Introduction
The antibacterial properties of silver (Ag) have been known for centuries. The increasing problems of antibiotic resistance, along with concerns about the safety and toxicity of topical antiseptics, has resulted in the need for an agent that can be used to treat colonised and infected wounds effectively. The presentation of silver in advanced wound care dressings has been found to be effective against bacterial, fungal and viral pathogens. This article describes two sustained-release silver product ranges ACTICOAT and ALLEVYN Ag (Smith & Nephew), which can be used to help prevent and reduce the risk of infection in a variety of wounds.

Authors: Roberts C, Ivins N, Widgerow A. Full author details can be found on page 5.

What is the role of sustained release silver dressings?
Recognising and managing wounds at risk of infection is vital for optimal wound management. Patients may present with minor symptoms such as pain, swelling or discharge, or more major life-threatening conditions such as sepsis. Wounds, particularly chronic wounds, support a variety of micro-organisms, many of which are pathogens, acting as a source for cross-infection. Such micro-organisms also provoke an increase in exudate and malodour.

Dressings are needed that provide an effective barrier together with a sustained release of an antimicrobial agent, such as silver, to reduce the bioburden throughout the dressing wear time, while providing limited opportunity for systemic absorption. The sustained release of effective levels of ionic silver over a period of time also removes the need for frequent dressing changes, with potential cost savings.

What amounts of silver are effective?
All topical silver products, regardless of their formulation (eg silver nitrate solution, silver sulfadiazine cream or dressings containing elemental or ionised silver), only exert antimicrobial effects when they release the ionic form of silver (Ag+). This usually occurs when the dressing comes into contact with wound fluid.

It is important to recognise that the amount of silver released from a wound dressing (bio-availability) will be different to the amount highlighted on the packaging of silver dressings. It has not been possible to measure bio-available levels, but it has been suggested that at least 20-40 parts per million (ppm) are required to be microbiologically effective (see box below).

What factors affect product choice?
When choosing an appropriate antimicrobial dressing, the priority should be to regain control of bacterial growth. In addition to reducing bacterial load, clinicians need to consider how different antimicrobial products support moist wound healing, manage exudate levels and assist wound bed preparation. Specific products should be chosen to reflect the overall requirements of the wound following a thorough wound assessment.

Two such products ACTICOAT and ALLEVYN Ag are considered here for use as topical antimicrobials in patients with full and partial thickness wounds where the wound is at risk of infection, showing early signs of local infection or where increased bacterial bioburden is suspected.

What is ACTICOAT?
The ACTICOAT range of antimicrobial barrier dressings includes ACTICOAT, ACTICOAT 7, ACTICOAT Absorbent and more recently ACTICOAT Flex 3 and 7, and ACTICOAT Site (see Table 3). A number of these dressing have absorptive capabilities but all of the dressings utilise SILCRYST™ technology, which provides fast-acting antimicrobial action. This technology was developed specifically to form the dressing interface that comes into direct contact with the wound surface (Box 1).

How does ACTICOAT work?
The SILCRYST silver layer in ACTICOAT, which comes into contact with the wound surface, is a highly soluble form of silver. These tiny crystals provide a larger surface area of silver than other silver technology systems and have a greater contact with the wound, releasing a highly effective concentration of silver over a sustained time period. This feature ensures that bacteria are killed rapidly and consistently over time.

Why is parts per million important?
PPM equals ‘parts per million’ and is a measure of concentration (ppm is also the same as milligrams per litre). PPM is important because in order to kill microbes effectively, the silver must be present in adequate concentrations (eg > 20ppm). If bacteria are not killed rapidly, there is the chance that they may survive and eventually become resistant to the silver. However, the clinical incidence of silver resistance remains low and, to date, has not been repeated through the clinical use of modern day silver dressings.
ACTICOAT™ AND ALLEVYN™ Ag made easy

ACTICOAT dressings release the positively charged silver ion (Ag⁺). SILCRYST silver also contains Ag⁺ which is present in the tiny atomic clusters and can be solubilised. This acts as a form of ‘back-up battery’ to replenish Ag⁺ to maximise effective kill. Additional data suggest that as a result of this antimicrobial action ACTICOAT may be responsible for modulating protease activity to promote healing. SILCRYST silver starts to work in as little as 30 minutes, which is particularly important for infected wounds in high-risk patients or wounds at high risk of infection.

