 in each arm) (Gago et al. 2008), finding statistically faster complete healing with Acticoat ionic silver compared to ionic silver Aquacel and ionic silver complex Comfeel/Biatain Ag'. We believe this is an incorrect interpretation of the study. Group two actually includes two different silver products Comfeel Ag, a hydrocolloid dressing for wounds with minimal exudate, and Biatain Ag, a polyurethane foam for wounds with moderate to high exudate levels which is clinically relevant and could lead to differences in healing rate. Please can the EAG re-review the evidence and their assumptions considering this.	Thank you for alerting us to this, we have edited this sentence to correct this.
192.	Coloplast	149	Table 7.2	The report states: 'The cohort remains on AMDs in the non-infected, unhealed wound health state". Please can you explain the rationale for this choice, since the EAG acknowledge that this is not best practice. Best practice is to discontinue AMDs once infection has resolved.	Thanks for the comment. The rationale for this is provided in the adjacent column of the same table. No change made to the report.
193.	Coloplast	155	Table 7.2	As with assumptions about ulcer healing, the EAG have provided no explanation of why "it was necessary to assume the rate of infection resolution was proportional to the rate of healing, because of lack of evidence.' The	Scenario analysis around infection resolution and healing rate has been conducted.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				clinical review identified 9 studies which reported evidence on the rate on infection resolution. Can you please provide an explanation of why this data was not used.	
194.	Coloplast	156	7.2.3.2	The healing rate for silver input was taken from Forlee et al 2014 which included a very small group of patients (14pts): 21,6% at 4 weeks. For example, the Dimakakos et al 2009 reported a healing rate at 9 weeks of 81% in the group treated with silver products compared to 48% in the non-silver group. Can you please confirm why the Forlee study was selected as the only input to the healing rate assumption in the model, when multiple silver studies were available that fully met the decision problem. No justification has been provided for this in the report.	See response to comment 6
195.	Coloplast	157	Table 7-3	Studies selected to inform the time to per-week healing rate: The infection status of the wounds enrolled in studies vary from “infected” to “hard to heal acute and chronic wounds”. We would highly recommend selecting studies that report healing outcomes on leg ulcers with similar infection status in order not to compare wounds that have different healing potential based on large differences in infection status.	
196.	Coloplast	157	Table 7-3	The studies selected to inform the time to per-week healing rate differ significantly in study type and sample size. Basing an important input on time to per-week healing rates on very small sample size for each agent type introduces a high level of uncertainty and bias as it is unknown whether the patients included are representative for patients with infected leg ulcers in the UK. Potential differences in patient demographics and comorbidities between studies do not seem to have been considered.	Uncertainty and limitations of evidence is described in Table 7-3 for clarity and transparency. This is further highlighted in the discussion of the report. Where possible, scenarios have also been conducted to explore the impact of these on the results. No change made to the report.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Can you please elaborate on how this has been accounted for?	
197.	Coloplast	160	Table 7.4	To determine the maximum time agents are prescribed a user should aways refer to the manufacturer's instructions for use for the individual products rather than using assumptions or reliance on single sources of evidence such as one formulary guide which could be inaccurately informed.	The EAG has used formulary data over manufacturer's instructions to reflect real world clinical practice. The impact of variation in these parameters are also further explored through scenarios and sensitivity analysis. No change made to the report.
198.	Coloplast	174	Table 7-8	Number of dressings required per week: There seems to be a discrepancy in the way that the number of dressings used per week per agent has been calculated. For agents where clinical studies are available (silver, silver salts and compounds) the most conversative reported outcome was used as input to the model, whereas for other agents without clinical evidence, a non-conservative estimate is used based on the guidance on maximum wear time. This favours agents without evidence which seems biased. Can further explanation please be provided.	Thank you for the comment. The use of maximum wear time is, by definition, a conservative approach where no further evidence is available. No change made to the report.
199.	Coloplast	173 & 174	7.2.4.2 & Table 78	Can the EAG confirm how the use of secondary dressings and their wear time are accounted for in the model? The need for secondary and even tertiary products will impact the number of products required per week, and cost. Other assumptions where data is limited have been made within the modelling; yet the need for secondary dressings appears to have been omitted, even though the AMD's that require a secondary dressing for appropriate use is known. Secondary dressings play an important role in exudate management, a key component of infection management, they also act as a bacteria and waterproof layer over the wound. In omitting the cost associated with secondary dressings when a number of the AMDs have a dual role in infection resolution and exudate absorption (acting as both	Costs associated with AMDs are varied to capture impact on the total costs estimated in the model.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				primary and secondary layer dressings) is misrepresentative in favour of primary layer only AMDs. This therefore misrepresents the total cost per treatment and adds bias to the analysis.	
200.	Coloplast	178 & 179	Table 7.9	Coloplast are seeking clarity on resource use parameters: - What is the relevance of including podiatry visits for leg ulcer patients, given the scope of the LSA? - A lack of doppler assessment is reported, however a doppler is best practice as recommended by the National Wound Care Strategy Programme and required for a patient to be safely put into compression. Secondary non-antimicrobial dressings are not reported, but would be used in conjunction with some AMDs, as per the manufacturer's instructions for use.	Podiatry visits were considered relevant as part of the total resource use sourced from Guest et al. This is also only applicable to 2% of the population. Doppler assessment was not considered. Recent data reporting on total resources used within this population, used in the model, did not report resources for Doppler and therefore while the model includes functionality to capture this it is set 0 to reflect published evidence. Paucity of evidence regarding secondary non-AMD use there this was not explicitly captured within the model. No change made to the report.
201.	Coloplast	246	8.1	Can you please confirm who will be involved in the clinical interpretation of the evidence given generalisability is poor. How will their credentials for involvement in this topic be judged?	Not a factual accuracy check, no change made to the report. We will review other comments at consultation stage.
202.	Coloplast	247	8.2	The report states 'Results from the model do not provide enough certainty to allow robust conclusions on the cost-effectiveness of AMDs when used to treat infected leg ulcers'. Due to this fact we presume no guidance /recommendations can be made based on this report alone.	Not a factual accuracy check, no change made to the report. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
203.	Coloplast	249	9.1	The report states 'The EAG recommends that further evidence should be collected to compare the performance of different agents and sub-agents within AMDs. Given that these dressings are in current use within the NHS, observational designs using hospital data may provide pragmatic means of evaluation'. Considering much of the cost of leg ulcer care sits in the community, it would be more relevant to collect clinical data in this healthcare setting.	Not a factual accuracy check, no change made to the report. We will review other comments at consultation stage.
204.	Coloplast	591, 595 & 597	Table 11.8	Please note that the full range of sizes of our products are not listed within the table or model. Can you please explain the rationale for this, as we understood all AMDs listed in Part IX were included.	AMD costs were sourced from Part IX of the Drug Tariff capturing relevant sizes reported, market shares were taken from CPRD data
205.	Coloplast	General Comment	All	Risk of Bias: There is a general issue with paucity of data and data sources used. The grouping of the products and the use of outcomes for one type of silver dressing for example, that seems to be applied to all other types of silver dressings. Very low-level evidence with high bias is used for some products compared to the higher-level, lower bias evidence for silver.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
206.	Coloplast	General Comment	All	These are complex documents and modelling that have been challenging to review in the timespan with available resource. We would like to highlight for future LSAs, given the potential consequences of this type of assessment, that industry requires time and resource to respond appropriately and assess impact. The lack of understanding at an industry level of the intent and use of the outcomes highlighted in Table 7-15 requires far greater transparency.	Not a factual accuracy check, no change made to the report. We will review other comments at consultation stage.
207.	Smith & Nephew	12, 15 and 21	1 2.2 2.4	Table 1-1, Table 2-2 and Table 2-3 We suggest adapting the sub category Cadexomer iodine to Cadexomer iodine with anti biofilm mechanisms. This is in line with sections on pages 27 and 28 of IWII 2022 which refers to	Thank you for your comment, the AMD categorisations were provided by NICE. We have not changed the report per this comment.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Cadexomer iodine as being able to provide the debridement necessary for Biofilm based woundcare.	
208.	Smith & Nephew	13	1	Table 1-1 It is inaccurate to include complete wound healing as an outcome. The primary outcome of resolution of signs and symptoms of infection which are affected by the intervention and comparator in review.	Comment queries the NICE scope and is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
209.	Smith & Nephew	Page 23	2.4	Table 2-3 Smith and Nephew Healthcare Ltd Algisite Ag dressing has been discontinued and is no longer available in UK.	Algisite Ag is listed on part IXa of the drug tariff and was in scope. We have not changed the report.
210.	Smith & Nephew	149	7.2.1	Why would patients with resolved infections continue using AMD? Does this suggest that costs are still being incurred?	Rationale provided in adjacent column of table. No change to report has been made.
211.	Smith & Nephew	151	7.2.1	Treating the costs and utility for infected and uninfected states as the same biases the results against more effective AMDs that resolve infections more quickly. Additionally, this contradicts the assumption in Table 7.2, where infected ulcers require more frequent dressing changes.	This was driven by paucity of evidence and the impact of was assessed through scenario analyses. No change to report has been made.
212.	Smith & Nephew	155	7.2.3.2	Typo- “**the”**	Updated in report.
213.	Smith & Nephew	168	7.2.3.4	Discontinuation only applies to Copper, PHMB, and silver salts and compounds. Is it correct that other AMDs have no discontinuation?	This is incorrect. Two types of discontinuations were considered. Data for discontinuation from AEs was only available for Copper, PHMB and silver salts and compounds. However, the second type of discontinuation (i.e., based on clinical indication, captured as maximum prescription time) was applicable for all AMDs considered in the model. No change to report has been made.
214.	Smith & Nephew	174 and 184	7.2.4.2 and 7.2.4.3	Tables 7-8 and 7-11 seem redundant since there is no difference in costs and utility between infected and uninfected health states	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
215.	Smith & Nephew	177	7.2.4.3	Delete repeated word “**the”**	Updated in report.
216.	Smith & Nephew	185	7.2.5	Assuming equal utility for infected and uninfected health states is an oversimplification. There should be at least some penalty for infection	This was driven by paucity of evidence and was explored through scenario analysis. No change to report has been made.
217.	Smith & Nephew	187 224	7.2.5, 7.3.4	Replace the word “principals” with “principle” for clarity to read for instance the principle of strong dominance or principle of extended dominance- replace this in the document.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
218.	Smith & Nephew	190	7.2.8.2	Why was 20% chosen as the variation? Is there a reference or justification for this choice?	This was based on EAG judgement to explore impact of alternative values. Where 20% variation was used, it was used consistently across all AMDs within each parameter category.
219.	Smith & Nephew	218 and 222	7.3.3.1 7.3.3.2	CEAC results appear to contradict the cost-effective plane despite the ERG’s attempt to explain within-group analysis for silvers and Honey	The cost and efficacy are very similar and sit very close to the threshold. Outliers pull the mean below the threshold, while the majority of the points sit above the threshold. This is explained in more detail in the report.
220.	Smith & Nephew	239	7.3.5	Missing word “AMD” from second last paragraph	Updated in report.
221.	Smith & Nephew	242	7.3.6	Typo word “**and”** second paragraph from the top	Updated in report.
222.	Smith & Nephew	243	7.3.6	Honey studies included DFU patients, but most of the leg ulcers in the review were VLUs. Did I miss something here?	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
223.	Smith & Nephew	249	9.1	Cullum et al. (2016) Was a research study conducted in the NHS between 2008 and 2012 gathered information on the outcomes most valued by patients and health professionals dealing with a range of chronic, complex wounds including leg ulcers; it identified healing (particularly time to healing) as a primary treatment	Thank you for your comment. While the Cullum et al research was not intended to look only at infected wounds, the study encompassed multiple wound types including infected leg ulcers. The researchers present the conclusions of their study as being broadly applicable to all wound types assessed, including infected leg

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				outcome alongside other important outcomes measuring pain, infection and discomfort. This study was not intended to look specifically at infected wounds and therefore conclusions should not be extrapolated to the scope of this review. The recommendation should amended acknowledge further research is required to determine patient benefit specifically for wounds with signs and symptoms of infection and not conflate conclusions of study not in scope of this assessment.	ulcers. The EAG agrees that further work focussing specifically outcomes of value to patients with infected leg ulcers would be of value, but as no such study has been identified, the broad conclusions of the Cullum work are relevant to this discussion. No factual inaccuracy is therefore identified. However, we have noted that the study does not focus on infected wounds as a caveat in parentheses.
224.	Surgical Dressings Manufacturer's Association (SDMA)			The SDMA recognises the conclusion of Late Stage Assessment (LSA), topical antimicrobial dressings (AMDs) for infected leg ulcers in people aged 16 in that the current evidence does not allow a clear assessment of the relative merits of the different types of antimicrobial dressings and welcomes the recommendation that further evidence should be collected to compare the performance of different agents and sub agents within AMDs. The wound care industry has invested heavily in developing clinical studies, evaluation and trials to demonstrate the clinical efficacy of both advanced wound dressing and topical antimicrobial dressings and our members have questioned why particular studies were not selected to inform the healing rate parameters in the model for example. We would welcome the opportunity to work alongside the DHSC, NICE, and the NWSCP to agree the level of evidence, protocols and clinical outcomes required in the future. We propose setting up a cross functional group to work on establishing a consensus in this area providing clarity and direction as described in the recommendation for future evidence generation	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
225.	Surgical Dressings Manufacturer's Association (SDMA)			Data Inaccuracies and exclusions Members are very concerned of the factual inaccuracies, particularly around inappropriate healing time endpoints, exclusion of relevant RCT data, inaccurate market share figures, infection rate estimates, utility assumptions, and scenario analysis limitations Incorrect and inaccurate product usage and market share assumption. Members suggest that alterative datasets for health economic generation such as the THIN database may offer a more representative perspective on wound care usage in the primary care setting. Member also express concerns about the lack of clinical relevance to weighted costings and the exclusion of biofilm and compression considerations in evidence review	Comment does not refer to specific inaccuracies for correction, no change to report has been made.
226.	Surgical Dressings Manufacturer's Association (SDMA)			Clinical Relevance and Endpoints Our members have criticised the focus on complete wound healing and its inappropriateness as a primary endpoint for antimicrobial dressings The clinical focus should be on reduction of wound bioburden and infection resolution rather than complete wound healing. The One-year time horizon with weekly cycles considered out of scope for antimicrobial evaluation.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
227.	Surgical Dressings Manufacturer's Association (SDMA)			Stakeholder Awareness and Input Members as concerned about the complete lack of patient input and limited clinician input into the user preference report. The low numbers reinforce our view of the overall poor awareness of the LSA process amongst wound care specialists and general nurses and the need for greater transparency and stakeholder involvement in the review process.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
228.	Integra LifeSciences			We do value the massive analysis have been conducted and the huge number of publications were investigated.	Thank you for sharing the additional sources. We will add a sentence to the report regarding the potential for varied impact of different

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				It is well appreciated that the Manuka honey was kept separated from the generic honey. As references, please consider the following ones. • Antibacterial activity of Manuka honey and its components: An overview 2018 • Methylglyoxal in Manuka Honey - Correlation with Antibacterial Properties 2009 • Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (Leptospermum scoparium) honeys from New Zealand 2008 We would also recommend to interview prof. Rose Cooper from Cardiff Metropolitan University; rcooper@cardiffmet.ac.uk, a biochemist that studies wound healing and agents. The analysis and report appear not to consider that the different types of technologies used with agents have a relevant impact on the clinical outcomes, for example, simple dressing is used for a specific type of wounds, while gel or alginate can benefit other type of wounds and patients. The huge difference is made by infected or not infected wound, if there is exudate or not, if there is bleeding or not. Grouping all different types of technologies might be misleading.	Manuka honey based on the presence of specific components, such as methylglyoxal. Regarding the latter comments, these are not factual inaccuracies, therefore, no further change has been made to report.

Section B: Economic model – Factual accuracy comments:

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
1.	The Leg Club Foundation	No comments from us.			
2.	Urgo	Number of AMDs required per weekly cycle' silver is given a value of 5 and is the highest value. Many silver dressings have a higher wear time than dressings of other technologies. We believe that this should be reviewed. The wear time of UrgoClean Ag is up to 7 days, and although dressing changes may be more frequent in a highly exuding infected wound, we would not expect there to be a need for significantly more dressing changes than other technologies.	This should be reviewed to make sure that this value is correct and more in line with other technologies. A value of between 1 and 2 seems more appropriate. It is unclear exactly how this value is calculated but based on a assumed wear time of 7 days the value for 'non-infected, unhealed' would be 1, making the maximum for 'infected, unhealed' 2.79. It is understood that different products in this category have different wear times, however 5 as an average seems far too high.	Reducing the number of dressings used would impact the cost-effectiveness significantly and could reduce the overall treatment cost for the silver category.	The base case has been updated which uses a lower resource use for silver.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
3.	Urgo	Number of AMDs required per weekly cycle' silver is given a value of 5 GID-HTE100041 Final Report page 174 Table 7=8 shows silver salts and compounds require 1.49 dressing per week for infected unhealed leg ulcers	Amend dressing changes to 1.49 in the model reflective of the reference and assumptions	Reducing the number of dressings used would impact the cost-effectiveness significantly and could reduce the overall treatment cost for the silver category.	Dressing change numbers have been explored in scenario analysis
4.	Urgo	'Antimicrobial dressing costs' Silver is given the value of £7.52. It is acknowledged in the report that the silver category has one of the widest price variations of any category. There are some highly priced outliers in the silver category that is taken into account when determining average price. This makes this average cost unrepresentative of the majority of the category.	Excluding products which are outliers from the group in price may make the economic model more representative of the majority of products in the category.	Excluding products with unusually high prices when compared with the rest of the category would impact the cost effectiveness of the silver category and could reduce the overall treatment cost for silver.	The weighted average cost uses CPRD data on market shares to weight the specific products, see Appendix H. As CPRD is the best readily available real world data on the usage of AMD products in the UK we consider this to be the most robust approach to costing the AMDs.
5.	Coloplast	General Comment: The economic model is very well laid-out and easy to follow. We have re-run the model and replicated all the reported results. The base-case results of the model indicate that Iodine is the			Thank you for your feedback.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
		most cost-effective agent, and all the other comparators are dominated by Iodine. The main driver of these results is differences in efficacy, and this is confirmed by the DSA and scenario results.			
6.	Coloplast	Healing rate. Report, Methods section (pg. 152-153: healing rate). There is no explanation of why particular studies have been selected to inform the healing rate parameters in the model	For example: the first line (1L) per week rate of ulcer healing for silver dressings was derived from a single study with 14 subjects carried out in South Africa (Forlee, 2014). The review of clinical literature identified 18 studies of silver dressings fully meeting the decision problem. Of these, 5 are UK studies; 6 are RCTs, 7 are judged to have low or moderate risk of bias, and 12 contain evidence of healing. There is no explanation in the report of why this evidence has not been used (and see point 7 below).		EAG provides comments on suitability in Table 7.2. Appendix G reports healing rates retrieved from studies, Dimakakos et al. 2009 (5/21 at 4 weeks); Forlee et al. 2014 (3/14 at 4 weeks); Miller et al 2010 (20/133 at 4 weeks); Woolstencroft 2018, (7% at 4 weeks); Harding 2016, (1/10 clinically infected); Lantis 2011; (1/24 at 4 weeks); Molle 2023: 16/25 at 4 weeks reported the percentage healed for silver at either 4 or 12 weeks (as required by the model) A conservative estimate using the silver salts and compounds study conducted by Forlee et al was chosen by the EAG. The efficacy was appropriate