**Box 1: SILCRYST Technology**

During manufacture, advanced processes are used to deposit extremely small clusters of water-soluble silver crystals onto the surface of the ACTICOAT dressing.

When ACTICOAT is moistened with sterile or drinking water and placed on the wound these small atomic clusters, which are very porous, rapidly release and replenish concentrations of silver ions at sufficient levels (in-vitro). This ensures that ionic silver is instantly provided in sustainable levels to reduce the levels of bacteria on the wound surface and in the surrounding tissue.

The small size of the crystals also ensures a large surface area is available for antimicrobial activity. SILCRYST technology appears to give the highest, sustained release of silver to a wound without apparent risk of toxicity.

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**Table 1 Summary of in-vivo evidence for ACTICOAT™ products**

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Title</th>
<th>Type</th>
<th>Purpose</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tredget EE et al. J Burn Care Rehabil 1998; 19(6): 531-7.</td>
<td>A matched-pair, randomised study evaluating the efficacy and safety of ACTICOAT silver-coated dressing for the treatment of burn wounds</td>
<td>Matched pair randomised, prospective study (n=30)</td>
<td>To assess the efficacy and ease of use of ACTICOAT dressing compared with the efficacy and ease of standard burn wound care (silver nitrate solution dressings)</td>
<td>Patients found dressing removal less painful with ACTICOAT than with silver nitrate. There was no statistically significant difference in the ease of use. The frequency of burn wound sepsis and secondary bacteraemia arising from infected wounds were less in the ACTICOAT group</td>
</tr>
<tr>
<td>Cuttle L et al. Burns 2007; 33(6): 701-7.</td>
<td>A retrospective cohort study of Acticoat versus Silvazine in a paediatric population</td>
<td>Retrospective cohort study examining 128 Silvazine-treated patients from January 2000 to June 2001 and 241 ACTICOAT-treated patients from July 2002 to July 2003</td>
<td>To assess whether using ACTICOAT instead of Silvazine as first-line burns dressing provided a better standard of care in terms of efficacy, cost and ease of use</td>
<td>In the Silvazine group, 25.6% of children required grafting compared to 13.4% in the ACTICOAT group (p=0.001). Time taken for re-epithelialisation in the ACTICOAT group (14.9 days) was significantly less than that for the Silvazine group (18.3 days), p=0.047</td>
</tr>
<tr>
<td>Fong J et al. Burns 2005;31(5): 562-7.</td>
<td>A silver-coated dressing reduces the incidence of early burn wound cellulitis and associated costs of inpatient treatment: comparative patient care audits</td>
<td>Two ‘before and after’ patient care audits</td>
<td>To compare the effectiveness and cost of Silvazine (silver sulphadiazine and chlorhexidine digluconate cream) and ACTICOAT for in-patient treatment of early burn wounds</td>
<td>Using ACTICOAT the incidence of infection and antibiotic use fell from 55% (28/51) and 57% (29/51) in 2000 to 10.5% (2/19) and 5.2% (1/19) in 2002. Total burn costs and inpatient stay were also reduced</td>
</tr>
<tr>
<td>Sibbald RG et al. Adv Skin Wound Care 2007; 20(10):549-58.</td>
<td>Bacteriology, inflammation, and healing: a study of nanocrystalline silver dressings in chronic venous leg ulcers</td>
<td>Case series with bacterial count (biopsy) monitoring and histological analyses (n=12)</td>
<td>To determine the effects of a nanocrystalline silver barrier dressing on wound microflora, wound inflammation, and healing in chronic venous leg ulcers</td>
<td>Healing was associated with a significant reduction in bacteria and neutrophilic inflammation with an associated persistent high lymphocyte count, as determined by wound biopsy</td>
</tr>
<tr>
<td>Childress BB et al. Ann Vasc Surg 2007; 21(5): 598-602.</td>
<td>Impact of an absorbent silver-eluting dressing system on lower extremity revascularisation wound complications</td>
<td>Non-concurrent cohort study in patients undergoing leg revascularisation</td>
<td>To assess whether immediate application of ACTICOAT would reduce wound complications in patients undergoing leg revascularisation compared to controls</td>
<td>Wound complications fell 64% in patients receiving the ACTICOAT dressing protocol (control 14% [17/118], treatment 5% [7/130]; p = 0.016)</td>
</tr>
<tr>
<td>Gago M et al. Wounds 2008; 20: 273-8.</td>
<td>A comparison of three silver-containing dressings in the treatment of infected chronic wounds</td>
<td>Prospective, comparative clinical trial n=40</td>
<td>To compare three types of silver dressing, looking at time to resolution of clinical signs of local infection and wound healing progress over eight weeks</td>
<td>Clinical signs of infection were resolved faster (p&lt;0.05) and wounds healed more quickly (p&lt;0.05) in the ACTICOAT group than in the other two groups (Aquacel Ag [Convatec] and Comfeel Ag/Biatain Ag, [Coloplast])</td>
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</table>
This provides exudate management combined with sustained antimicrobial protection for up to seven days. ALLEVYN Ag is available in a wide range of sizes and formats (see Table 3). ALLEVYN Ag Adhesive is designed to provide extra security of retention where fixation is important, while ALLEVYN Ag Non-Adhesive offers a versatile option that can be cut and shaped for wounds and patients where an adhesive-free dressing is preferred. In addition ALLEVYN Ag Heel and Sacrum provide bespoke dressings for an improved fit on awkward-shaped areas. The ALLEVYN Ag Gentle range is designed to minimise pain and trauma on dressing removal for patients with fragile skin. SSD has been used as a topical antimicrobial agent in burns and other wound types for more than half a century. It is well documented to be effective against a broad spectrum of common wound pathogens.

How does ALLEVYN™ Ag work?

The dressing properties are designed to ensure that a moist wound environment is maintained. Excess exudate is absorbed into the hydrocellular foam core. As exudate reaches the top of the dressing, it evaporates through the breathable film layer. In turn, this increases the dressing’s moisture vapour transmission rate as exudate builds up to prevent the dressing from becoming saturated and reduces the risk of periwound skin maceration or leakage from occurring.

SSD particles are incorporated within the cellular structure of the central absorbent polyurethane foam layer of the dressing. As the exudate is absorbed into this central layer away from the wound, the antimicrobial activity of the dressing is triggered. This results in the release of positively charged silver ions at concentrations greater than 40ppm for up to seven days.

When to use ACTICOAT?

ACTICOAT can be used as an antimicrobial barrier layer for partial and full-thickness wounds such as burns and recipient graft sites, pressure ulcers, diabetic foot ulcers and venous leg ulcers that are judged to be at risk from infection.

ACTICOAT should not be used:
- On patients with known sensitivity to silver
- During radiation therapy (current dressing should be removed prior to therapy and a new dressing applied post treatment)
- On patients undergoing magnetic resonance imaging (MRI) examination.

For further product information, see Useful links on page 5.

What evidence is there to support the use of ACTICOAT?

In-vivo, ACTICOAT has been shown to reduce bacteria in chronic leg ulcers and reduce both infection rates and signs and symptoms of infection (see Table 1). In addition, there are a number of in-vitro studies to assess the antimicrobial efficacy of ACTICOAT. These have demonstrated an ability to reduce the bioburden and to be effective against a broad range of bacteria.

In addition, it has been shown to have a faster killing rate when compared to silver nitrate solution and silver sulfadiazine. It has also been shown to be effective against fungi.

What is ALLEVYN Ag?

ALLEVYN Ag is a highly absorbent antimicrobial foam dressing, which consists of an absorbent foam layer containing silver sulfadiazine (SSD), a perforated wound contact layer and a breathable top film.

ACTICOAT Flex 3 case report

A 22-year-old man presented with a large ulcer (Fig 1) to the medial malleolus on his left leg. Treatment included debridement, hydofibre dressing and multilayer compression bandaging. There had been no improvement in the ulcer over the previous two years, with the ulcer increasing in size.

The patient had chronic venous disease and was receiving hospital care for a wound biopsy and scan. The patient complained of increased pain and the ulcer showed signs of clinical infection with erythema, malodour and increased exudate. A referral was made to the tissue viability team.