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
					compared with other efficacy studies, including Dimakakos et al. 2009 (23%) and sat centrally between extreme study outcomes such as Molle (64%) and Lantis (4.2%). Sensitivity analysis explored the impact of changing the efficacy by 20% and the efficacy was further varied in the sensitivity analysis.
7.	Coloplast	Infection resolution rate. Report, Methods section (pg.155). "it was necessary to assume the rate of infection resolution was proportional to the rate of healing, because of lack of evidence."	As with assumptions about ulcer healing, EAG have provided no explanation of why this assumption was necessary. The clinical review identified 9 studies which reported evidence on the rate on infection resolution. Some explanation should be provided for why this evidence was not used.		The EAG acknowledged the limitations in this assumption in the report. A relationship between infection resolution and healing rate was deemed appropriate by the EAG and clinical opinion. Additional scenarios have been performed to test this assumption further, see Table 7.24.
8.	Coloplast	Definition of transition probabilities. Model structure and data library Is there a risk of double counting?	The two efficacy 1L transitions are "infected unhealed to not infected unhealed" informed by the rate of infection resolution; and "not infected unhealed to healed". In the model this transition is derived from the 4-week, or 12-week rate of		Thank you for your comment, we can confirm there was no risk of double counting. See page 153-4 of the report for more detail. No changes to the report were made.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
			healing reported the literature. Because the population of reported studies is predominately patients with an infected leg ulcer, it appears the transition from "not infected unhealed to healed" is in fact a transition from "infected not healed to healed". Is there a risk of double counting here?		
9.	Coloplast	DSA. Report Table 7.13 (pg. 191). The two important 1L transitions based on assumptions about efficacy are not independent. These values are varied in the DSA by ±20%	Does the DSA take account of the fact that these two variables are not independent because the infection rate is set to be proportional to the healing rate? Interdependence makes it difficult to interpret the effect of varying these assumptions. A variation of 20% is quite arbitrary. Is there not a more objective means of estimating confidence intervals?		The baseline calculation for infection resolution is proportional to healing rate. In the DSA these inputs are varied independently of each other. No change to report has been made. Where an uncertainty estimate or range was available, these values informed the DSA.
10.	Coloplast	Scenario analysis. Report Pg 226- Given the importance of assumptions about efficacy, none of the scenarios	Five of the scenarios (Pg. 241-242) vary assumptions about efficacy and prescription time. None of these varies the rates of healing or infection resolution except for the		Thank you for your comment. Scenario analysis has been conducted around healing rates.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
		adequately tests these assumptions	second line basket of treatments for patients who have discontinued the first line antimicrobial dressings (AMD) (Table 7.45, Pg 165). Estimates of the efficacy parameter values in the model are acknowledged to be highly uncertain. It is surprising there is not a more in-depth consideration of the importance of these assumptions. PSA alone is not able to capture the full impact where one dominant parameter is significantly more uncertain than others.		
11.	Coloplast	Appendix D: Feasibility of quantitative analysis. Report Pg. 387 Given the number of silver studies which were identified, why was it not possible to pool data on healing rates? Similarly, why was it not possible to pool data from some of the 9 studies reporting the rate of infection resolution?	Given the fact that there were 18 silver studies, 6 of which are RCTs which fully met the decision problem, was it not possible to pool healing data to provide a more reliable estimate for the model? EAG concludes that no quantitative analysis was possible because (a) the comparators in these trials were not sufficiently similar to be combined, and (b) because the type of silver		Pooling data/ conducting a meta-analysis was not feasible, this was supported by clinical input. See Appendix D. No change to report has been made.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
			dressings used in each study were different. The first point would be relevant if the aim of a meta-analysis is to derive an estimate of relative treatment effects. But in the present case the aim is to obtain estimates of individual parameter values, so the comparator arm is not relevant? The model compares different types of AMD grouped into broad categories (silver, Iodine, honey, copper, PHMB and chitosan). The base case analysis does not distinguish different forms of silver, so in principle it should be possible to pool data from the silver arms of these studies to provide a more robust estimate of the healing rate. All the study populations are patients with an infected leg ulcer.		
12.	Paul Hartmann Ltd	While the model itself is not factually incorrect, we would like to highlight significant concerns regarding the use of CPRD as the base dataset. Specifically, it does not	We believe the THIN database would provide a more representative basis for the model.	Using THIN could yield valuable insights, as many primary care practitioners rely on traditional wound management methods, such as iodine, due to varying levels of knowledge in wound	CPRD was used as this is a large dataset which was readily available for the analysis. No change to report has been made.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
		account for the community care setting, where the majority of wound care (60–70%, according to BOW) occurs.		care. This reliance would influence market share and weightings within the model.	
13.	Paul Hartmann Ltd	We wish to reiterate our concerns regarding the unintended consequences of the narrow scope of the LSA, while acknowledging the rationale behind it. Most formularies recommend the use of antimicrobials as a preventative measure prior to infection, aiming to treat locally and thereby avoid systemic infection, the need for antibiotics, and potential acute admissions. This is especially pertinent considering that chronic wound patients typically present with an average of 4.1 comorbidities (BOW).	Scope would include risk of infection or localised infection/critically colonised to fully capture the use and efficacy of these products.		Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
14.	Integra LifeSciences	Different typology and technologies of wound dressing. We appreciate the structure of the analysis by active agents, however the technology (dressing, gel,	The analysis should consider the comparison by active principle/agent and type of technology to provide correct results.	Add the opportunity to introduce the input data by agent and type of technology.	The focus of this analysis was to compare AMD agents only. See decision problem, pg12 of report.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
		adsorbable material, alginate …) plays a relevant aspect in the outcomes.			
15.	Integra LifeSciences	The structure of the Markov model should be changed.	The Markov structure status should be (infected) and (not infected) and then as further status (healed) and (not healed).	As the healing from infection is a relevant outcome for some agent and it brings to different treatments in case they wound is stalled (not healing). Treatments are set up based on the time the wound remains not healed.	See model structure justification pg148 in report.
16.	Integra LifeSciences	Structure of patient's management and resources consumption.	The length of the period in which the wound remains in the status of infected and not healed and not infected not healed requires different type of treatments.	Adjust the model structure according to resources and treatments are provided to patients for the type and chronicity of the wounds.	Comment is not a factual inaccuracy, no change to report has been made. We will review other comments at consultation stage.
17.	Integra LifeSciences	Patients' status has an impact on the outcomes results and the study cohort can be is different from one study from another.	Consider defining comparable efficacy input data for the different products.	Verify input clinical data based on the cohort characteristics of the clinical study and adjust if the patients' characteristics in the study differs from the model structure.	Adjusting for patient characteristics in the clinical studies used for efficacy data was not feasible for this analysis. No change to report has been made.
18.	Integra LifeSciences	As above, antimicrobial wound dressings can be used in association to other treatments and it's important to verify the coherence with the clinical study and the model cohort and its characteristics.	Consider defining coherent input and efficacy data for the different products in combination with other treatments.	Verify input clinical data based on the cohort characteristics of the clinical study and adjust if the patients' characteristics in the study differs from the model structure.	Adjusting for patient characteristics in the clinical studies used for efficacy data was not feasible for this analysis. No change to report has been made.

Comment no.	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
19.	Integra LifeSciences	Not only venous leg ulcers are treated with antimicrobial wound dressings and the model for this reason is limited. Patients might suffer from unhealed wound that are different from venous ulcers	Consider the efficacy data in several studies refer to multiple types of patients, not only those suffering form leg ulcers.	Verify input clinical data based on the cohort characteristics of the clinical study and adjust if the patients' characteristics in the study differs from the model structure.	Adjusting for patient characteristics in the clinical studies used for efficacy data was not feasible for this analysis. No change to report has been made.

NICE National Institute for Health and Care Excellence

HealthTech Programme

Late-stage assessment

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

User preference report

Produced by: **NICE**

Date completed: 13 November 2024

Contains confidential information: No

Number of attached appendices: 4

Table of Contents

1. Introduction

Alongside the assessment of a technology's value based on costs and effectiveness, the late-stage assessment on topical antimicrobial dressings for treating infected leg ulcers includes an assessment of user preferences that influence decision making when selecting which technology to use (NICE's Interim methods and process statement for late-stage assessment). This report presents the key findings from the user preference assessment that was done to understand:

- the criteria that are important to users when choosing an antimicrobial dressing
- the relative importance of the criteria, and
- how the criteria can be measured.

The user preference report should be read alongside the external assessment group (EAG)'s assessment report.

2. Background

This late stage assessment focuses on topical antimicrobial dressings for infected leg ulcers in people aged 16 and over. A leg ulcer can be defined as an ulcer between the knee and ankle that has not healed within 2 weeks (NWCSP 2023). The assessment, diagnosis and management of infected leg ulcers is a nurse-led discipline typically managed in the community (Guest 2020). According to the International Wound Infection Institute (IWII), signs and symptoms of local infection can be covert (subtle) 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. Once an infection has been identified, a topical

antimicrobial dressing can be used to reduce the level of bacteria at the wound surface.

There are over 300 different product variations from at least 30 manufacturers included in the late-stage assessment of topical antimicrobial dressings for infected leg ulcers in people aged 16 and over. These include dressings with different agents that have an antimicrobial effect and different formats, such as foam or alginate. Dressing products are chosen to suit a particular wound presentation and individual patient needs at a particular stage of healing.

3. Methods

This user preference assessment was conducted in line with NICE's Interim methods and process statement for late-stage assessment. The aim of capturing user preferences is to transparently collect and present information to the committee on the criteria that users consider important when deciding which technology to choose. Users are defined as those who will use the technology and are directly involved in the decision to choose one technology over another.

When choosing a dressing, it was assumed that appropriate clinical reasoning had taken place, the wound was adequately prepared before the dressing was applied and that an antimicrobial dressing was indicated.

3.1 Participants

For this user preference assessment, users were identified as district nurses, practice nurses, tissue viability nurses, specialist clinic nurses and vascular nurses. This is because they decide which dressing is best suited to meet the needs of a specific patient. Although it was acknowledged that patient preference plays a role in dressing selection, the choice is ultimately made by the healthcare professional. In addition to the user preference assessment, a patient survey is being used to capture patients' views and preferences about the use of dressings for treating infected leg ulcers. Users were recruited in line with NICE's Interim methods and process statement for late-stage

assessment. NICE's policy on declaring and managing interests for NICE advisory committees was considered during the recruitment process. A declarations of interest register will be published alongside the guidance document on NICE's topic page.

3.2 Assessment stages

This user preference assessment has been designed with Multicriteria Decision Analysis (MCDA) principles (ISPOR Task Force Report, 2016). Data on user preference was collated through participation in 2 online workshops and through communication via email. The process followed 4 stages:

- Stage 1: identifying and defining criteria (workshop 1)
- Stage 2: ranking criteria in order of importance (email task 1)
- Stage 3: weighting of criteria (email task 2)
- Stage 4: development of performance rules (workshop 2).

Stage 1: identifying and defining criteria

Users were asked to identify key factors that are important when choosing a topical antimicrobial dressing for an infected leg ulcer. A list of criteria and definitions were identified and agreed on during an online workshop with users.

Stage 2: ranking criteria in order of importance

Users were then asked to rank the criteria in order of importance to them via email. Ranked lists from all respondents were collated, averaged and ordered from most important to least important, creating a final ranked list of criteria and definitions (using the SMART ranking technique; see appendix C for a detailed definition).

Stage 3: weighting criteria

Users were asked to weight the criteria to show how much more important 1 criterion was compared with the criterion ranked below (using the swing weighted technique, see appendix C for a detailed definition). To weight the

criteria, users were asked to give each criterion a score from 0 to 100%. A score of 0% meant that there was no difference in importance between a criterion and the criterion ranked below, and a score of 100% meant that it was considered twice as important. Weighted lists for all respondents were collated, averaged and weights were calculated.

Stage 4: developing performance rules

During the second online workshop, performance rules were created by consensus for each criterion. To do this, users were asked how they would measure performance of a dressing against each criterion. For rules with multiple answers, users were asked what would be considered acceptable or unacceptable levels of performance. In some cases, a level of acceptable performance could not be reached due to variation in opinion and the group being unable to come to a consensus. Where this was the case, it is highlighted in table 4.

3.3 Patient survey

NICE conducted a survey of people with lived experience of using AMDs to treat infected leg ulcers. 19 people responded to the survey, of whom 12 had used an AMD for an infected leg ulcer. Most people (10/12) did not know what type of dressing they were prescribed and were not involved in the selection of the AMD. When asked if they knew what agent they were prescribed, 5 people said their dressing contained honey as an agent, 1 silver, 1 iodine, and 5 people did not know. When asked what factors would make them choose a dressing over another the results were as follows (people could select more than one answer):

- Comfort (n=9)
- Ease of removal of dressing (n=8)
- Effectiveness in reducing healing time of wound (n=7)
- Effectiveness in reducing healing time of infection (n=6)

- Dressing staying in place for as long as needed (n=5)
- Avoidance of reactions to the dressing (n=5)
- Ease of applying the dressing (n=5)
- How often the dressing needs to be changed (n=4)
- Odour control (n=3)
- Appearance (n=2)
- Cost (n=1)

4. Results of user preference exercise

A total of 15 people took part in the user preference exercise, most of whom were tissue viability nurses. Their engagement varied at each stage as follows: 10 participated in stage 1, 14 in stage 2, 12 in stages 3 and 4. The engagement for individual users is shown in table 1.

Table 1. User engagement for all stages of the assessment

Stage	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	Total
1	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	N	N	**10**
2	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	**14**
3	Y	Y	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	**12**
4	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	N	**12**
Total	**4**	**4**	**4**	**3**	**4**	**3**	**3**	**2**	**4**	**2**	**3**	**3**	**4**	**3**	**2**	

Identifying and defining criteria

An initial list of criteria was drafted before the first workshop by a participant. This formed the basis of discussion for the workshop. Users were asked to suggest additional criteria and to confirm if the existing list was appropriate. Definitions for the criteria were drafted by consensus during the workshop. At the end of the workshop, users were asked to consider each criterion in the

list and confirm that they agreed with its inclusion and definition. Two sets of criteria were created, one for those related to clinical presentation and the other for criteria that are independent of clinical presentation.

The following two sections describe the discussions between the users when developing the criteria.

Development of criteria related to clinical presentation

Criteria related to clinical presentation were wound presentation, medical history and patient characteristics, previous dressing regimes and efficacy, mode of action of agent or dressing, and cytotoxicity of antimicrobial agent (table 2).

Users discussed that wound presentation includes details of the wound such as size, depth, presentation of wound bed (such as sloughy, necrotic, hypergranulation) appearance of periwound (including colour, inflammation, maceration and temperature), malodour and volume and type of exudate. It also includes the duration of the wound, whether there are multiple wounds and the results of any swabs or biopsies. Some users mentioned that there can be confusion between inflammation and infection, and antimicrobial dressings may be used inappropriately in this situation. Users also noted that it is usual to compare the affected limb with the non-affected limb to assess the effect of the wound on the whole limb.

Users discussed that medical history and patient characteristics include factors such as age, past and current medical history (including current medication), comorbidities, allergies and sensitivities. It was agreed that genetic predisposition should be included because it is becoming more prominent in the delivery of care. Compliance and concordance are also factors that would be considered by users if shared-care is an option. If a patient has physical or mental impairment, they may not be able to dress their own ulcer and they may be less compliant with treatment. This overlaps with the definitions under criterion ‘Application directions from manufacturer’ that

was considered to be independent of clinical presentation (table 2). The group discussed whether contraindications should be included under this criterion. A medicated dressing with a particular agent may be contraindicated for certain groups of people, such as those who are having radiotherapy or people with thyroid dysfunction. There was consensus that this is taken into account by following the 'Instructions for Use' (IFU) for a particular dressing.

The group highlighted that previous dressing regimes and efficacy includes wound duration as an important factor and that the frequency and duration of previous treatments is considered when choosing a dressing. The group discussed that if a particular dressing has only been used once for a short period of time, it is difficult to make any conclusions about its efficacy. Users reported that in chronic wounds, antimicrobial dressings might be 'cycled' so that different types of dressing are used rather than repeatedly using the same type of dressing. The group reported that this might be useful to limit the duration of a single agent.

Patient preference is included in the definition for 2 criteria - medical history and patient characteristics, and previous dressing regimes and efficacy. The group discussed that some dressings include animal products such as collagen, which might be unacceptable because of personal or religious beliefs. Users reported that some people may have had a negative experience with a particular type of dressing before and express a preference for a different type. The group discussed that preferences would be considered when a healthcare professional chooses a dressing.

The group reported that the mode of action of a dressing or agent is also relevant to wound presentation and that dressings may be tailored according to wound characteristics and a multi-action primary dressing might be chosen rather than layering multiple dressing. Users discussed that different dressings have different effects on the periwound, and wound characteristics, such as the amount of exudate, are also important to consider. They stated that a dressing with odour control properties might be preferentially chosen in

some circumstances. Users also said that antimicrobial dressings can be medicated, with an active agent such as silver, iodine or honey or non-medicated, such as those coated with Dialkylcarbamoyl chloride (DACC). Some dressings act on a wider range of microorganisms. Users agreed that this might be useful in the absence of results from a swab.

The group discussed that pain during dressing removal might be associated with the mode of action of the dressing or agent, and this is also covered by 'ease of removal' in the second group of criteria, independent of clinical presentation.

It was noted by the group that cytotoxicity of antimicrobial agents that are absorbed systemically, such as silver and iodine is a consideration when choosing a dressing. One user noted that silver could be killing good bacteria as well as bad. Users reported that inappropriate use of the agent regarding dosage of agent or length of time of use (over the manufacturer's IFU or specialist advice) should be avoided. Users agreed that there should be regular reviewing of efficacy at least every 2 weeks.

Table 2. Criteria that were considered to be related to clinical presentation

Criterion	Definition
Wound presentation	• Size of wound • Depth of wound e.g. cavity, tunnelling, undermining • Presentation of wound bed e.g. sloughy, necrosed, hyper-granulation, friable • Exposed anatomical structures e.g. tendon • Exudate volume and type e.g. purulent, turbid, sanguinous • Results of wound swab • Results of wound biopsy • Duration of the wound • Condition of peri-wound e.g. colour of peri-wound, maceration, temperature • Malodour

	• Presentation of whole limb in comparison to contralateral limb • Presence of multiple wounds
Medical history and patient characteristics	• Age • Current and past medical history • Genetic predisposition • Comorbidities • Allergies/sensitivities • Pain • Compliance and concordance with the dressings e.g. patient preference, social circumstances e.g. does the patient have a carer, mental capacity • Current medication • Patient preference because of personal beliefs e.g. religion, animal products
Previous dressing regimes and efficacy	• Duration of wound • Other historical treatments of AMDs including frequency, variability, length of treatments, cycling of AMDs • Patient preference
Mode of action of agent or dressing	• Medicated versus unmedicated (agent released into the wound versus the agent locking the bacteria in the dressing) • Autolytic debridement • Exudate management • Peri-wound protection • Ability to manage or eliminate wound malodour • Ability to affect a range of micro-organisms
Cytotoxicity of antimicrobial agent	• Cytotoxicity of antimicrobial agents that are absorbed systemically, e.g. silver, iodine. • Inappropriate use of the agent regarding dosage of agent or length of time of use (over the manufacturer's IFU or specialist advice) • Regular reviewing of efficacy every 2 weeks minimum

Development of criteria independent of clinical presentation

There was general agreement on 5 criteria independent of clinical presentation to be considered: cost, conformability, ease of removal,

application directions from the manufacturer, and sustainability. The definitions agreed for these criteria are described in table 3.

The group agreed that cost was a criterion that is considered when choosing a dressing. This would encompass whether the dressing has multiple actions and whether additional products are needed. Wear time was initially included as a separate criterion, but it was moved to ‘cost’ because it was noted that a cheaper product might be chosen if it is going to be changed more frequently. Users discussed that in primary and community care settings, a longer wear time may facilitate less frequent nursing visits, although 1 user commented that it would be unusual to leave a dressing on for as long as 7 days. There was some concern about antimicrobial dressings being chosen inappropriately when a cheaper alternative could be used, but the users reported that this should not happen if proper clinical reasoning is followed.

Conformability was discussed by the group. They stated that conformability is something they consider when prescribing a dressing. They were in agreement that conformability was defined by how conformable the dressing was to the anatomical landscape and that it stayed in place after it had been placed there. Users also stated that comfort whilst wearing was an aspect of conformability.

The discussion of ease of removal focussed on pain during removal and the protection of the wound bed and peri-wound skin. The group agreed that pain and protection were linked and that if the dressing was not adhered to the wound bed and the appropriate dressing was selected then pain free removal should be possible. It was noted that comfort while wearing and pain on removal of a dressing are two separate aspects of AMD use.

When discussing the application directions from the manufacturer the group discussed if this was in the context of shared care with a clinician, or directed self-care. The group decided that it was more appropriate to develop this criterion from the perspective of shared care, as this is more likely to be the case with an infected leg ulcer. Users discussed how the ease of applicability

is influenced by the directions from the manufacturer if for example an additional product is needed or not. Users observed that some super absorbent dressings cannot be cut to size, so the need for cutting was included as part of the definition. A user commented that for infected leg ulcers cutting dressings to size was not normally needed.