Treatment

ACTICOAT Flex was used as a primary dressing to eliminate odour and PROFORE™ (Smith & Nephew) multilayer compression bandaging was applied.

Results

An improvement was seen after 3 weeks (Fig 2). The patient was discharged under the care of the leg ulcer clinic. At four months following referral to the tissue viability team, the wound was healed.

When to use ALLEVYN Ag?

This dressing can be used in the management of infected, exuding chronic and acute full or partial thickness or shallow granulating, exudating wounds such as pressure ulcers, venous ulcers, diabetic ulcers, burns, donor sites, fungating/malignant wounds and surgically dehisced wounds.

ALLEVYN Ag should not be used:
- On patients with known sensitivity to silver sulfadiazine or sulphonamides
- On women who are at, or near term pregnancy or lactating
- On premature infants or newborn infants during the first months of life.

For further product information, see Useful links on page 5.

What evidence is there to support the use of ALLEVYN Ag?

An in-vivo study by Kotz et al\(^{17}\) found ALLEVYN Ag to achieve a significant reduction in the percentage of patients presenting with clinical signs of infection from initial to final assessment, together with a significant reduction in the wound area and level of exudate present.

A recent prospective study by Lantis and Gendics using ALLEVYN Ag demonstrated a 45.8% closure rate within a cohort of patients with hard to heal leg ulcers\(^{34}\). This was deemed to compare favourably with previously published wound closure rates with active agents. This benchmark study also achieved a significant reduction in bioburden, a significant decrease in the level of pain and a good level of patient concordance. Dressings were changed on average every seven days (compared to standard dressing frequency of 2.7 days)\(^{15}\).

In-vivo ALLEVYN Ag has shown a broad spectrum of bactericidal activity against gram positive and gram negative bacteria, antibiotic resistant strains, anaerobes, fungi and yeast within 24 hours\(^{35,37}\).

When should treatment be stopped?

Treatment with ACTICOAT or ALLEVYN Ag should be stopped when the wound bed appears healthy and signs of infection have resolved. Regular re-assessment of the wound should be undertaken by a suitably qualified clinician to ensure that the dressing is appropriate and discontinued at the appropriate time — ie when the infection has resolved — this should be within 10–14 days of the start of treatment.

If a chronic wound with localised infection shows no improvement after 10-14 days, it is important to re-evaluate the patient and the wound, which may necessitate a change to the management plan\(^{17}\).

What are the cost benefits of using ACTICOAT or ALLEVYN Ag?

Evidence from clinical trials and case reports suggest that the use of ACTICOAT is cost-effective\(^{36,39}\). The longer wear times associated with both ACTICOAT and ALLEVYN Ag compared with standard therapy\(^{16,37}\), may offer potential cost savings in terms of resource use and nursing time.

This is supported by a clinical evaluation of ALLEVYN Ag on 25 patients in an Accident and Emergency department. Interpretation of the data suggests a cost saving of 40 euros per week. Dressing changes were also reduced by 1.6 per week, resulting in 160 minutes of saved nursing time per 10 patients treated with ALLEVYN Ag\(^{36}\).

Similarly, in a comparison of three silver-containing dressings, ACTICOAT was shown to resolve the clinical signs of infection faster (p<0.05) and heal wounds more quickly (p<0.05), reducing length of treatment and number of dressings used\(^{41}\).

<table>
<thead>
<tr>
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<th>Purpose</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Kotz P et al. Int Wound J 2009; 6(3): 186-94.</td>
<td>Use of a new silver barrier dressing ALLEVYN Ag in exuding chronic wounds</td>
<td>Multicentre case series (n=126)</td>
<td>To assess the performance of ALLEVYN Ag (Adhesive, Non Adhesive and Sacrum dressings) in a range of indications</td>
<td>Clinicians rated the dressings as acceptable for use in various wound types in 88% of patients. The majority of clinical signs of infection reduced between the initial and the final assessment. The condition of wound tissue and surrounding skin was observed to improve, and there was significant evidence of a reduction in the level of exudate from initial to final assessment (p &lt; 0.001). Clinicians rated ALLEVYN Ag as satisfying or exceeding expectations in over 90% of patients</td>
</tr>
<tr>
<td>Lantis J and Gendics C. J Wound Care 2011; 20(2): 90-6.</td>
<td>In-vivo effect of sustained release silver sulfadiazine foam on bioburden and wound closure in infected venous leg ulcers</td>
<td>Single centre prospective case series (n=24)</td>
<td>To address the lack of data on in vivo efficacy of topical antibacterials in the treatment of VLU. To provide a benchmark for the treatment of the hard to heal ulcer</td>
<td>A 45.8% closure rate reported within 80.5 day median treatment duration. There was a statistically significant (p&lt;0.001) reduction in wound bioburden by week eight. There was also a significant reduction (p&lt;0.001) in pain in the last week and exudate burden by week eight. There was also a significant reduction (p&lt;0.001) in pain in the last week and exudate burden by week eight.</td>
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ALLEVYN Ag case report