There was some disagreement about whether the carbon footprint of a company was a consideration when choosing a dressing for an individual patient. Some users stated that it could affect a clinician's attitude towards an overall brand and the group decided to include it as a criterion. Users agreed that packaging was an important consideration, with several people commenting on the amount of waste currently produced. Limited storage space was also mentioned as a factor. It was also noted that ethical and environmental concerns, including biodegradability, are becoming more prominent.

Table 3. Criteria considered to be independent of clinical presentation

Criterion	**Definition**
Cost	Is the primary dressing multi-action? Need for, and cost of, secondary or tertiary products; wear time versus cost: number of days the dressing can be worn for before it needs changing as per the manufacturer IFU or the clinical need for changing
Conformability	How conformable is the dressing material to the anatomical landscape; stays fixed to site after it has been placed there; comfort and conformability whilst wearing
Ease of removal	Pain free removal; wound bed protection; protection of surrounding skin from peri-wound stripping
Application directions from manufacturer	Ease of applicability for shared care between clinician and patient: the dressing does not need to be cut to size; the dressing does not need additional products e.g. for peri-wound care
Sustainability	Biodegradable, environmentally friendly, how recyclable is the packaging; multiple layers of unnecessary packaging

Ranking criteria in order of importance and assigning weights

There was consensus among the group that it was inappropriate to rank the clinical presentation criteria because it is not appropriate to rank one clinical presentation more important than another.

Each of the criteria that was independent of clinical presentation was ranked in order of importance and a weight was then assigned to show how much more important 1 criterion was over another. The average rank and weighting are shown in table 4. Anonymised individual responses from the ranking and weighting exercises are in appendix B (tables 5 and 6).

For the ranking exercise, there was most agreement for 'sustainability' with 11 respondents ranking it last and 3 ranking it fourth out of 5. 'Ease of removal' was ranked in the top 3 by all respondents, although only 1 thought it was the most important criterion. Out of 14 responses, 7 ranked 'conformability' as the most important criterion, 6 ranked it second or third and only 1 ranked it fourth. Ranking for cost ranged from first to last, but most respondents ranked it third or fourth. 'Application directions from manufacturer' also had mixed responses, ranging from first to last; 6 respondents ranked it in the top 2 criteria and 6 ranked it in the bottom 2 criteria.

The individual weighting scores for each criterion ranged from 0 to 100%. Of the 12 users who took part in this stage, 5 weighted at least 1 criterion as equally as important as another. More than a third of the total weighting score was given to conformability (35.3%), which was ranked as the most important criterion, although only 1 user weighted conformability as being above 50% more important than the second ranked criterion, which was ease of removal, and 6 of the 12 weighted it 25% or less more important. Just over a quarter of the total weighting score (27.3%) was given to ease of removal. Less than 10% of the total weighting score (8.3%) was given to the bottom ranked criterion, which was sustainability.

Creating performance rules

All users agreed that because the criteria related to clinical presentation resemble an objective and subjective assessment of an infected leg ulcer, and the fact that there is no national clinical guideline available for the prescription of AMDs, that there was a risk that performance rules for these criteria could be used as a clinical reasoning tool. This would be outside the scope of their remit and would be unvalidated. Therefore the group decided by consensus not to develop performance rules for the criteria related to clinical presentation.

Users were able to create performance rules for all criteria determined to be independent of clinical presentation. Some rules can be answered as a simple yes or no answer whereas others may have a range of answers. For those non-binary answers, users were asked to state acceptable or unacceptable levels of performance. This was achieved for most of the rules but consensus could not be reached for a small proportion.

The following 5 sections describe the discussions between the users when developing the performance rules.

Criterion 1: Conformability

Performance rules included whether the dressing conforms to the shape of wound and wound bed and sits flush to the skin without creases; whether it stays in place while the initial dressing preparation takes place; whether it stays in place until it needs changing clinically and whether it is comfortable and conforms while it is being worn. It was decided that no amount of gaping of the dressing would be acceptable. Wear time was discussed as possibly being relevant to this criterion, but it was agreed not to include for this rule. Users reported that wear time can be related to how long the agent lasts rather than conformability, for example, iodine tends to absorb into a wound faster and iodine dressings typically need to be changed more frequently.

Comfort and conformability while wearing was considered to be patient specific, largely subjective and difficult to define, although it was agreed that healthcare professionals can give feedback on how a product works based on experience and patient feedback. If a patient has found a particular dressing uncomfortable, they might not allow the same dressing to be used again. The group discussed how this could also include skin sensitivity or reaction, which is covered by the clinical criterion of wound presentation. Users considered that community nurses see patients regularly and are likely to have more information on conformability. There was consensus that because of these reasons this rule is situation specific and not measurable.

Criterion 2: Ease of removal

It was agreed that pain free removal largely depends on how much the dressing sticks to the wound bed and surrounding skin when it is being removed. Users discussed how this is related to the contact layer and the performance rule was agreed as ‘lack of adherence to the wound bed’. The same performance rule was agreed for wound bed protection. Although several users stated that they would avoid using adhesive dressings for infected leg ulcers, it was noted that it might be appropriate to use them in certain populations. For example, homeless people or those who are less likely to access regular dressing changes. The third definition included in this criterion was protection of surrounding skin. The group reported that this relates to the dressing stripping the skin around the wound. Users stated that most of the factors that had already been discussed about adhesive dressings were relevant to this criterion as well. In addition, it was noted that adhesive dressings might be used with hosiery and if the dressing comes off when the hosiery is removed, it could strip the skin. It was also noted that there is an increasing level of self-care, for which adhesive dressings may be used more frequently. The group considered that some non-adhesive dressings will also adhere to a wound and strip the surrounding skin. The group felt that this is situation specific as well as patient specific. There was consensus that this is

an important criterion and it could be captured by a single binary measure 'Does the dressing cause periwound stripping or irritation?'

Criterion 3: Application directions from manufacturer

The group discussed how this criterion relates to the ease of dressing application for shared care between the healthcare professional and patient. The first definition under this criterion is that the dressing does not need to be cut to size. The group considered that if a product is available in a range of sizes there may be less need to cut it to size. Users felt this might be an important consideration when family members or carers are changing the dressing rather than a healthcare professional. There was consensus that this would be patient and wound specific but can be measured with a binary outcome of yes or no.

The group noted that periwound care is important and extra products might be needed for periwound protection. This could make applying the dressing more difficult, but several users noted that the use of an additional product is not necessarily a negative factor. Not everyone agreed with the view that a single product would be easier for shared-care. Some users felt that many patients can manage multiple products. For infected leg ulcers in particular, it was noted that more products would probably be necessary, for example if a patient had more friable skin that needed protecting. There was concern from the group that a performance rule promoting the use of a single product may lead to inappropriate clinical decisions. For simplicity and shared care, a single product would be preferred by users but they reported there is a need to consider clinical criteria as well. It was noted that shared care is likely to be more common for straightforward wounds that can be treated with a single dressing and more complex wounds are more likely to be managed by a healthcare professional. The conclusion was that there was a lack of consensus for this performance rule.

It was agreed that the definition of 'simplicity in application procedure' is situation and patient specific, based on the patient's understanding, mental

capacity and dexterity. The group felt instructions on placing the dressing should be simple enough for a lay person to follow. They reported that accessibility of instructions is important and they should be available in a variety of formats such as visual, easy-read, digital, and multiple languages.

Criterion 4: Cost

It was agreed that the performance rule for all the definitions under the cost criterion should be ‘the most cost-effective option for the clinical presentation’. This was because the group felt they were all related and that factors that were considered such as ‘multi-action’ were only of benefit in relation to cost and the cost of the alternative.

There was general agreement that whether a dressing is ‘multi-action’ can be measured with a binary yes or no. It was agreed that factors such as the frequency of dressing changes as well as the need for other products contribute to the decision making, so cost-effectiveness is important rather than just direct cost. The group noted that a multi-action dressing is not necessarily cheaper or preferable, because it might need to be changed more frequently.

The users discussed how the use of a primary and secondary dressing might be cheaper than using a single product. Most people with leg ulcers will benefit from compression and a retention bandage might be part of a compression therapy system. It was noted that a patient may be under the care of a vascular team who want specific bandages to be used. Again, cost-effectiveness was agreed as the appropriate measure.

The group discussed wear time being proportional to cost, and if the dressing performed as per the Instructions for Use (IFU) in terms of wear time. One user noted that there have been recent occurrences of infected leg ulcers leading to serious sequelae including amputation. The group expressed concern that this assessment should not be used as guidance on clinical reasoning and that healthcare practitioners should continue to follow locally agreed infection control pathways.

Criterion 5: Sustainability

The first definition under this criterion was biodegradability. It was agreed that this is mainly relevant to the packaging rather than the dressing itself. The group noted that different trusts have different processes for dealing with clinical waste and it might vary according to infection status. In some centres, all clinical waste goes into burn bins. The dressing may also be placed into a non-biodegradable bag before being disposed of. It was agreed to add the measure of 'Is it toxic when the dressing is burnt?', which has a binary measure yes or no. Two users stated that this isn't a consideration for them when choosing a dressing for an individual patient, but it might be more of a consideration when choosing dressings for formularies.

There was consensus that whether packaging is recyclable can be measured with a binary yes or no.

It was agreed that it is difficult to define 'unnecessary' packaging. What is deemed to be unnecessary by the user may be considered necessary by the manufacturer. It was agreed that packaging needs to be proportional. One member of the group mentioned that the number of dressings per box is a consideration, but procurement arrangements may stipulate the number of dressings that can be bought. There was consensus that it is not possible to define this measure numerically.

The group also had difficulty in defining a measurement of ethical sourcing of dressing materials and carbon footprint of the company. Some users noted that this wouldn't be a consideration for them when choosing a dressing for an individual patient. It was agreed that transparency of information is important, and it was noted that companies do mention this in their training talks. One member of the group noted that it was important to have sustainability criterion as we have a duty to set standards for the future. There was consensus that it is not possible to define ethical practice in this context or to define an acceptable level of carbon footprint.

Table 4 presents the resulting performance matrix. Anonymised raw data of the ranking and weighting stages can be found in Appendix B.

Table 4. Performance matrix

Order of importance	Weight (%)	Criteria	Performance rule (how to measure criteria and levels of performance considered acceptable)
1	35.3	**Conformability**	• Conforms to shape of wound and wound bed, sits flush to skin, lack of creases. (Y/N) • No level of gaping is acceptable. • Dressing stays in place while rest of dressing preparation takes place. (Y/N) • Dressing stays in place until it needs changing clinically. (Y/N) • Comfort and conformability while wearing. Patient specific, based on patient feedback and healthcare professional feedback.
2	27.3	**Ease of removal**	• Does the dressing cause peri-wound stripping or irritation? (Y/N)
3	16.9	**Application directions from manufacturer**	• Does the dressing need to be cut to size? (Y/N) Binary measure, but patient and wound specific. • Are there a variety of sizes? (Y/N) • Instructions should be simple enough for a lay person to follow. This is situation and patient specific, based on understanding, capacity, dexterity. • Instructions should be accessible and available in various formats e.g. digitally, aphasia friendly and various languages. Unable to reach consensus on how to measure whether additional products are needed.
4	12.2	**Cost**	• Cost of primary dressing • Cost of additional dressings or products • Wear time proportional to cost, does the dressing perform as per the IFU in terms of wear time? (Y/N)

			Most cost-effective option for the clinical presentation should be chosen.
5	8.3	**Sustainability**	• Is the dressing biodegradable? (Y/N) • Is the dressing toxic when burnt as part of clinical waste? (Y/N) • Is the packing recyclable? (Y/N) • Is the packaging proportional to dressing numbers and context of use? (Y/N) The group was unable to define ethical practice in this context or to define an acceptable level of carbon footprint.

5. Additional considerations

Of the 5 criteria identified by the users that were independent of clinical presentation, costs data were captured by the economic evidence review done by the EAG. Data on ease of removal were captured as safety outcomes in the evidence base but there were no explicit data measuring conformability, application, or sustainability.

6. Conclusion

There were 15 people who took part in the user preference assessment to determine the most important criteria when selecting an antimicrobial dressing for infected leg ulcers. They identified 5 main criteria that were related to clinical presentation but it was agreed that these should not be ranked because it is not appropriate to rank one clinical presentation more important than another. The 5 criteria were wound presentation, medical history and patient characteristics, previous dressing regimes and efficacy, mode of action of agent or dressing, and cytotoxicity of antimicrobial agent.

In addition to the 5 criteria related to clinical presentation, 5 criteria that were considered to be independent of clinical presentation were identified. These were ranked and weighted and performance rules were created. In order of importance, the 5 additional criteria were conformability, ease of removal,

application directions, cost and sustainability. It is notable that none of these criteria are specific features of individual dressings, but instead quite generic and related to the performance of the dressing.

There was some disagreement about the relative importance of the criteria that could be ranked. In particular, cost and application directions both ranged from first to last in the individual rankings. Most users ranked conformability in the top 3 and it received more than a third of the total weighting score.

A limitation of the user preference assessment is volunteer bias. NICE recruited a sample of users who volunteered to take part in the assessment, and it is possible that the sample of healthcare professionals is not fully representative of the wider population of people who choose which antimicrobial dressings to use. In addition, there were no applicants to participate in the user preference assessment from practice nurses meaning this aspect of practice may not be represented if it were different from the other disciplines represented. However, the participating users came from a range of NHS trusts in England and Scotland and included experienced tissue viability nurses and those who work in community settings.

The user preference exercise only included healthcare professionals but they agreed that patient preference is also important when choosing an antimicrobial dressing. Patient preference was included in the definition for 2 criteria that were related to clinical presentation. To gain feedback from a patient's perspective, a patient survey was circulated to relevant patient groups.

When comparing the criteria that were ranked and weighted to the EAG's assessment report, only cost and ease of removal were captured either well or partly. Cost of the dressings was captured well by the report and informed the EAG's health economic analysis. However, ease of removal was only partly captured in some of the evidence identified in the form of adverse events. The EAG observed that for this latter criteria the evidence was low in volume and poor in quality. The other three criteria (conformability, application

directions from manufacturer and sustainability) were not captured in the evidence identified by the EAG. This signals that the current evidence base may not be capturing approximately 60% of what is important to users when selecting an AMD for use, and indicates a gap in the evidence. While criteria like sustainability and application directions from manufacturer may be difficult topics to research, conformability of a dressing is a measure of performance and could be evaluated.

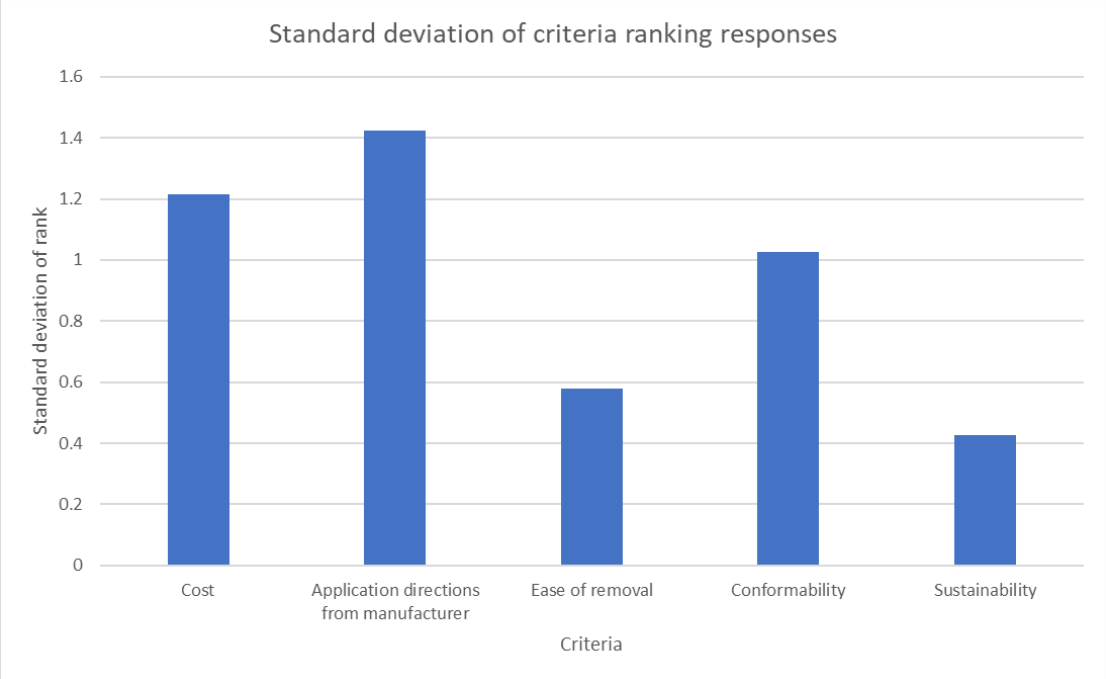
Appendix A. Uncertainty in the user preference exercise

Agreement of users for ranking and weighting stage

Ranking stage

Figure 1 shows the standard deviation (SD) of responses representing the level of agreement between the users in their responses to the ranking exercise for the criteria considered to be independent of clinical presentation. Fourteen users contributed to the ranking exercise. The SD ranged from 0.43 for 'sustainability' to 1.42 for 'application directions from manufacturer'.

Figure 1. Standard deviation of mean of rank

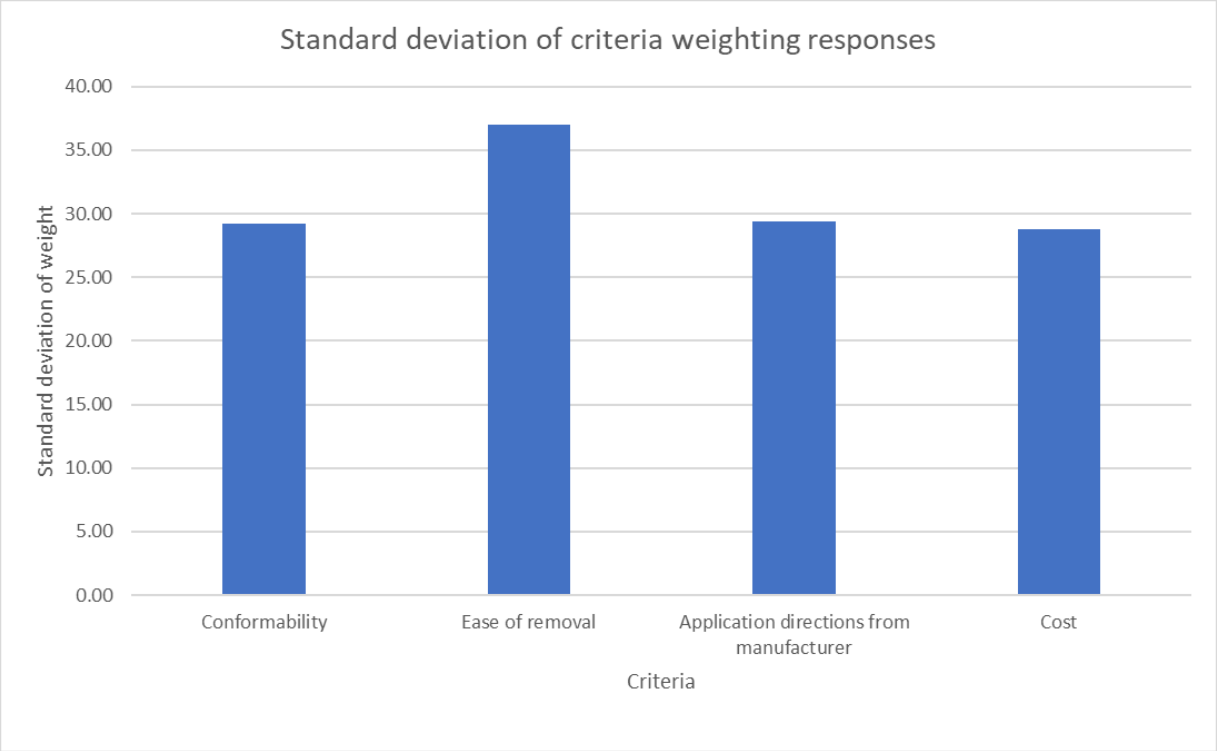


Weighting stage

The SD of responses representing the level of agreement between the users in their responses to the weighting exercise for the criteria considered to be independent of clinical presentation is in figure 2. Twelve users contributed to the weighting exercise. Responses could range from 0 to 100 meaning the

maximum SD was approximately 50. The SD of weighting responses ranged from 28.8 for ‘cost’ to 37 for ‘ease of removal’.