A 65-year-old woman presented with a venous ulcer on the lower leg, which had been present for eight weeks with no progression. It measured 90cm² and had the following clinical signs and symptoms of infection: discoloured granulation tissue, local erythema, malodour and heavy exudate (Fig 1). The patient also complained of increasing levels of pain and found the wound very painful.

Treatment

The primary aim was to treat the signs and symptoms of infection. The secondary aims were to manage the exudate and improve the patient’s quality of life by reducing her pain level. ALLEVYN Ag Non-Adhesive was applied under PROGUIDE™ (Smith & Nephew) two-layer compression bandage system.

Results

The patient found the dressing comfortable and she experienced less pain. Her flabby surrounding the ulcer remained intact on dressing removal and there was no pseudomembrane present. The exudate level reduced from heavy to light and all signs and symptoms of infection were eradicated within two weeks. The wound decreased in size rapidly, reducing from 90cm² to 45cm² in two dressing changes. The wound went on to fully heal in less than six weeks.


References

31. Myers D. The clinical and physical properties of ALLEVYN Ag Gentle Border dressings and the moist wound environment, April 2009.

Useful links

For further information on ACTICOAT range go to: http://global.smith-nephew.com/master/ACTICOAT_27517.htm

For further information on ALLEVYN Ag range go to: http://wound.smith-nephew.com/uk/Standard.asp?ModeId=3774

Author details

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Fig 1: On presentation

Fig 2: At six weeks
Table 3 List of products in the ACTICOAT and ALLEVYN AG ranges. For full product information and instructions for use go to: global.smith-nephew.com