Figure 2. Standard deviation of mean weight



Appendix B. Raw data from ranking and weighting stages

Table 5. Raw data from ranking exercise

Criteria	User 1	User 2	User 3	User 4	User 5	User 6	User 7	User 8	User 9	User 10	User 11	User 12	User 13	User 14	Mean	SD	Final rank
Conformability	2	1	3	3	1	1	3	1	2	4	1	2	1	1	1.86	1.03	1
Ease of removal	3	2	2	1	2	3	2	2	3	2	2	3	2	2	2.21	0.58	2
Application directions from manufacturer	1	3	1	2	3	2	4	4	4	1	4	1	5	4	2.79	1.42	3
Cost	4	4	4	4	4	5	1	3	1	3	3	5	3	3	3.36	1.22	4
Sustainability	5	5	5	5	5	4	5	5	5	5	5	4	4	5	4.79	0.43	5

Table 6. Raw data from weighting exercise

Rank	Criteria	User 1	User 2	User 3	User 4	User 5	User 6	User 7	User 8	User 9	User 10	User 11	User 12	mean	SD	Overall weight*
1	Conformability	35	15	40	50	25	100	0	30	5	0	50	0	29.2	29.2	0.353
2	Ease of removal	75	50	10	50	85	100	100	80	10	0	75	100	61.3	37.0	0.273
3	Application directions from manufacturer	100	25	50	25	0	75	50	50	0	50	25	20	39.2	29.4	0.169
4	Cost	50	60	60	0	0	50	50	50	20	50	75	100	47.1	28.8	0.122
5	Sustainability															0.083

*points are attributed to the criterion based on the mean importance relative to the criterion below. These are used to calculate the final weight

Appendix C. Glossary

Term	Definition
SMART ranking technique	Simple Multi-Attribute Rating Technique is a process mainly used in Multi Criteria Decision Analysis. It allows a group of alternatives to be ordered by importance. Individual responses from each member of the sample are collated and then meaned ensuring equal say among the group (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioral research. Cambridge: Cambridge University Press).
Swing weighting technique	Swing weighting is also a process often used in Multi Criteria Decision Analysis. It is a method used for calculating and reporting the relative importance (weight) of each of the alternatives from a ranked group. Each member of the provides individual answers to questions asking them to decide (on a scale of 0-100%) how important each criterion is over the criterion below it. All of the responses from each member of the sample are then collated and meaned. After this, weights are calculated (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioral research. Cambridge: Cambridge University Press).
Performance rule	A rule which describes how the users measure performance of the technology in question against the criteria.
Performance matrix	A list of the most important criteria to users, and the performance rules associated with these criteria.

Appendix D. Participants in the user preference assessment

Mikyung Bailey, Tissue Viability Nurse, Berkshire Healthcare NHS Foundation Trust

Lindsay Banks, Medicines Optimisation Pharmacist and Non-Medical Prescribing Lead, Bridgewater Community Healthcare NHS Trust

Priti Bhatt, Tissue Viability Lead Community Services, Guy's and St Thomas' NHS Foundation Trust

Keira Bradley, Senior Tissue Viability Clinical Nurse Specialist, Leeds Teaching Hospitals NHS Trust

Lucy Cook, Nurse Practitioner, Guy's & St Thomas' NHS Foundation Trust

Stacey Evans-Charles, Lead Nurse Tissue Viability, Highland HSCP, NHS Highland

Clare Greenwood, Clinical Academic Researcher in Tissue Viability, Leeds Teaching Hospitals

Lisa Hill, Lead Nurse Tissue Viability, St James's University Hospital

Sam Lane, Lead Wound Management Specialist and Tissue Viability Nurse, Surrey Heartlands Integrated Care System

Emma Mallinson, Practice Development Lead for Tissue Viability Service, Tissue Viability Nurse Specialist, Leeds

Sarah Marquis, Matron District Nursing, Lancashire and South Cumbria NHS Foundation Trust

Keith Moore, Tissue Viability Clinical Nurse Specialist, Bridgewater Community Healthcare NHS Foundation Trust

Kathryn Morgan, Matron for Infection Prevention & Safety (Tissue Viability), Lancashire & South Cumbria NHS Foundation Trust

Jane Todhunter, Advanced Vascular Nurse Practitioner, North Cumbria Integrated Care Trust

Kate Williams, Senior Lecturer and Honorary Tissue Viability Nurse, University of Huddersfield

NICE National Institute for Health and Care Excellence

User Preference Report – Factual accuracy comments:

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
1.	Essity	19	TABLE 4	Clinical group did not highlight healing rate as a key performance metrix – why was this included in economic model if clinical group don't see this as a key metric for choice	Thank you for your comment. The scope was developed by all stakeholders, this is when the outcome measures for the model are decided. The purpose of the user preference assessment is not to inform the model, but to determine if there is anything external to the model which factors in decision making to select one device over another for use. No change made to report.
2.	Essity	9	4	The clinical group recognise different types of dressings are needed with medicated and non medicated dressings the exclusion of DACC from the economic model does not reflect current clinical practice Users also said that antimicrobial dressings can be medicated, with an active agent such as silver, iodine or honey or non-medicated, such as those coated with Dialkylcarbamoyl chloride (DACC).	Thank you for your comment. The reasons for DACC not being included in the modelling are described in sections 7.2.3.2 and 7.3.1.1 of the external assessment report. No change made to report.
3.	Essity	6	3.3	Patient feedback is essential and not included in any documents – how has the decision been made with no user input ?	Thank you for your comment. No decision has been made at this point in time (December 2024). Recommendations will

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
					be made by the committee on 16th January 2025. There are two specialist committee members who have relevant lived experience and NICE are conducting a survey of people with lived experience. The user preference assessment focuses on those who are making the decision to select on technology over another. The question of who this is was put to all stakeholders during scoping, and the groups identified were deemed appropriate. Feedback received from stakeholders was that people with ulcers, while involved in discussions, were not the main decision makers in selecting which AMD to use.
4.	Urgo	6	4	District nurses, practice nurses, tissue viability nurses, specialist clinic nurses and vascular nurses were identified as user for the user preference assessment. There are no practice nurses within the group of 15 that formed the user assessment group. How will the practice nurse user view be considered and incorporated within the user assessment report?	Thank you for your comment. This has now been added as a limitation to the report.
5.	Urgo	8	2	The decision to include contraindications in the IFU does not allow significant enough consideration to this factor. In	Thank you for your comment. This part of the report describes the consensus opinion of the users. further

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				particular an iodine dressing this year has changed it's IFU so it is now contra-indicated for patients with renal disease and any thyroid disease which will make this dressing inappropriate for a large proportion of the patient pool. See comments and information provided in Section A Comment no. 7	detail to the users' discussion cannot be added retrospectively. No change made to the report
6.	Coloplast	6	3.3	Coloplast is concerned that, if the patient survey forms part of the evidence presented to the committee, stakeholders should be given the opportunity for factual accuracy checking. Please can this be incorporated into the report's development?	Thank you for your comment. NICE has developed a survey for people with lived experience of leg ulcers and AMDs. Headline results of this will be incorporated into the user preference report and supplied to committee ahead of the committee meeting for their consideration. Full details of the survey will be presented to committee in the slides. As the results of the survey will be reporting the experiences and opinions of people with lived experience these are not subject to factual accuracy checking. No change made to the report.
7.	Coloplast	21	6	The conclusions on the ranking, weighting and performance rules for the criteria which were considered to be independent of clinical presentation cannot be considered to be factually complete or	Thank you for your comment. The user preference assessment focuses on those who are making the decision to select on technology over another. The question of who this is was put to all stakeholders

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				accurate because no patients were included in the user sample. This limits the value of the evidence and should be more prominently and strongly reflected both in the limitations section of the report and when the data are presented to the committee.	during scoping, and the groups identified were deemed appropriate. Feedback received from stakeholders was that people with ulcers, while involved in discussions, were not the main decision makers in selecting which AMD to use. However, there are two specialist committee members who have relevant lived experience and NICE are conducting a survey of people with lived experience. No change made to the report.
8.	Coloplast	26	Appendix D	List of participants Given the specificity of the topic, it would be relevant to include a microbiologist.	Thank you for your comment. Please responses to comments 3 and 7 which already discuss how users were defined and identified for this user preference assessment. No change made to the report.
9.	Smith & Nephew	13	Table 3.	We would have expected to see a criteria specific to dose and release of AMD which can effect wear time. These criteria should seek input from larger number of clinical experts involved in infected wound management where broader consensus should be sought.	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to add extra criteria retrospectively. No change made to the report
10.	Convatec	4	2	Background could benefit from describing what AMDs are indicated for, i.e., for	Thank you for your comment. It is stated in the introduction that the user preference

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				infected wounds and wounds at risk of infection, e.g., three commonly used AMDs: "**INADINE**™ Dressing is designed to protect the wound, even if infected. INADINE™ Dressings can be used for the management of ulcerative wounds and may also be used for the prevention of infection in minor burns and minor traumatic skin loss injuries. In heavily infected wounds, it may also be used in conjunction with systemic antibiotics" "**ACTICOAT** helps to minimise infection. Prophylactic use of ACTICOAT Dressings helps to prevent infection. Early intervention as part of an infection management protocol has been shown to reduce the risk of progression to infection." "**Aquacel™ Ag+ EXTRA**™ Dressings… for wounds, which are at risk of infection or show signs of infection, or where biofilm is suspected to be present"	report should be read alongside the external assessment report. This external assessment report contains a detailed description of the technologies under assessment. No change made to the report.
11.	Convatec	7 and 11	4	**"cytotoxicity of antimicrobial agent"**	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				Cytotoxicity can only be confirmed in the laboratory, so is not a criterion related to clinical presentation.	possible to change or add details retrospectively. No change made to the report.
12.		11	4 Table 11	**"Cytotoxicity of antimicrobial agents that are absorbed systemically, e.g. silver, iodine"** Cytotoxicity and systemic toxicity are different things. Not all antimicrobial agents may be absorbed systemically. E.g., of the low amounts of ionic silver that are released into gelled dressing when H_2O molecules replace some Ag^+ ions from the silver sodium CMC dressing in Aquacel Ag+ Extra, some Ag^+ ions actually re-bind to the CMC, some Ag^+ ions react with proteins in wound fluid and tissues that have been taken up into the gelled dressing, some react Ag^+ ions with negatively charged anions (e.g., Cl^-) to form the inactive silver chloride (AgCl), and some obviously are taken up into microbial cells and react with cellular components, rendering the Ag^+ ions inactive. That is, most ionic silver does not leave the gelled dressing, and any that does will further react with proteins, anions and microorganisms (for which Ag^+	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. No change made to the report.

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				ions have affinity for due to the negatively charged peptidoglycan cell wall) in the local wound environment.	
13.	Convatec			**"although 1 user commented that it would be unusual to leave a dressing on for as long as 7 days"** Yet as part of the cost-effectiveness analysis on p174-175 of the main document, 1 dressing change per week was used for silver salts and compounds, honey, PHMB and copper AMDs.	Thank you for your comment. This is related to external assessment group's assumptions on the frequency of dressing changes in the model. Queries on the assumptions made on frequency of dressing changes are included in the comments on the external assessment group's report. No change made to the report.
14.	Convatec	22	Criterion 1: Conformability	Omission of a criterion related to use and performance of dressing under compression. Relevant given the scope and high ratio of patients who would be clinical prescribed compression therapy (as cited on P25)	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to add extra criteria retrospectively. However, the use of compression products was discussed under criterion 4. No change made to the report.
15.	Convatec	27-29	Criterion 5: Sustainability	Whilst of positive intent, clarity is sought re how the criterion can be measured and recorded? Eg: 'Is the dressing Biodegradable'? 'Is it toxic when the dressing is burnt?' These aspects of dressing design are dependent upon raw materials used and EU	Thank you for your comment. The performance rules are developed by consensus opinion of the participants. The user preference report details these discussions as much as possible. The terms 'biodegradable' or 'toxic' were those used by the participants, which they

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				Regulation related to use of such materials.	deemed to be measurable as binary measures. It is not possible to amend these retrospectively. No change made to the report.
16.	Convatec	29	Table 4 performance matrix	Whist many performance questions may be suitable for binary measure, there still remains the matter of subjectivity and reliance upon interpretation by user/reader. Eg Ease of removal; Does the dressing cause peri-wound stripping or irritation? (Y/N): any visual evidence of skin irritation may indeed be due to exudate toxicity on peri wound skin and not caused by dressing design. One of many examples within the table.	Thank you for your comment. The performance rules are developed by consensus opinion of the participants. It is not possible to amend the performance rules retrospectively. No change made to the report.

NICE National Institute for Health and Care Excellence

Advisory Committee Interests Register

Topic: Topical antimicrobial dressings for infected leg ulcers in people aged 16 and over: Late stage assessment

NICE's declaration of interest policy can be accessed here

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Kathryn Morgan	Specialist Committee Member	Financial Interest	NIL	-	14/05/2024	-	No action other than open declaration
Kathryn Morgan	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	14/05/2024	-	No action other than open declaration
Kathryn Morgan	Specialist Committee Member	Indirect Interest	NIL	-	14/05/2024	-	No action other than open declaration
Jane Todhunter	Specialist Committee Member	Financial Interest	CEMAG advisory board	May 2024	08/05/2024	Ongoing	No action other than open declaration
Jane Todhunter	Specialist Committee Member	Financial Interest	OVIK Research studies	Oct 2023	08/05/2024	Ongoing	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Jane Todhunter	Specialist Committee Member	Non-Financial Professional and Personal Interest	Vascular & Venous All Party Parliamentary Group	2023	08/05/2024	Ongoing	No action other than open declaration
Jane Todhunter	Specialist Committee Member	Non-Financial Professional and Personal Interest	Co -PI Dressing Trial	April 2024	08/05/2024	Ongoing	No action other than open declaration
Jane Todhunter	Specialist Committee Member	Indirect Interest	NIL	-	08/05/2024	-	No action other than open declaration
Jo Dumville	Specialist Committee Member	Financial Interest	NIL	-	31/05/2024	-	No action other than open declaration
Jo Dumville	Specialist Committee Member	Non-Financial Professional and Personal Interest	Published research in field and member of University	2003	31/05/2024	Ongoing	No action other than open declaration
Jo Dumville	Specialist Committee Member	Indirect Interest	NIL	-	31/05/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Lindsay Banks	Specialist Committee Member	Financial Interest	NIL	-	03/06/2024	-	No action other than open declaration
Lindsay Banks	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	03/06/2024	-	No action other than open declaration
Lindsay Banks	Specialist Committee Member	Indirect Interest	Chair of Wound Care Formulary Group, Bridgewater Community Healthcare NHS Trust	2020	03/06/2024	Ongoing	No action other than open declaration
Priti Bhatt	Specialist Committee Member	Financial Interest	NIL	-	05/06/2024	-	No action other than open declaration
Priti Bhatt	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	05/06/2024	-	No action other than open declaration
Priti Bhatt	Specialist Committee Member	Indirect Interest	NIL	-	05/06/2024	-	No action other than open declaration
Sam Lane	Specialist Committee Member	Financial Interest	NIL	-	05/06/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Sam Lane	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	05/06/2024	-	No action other than open declaration
Sam Lane	Specialist Committee Member	Indirect Interest	NIL	-	05/06/2024	-	No action other than open declaration
Sarah Marquis	Specialist Committee Member	Financial Interest	NIL	-	04/06/2024	-	No action other than open declaration
Sarah Marquis	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	04/06/2024	-	No action other than open declaration
Sarah Marquis	Specialist Committee Member	Indirect Interest	NIL	-	04/06/2024	-	No action other than open declaration
Stacey Evan-Charles	Specialist Committee Member	Indirect Interest	NIL	-	22/05/2024	-	No action other than open declaration
Stacey Evan-Charles	Specialist Committee Member	Financial Interest	NIL	-	22/05/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Stacey Evan-Charles	Specialist Committee Member	Non-Financial Professional and Personal Interest	NIL	-	22/05/2024	-	No action other than open declaration
Kate Hawley	Lay Member	Indirect Interest	NIL	-	30/04/2024	-	No action other than open declaration
Kate Hawley	Lay Member	Financial Interest	NIL	-	30/04/2024	-	No action other than open declaration
Kate Hawley	Lay Member	Non-Financial Professional and Personal Interest	NIL	-	30/04/2024	-	No action other than open declaration
Elizabeth McCall	Lay Member	Financial Interest	NIL	-	04/06/2024	-	No action other than open declaration
Elizabeth McCall	Lay Member	Non-Financial Professional and Personal Interest	NIL	-	04/06/2024	-	No action other than open declaration
Elizabeth McCall	Lay Member	Indirect Interest	NIL	-	04/06/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Kate Williams	Professional Expert	Financial Interest	NIL	-	23/05/2024	-	No action other than open declaration
Kate Williams	Professional Expert	Non-Financial Professional and Personal Interest	Trustee for the Society of Tissue Viability (registered charity)	2018	23/05/2024	Ongoing	No action other than open declaration
Kate Williams	Professional Expert	Indirect Interest	NIL	-	23/05/2024	-	No action other than open declaration
Ayesha Marshall	Professional Expert	Financial Interest	Investigation work for TMLEP to provide reports for breach of duty and causation for pressure ulcers	June 2022	26/07/2024	Ongoing	No action other than open declaration
Ayesha Marshall	Professional Expert	Non-Financial Professional and Personal Interest	Trustee for the Society of Tissue Viability	June 2022	26/07/2024	Ongoing	No action other than open declaration
Ayesha Marshall	Professional Expert	Indirect Interest	NIL	-	26/07/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Clare Greenwood	Professional Expert	Financial Interest	NIL	-	18/07/2024	-	No action other than open declaration
Clare Greenwood	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	18/07/2024	-	No action other than open declaration
Clare Greenwood	Professional Expert	Indirect Interest	NIL	-	18/07/2024	-	No action other than open declaration
Emma Mallinson	Professional Expert	Financial Interest	NIL	-	13/08/2024	-	No action other than open declaration
Emma Mallinson	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	13/08/2024	-	No action other than open declaration
Emma Mallinson	Professional Expert	Indirect Interest	NIL	-	13/08/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Keira Bradley	Professional Expert	Financial Interest	NIL	-	06/08/2024	-	No action other than open declaration
Keira Bradley	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	06/08/2024	-	No action other than open declaration
Keira Bradley	Professional Expert	Indirect Interest	NIL	-	06/08/2024	-	No action other than open declaration
Keith Moore	Professional Expert	Financial Interest	NIL	-	13/07/2024	-	No action other than open declaration
Keith Moore	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	13/07/2024	-	No action other than open declaration
Keith Moore	Professional Expert	Indirect Interest	NIL	-	13/07/2024	-	No action other than open declaration
Lisa Hill	Professional Expert	Financial Interest	NIL	-	07/08/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Lisa Hill	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	07/08/2024	-	No action other than open declaration
Lisa Hill	Professional Expert	Indirect Interest	Member of the Society of Tissue Viability	Approx. 2019	07/08/2024	Ongoing	No action other than open declaration
Lisa Hill	Professional Expert	Indirect Interest	Member of the North East TVNA Group	Approx 2015	07/08/2024	Ongoing	No action other than open declaration
Lucy Cook	Professional Expert	Financial Interest	NIL	-	23/07/2024	-	No action other than open declaration
Lucy Cook	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	23/07/2024	-	No action other than open declaration
Lucy Cook	Professional Expert	Indirect Interest	NIL	-	23/07/2024	-	No action other than open declaration
Mikyung Bailey	Professional Expert	Financial Interest	NIL	-	26/07/2024	-	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Mikyung Bailey	Professional Expert	Non-Financial Professional and Personal Interest	NIL	-	26/07/2024	-	No action other than open declaration
Mikyung Bailey	Professional Expert	Indirect Interest	NIL	-	26/07/2024	-	No action other than open declaration