<table>
<thead>
<tr>
<th>Product</th>
<th>Silver type/content</th>
<th>Method of use</th>
<th>Frequency of change</th>
<th>When to use</th>
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</thead>
<tbody>
<tr>
<td>ACTICOAT and ACTICOAT 7</td>
<td>High density dressing comprising two or five layers with an absorbent inner core sandwiched between outer layers of SILCRYST silver coated, low adherent polyethylene net</td>
<td>Before application moisten with water (not saline). Dressing can be cut to size. Apply either side down and secure with a secondary dressing</td>
<td>ACTICOAT can be left in place up to three days. ACTICOAT 7 can be left in place for up to seven days. Secondary dressing may be changed more frequently. Soak the primary dressing to facilitate removal if necessary</td>
<td>FOR LOW TO MODERATELY EXUDING WOUNDS, including partial and full thickness wounds (eg pressure ulcers, leg ulcers, diabetic foot ulcers and burns)</td>
</tr>
<tr>
<td>ACTICOAT Absorbent</td>
<td>Calcium alginate dressing utilising SILCRYST silver technology</td>
<td>Do not moisten. Cut to the appropriate size and shape. Place in wound bed and secure with secondary dressing</td>
<td>Replace up to every seven days depending on exudate level. Remove dressing when saturated with exudate. If necessary, soak the primary dressing to facilitate removal</td>
<td>FOR MODERATE TO HIGHLY EXUDING WOUNDS, including pressure ulcers, venous leg ulcers, diabetic foot ulcers, burns, recipient graft sites and cavity wounds</td>
</tr>
<tr>
<td>ACTICOAT Flex 3 and ACTICOAT Flex 7</td>
<td>Conformable dressing comprising low adherent polyester layer coated with SILCRYST silver</td>
<td>Without stretching the dressing, apply either side down, ensuring no creases. If the wound is dry or minimal exudate, moisten with water (not saline). Apply a secondary dressing (eg hydrogel)</td>
<td>ACTICOAT Flex 3 can be left in place up to three days. ACTICOAT Flex 7 can be left in place up to seven days. The dressing should be changed depending on amount of exudate and condition of wound. When used under compression, check the entire dressing system and change if strike-through occurs</td>
<td>FOR LOW TO MODERATELY EXUDING WOUNDS, including pressure ulcers, venous leg ulcers, diabetic foot ulcers, burns, recipient graft sites and surgical sites. It can also be used with negative pressure wound therapy</td>
</tr>
<tr>
<td>ACTICOAT Site</td>
<td>Absorbent three-layer dressing comprising SILCRYST silver coated polyurethane wound contact layer, a white polyurethane foam layer and a blue waterproof polyurethane film layer</td>
<td>Ensure silver layer is in intimate contact with the insertion site and the blue side is away from the skin. The pre-cut slit must be placed near or under the inserted device and the edges of the slit must meet to allow full contact with the surrounding skin. Secure with a secondary retention dressing</td>
<td>ACTICOAT Site may be left in place for up to seven days, but more frequent dressing changes may be required if a strike-through of exudate occurs</td>
<td>For use around vascular and non-vascular percutaneous device sites, eg intravenous catheter insertion and external fixation sites. ACTICOAT Site may be used on infected insertion sites as per local clinical protocols</td>
</tr>
<tr>
<td>ALLEVYN Ag Non-Adhesive and ALLEVYN Ag Heel</td>
<td>Absorbent hydrocellular pad containing silver sulfadiazine sandwiched between a perforated non-adherent wound contact layer and a waterproof outer film</td>
<td>Apply with white face to the wound, ensuring good contact. Use retention sheet, tape or bandage to secure. May be used under compression. Can be cut to dress awkward areas or use ALLEVYN Heel to dress heels</td>
<td>Dressings may be left in place for up to seven days. Dressings should be changed when exudate is visible and approaches 0.5cm from the edge of the dressing pad</td>
<td>LIGHT TO MODERATELY EXUDING WOUNDS, including pressure ulcers, burns, surgical wounds and donor sites. Not suitable for use alone on cavity wounds</td>
</tr>
<tr>
<td>ALLEVYN Ag Adhesive and ALLEVYN Ag Sacrum</td>
<td>Absorbent hydrocellular pad containing silver sulfadiazine, sandwiched between a perforated adherent wound contact layer and a waterproof outer film</td>
<td>Remove protector material and anchor the dressing. When positioning ALLEVYN Ag Sacrum, place the narrow end of the dressing a minimum of 2cm above anal sphincter. Smooth the dressing in place. No secondary retention dressing required</td>
<td>Dressings may be left in place for up to seven days, except for the sacral area where dressings can be left for up to five days or until exudate is visible and approaches 0.5cm from the edge of the dressing pad</td>
<td>LIGHT TO MODERATELY EXUDING WOUNDS (as indicated for ALLEVYN Ag Non-Adhesive)</td>
</tr>
<tr>
<td>ALLEVYN Ag Gentle and ALLEVYN Ag Gentle Border</td>
<td>Soft gel and soft silicone gel adhesive dressings containing silver sulfadiazine</td>
<td>Remove protector material and apply adherent side to the wound ensuring good contact. Secure ALLEVYN Ag Gentle with tape or bandage. ALLEVYN Ag Gentle Border does not require secondary retention</td>
<td>Dressings may be left in place for up to seven days. Dressings should be changed when exudate is visible and approaches 0.5cm from the edge of the dressing pad</td>
<td>LIGHT TO MODERATELY EXUDING WOUNDS (as indicated for ALLEVYN Ag Non-Adhesive). Can be used on fragile skin or cut to fit awkward areas (eg heels)</td>
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</table>

Summary
Modern day silver releasing dressings are an important part of the antimicrobial armoury. Speed of bacterial kill and rapid availability and replenishment of the active Ag⁺ silver ions are important in achieving successful clinical outcomes. The ACTICOAT and ALLEVYN Ag ranges show good evidence of antimicrobial efficacy, reducing bacterial load in wounds and helping to prevent and reduce the clinical signs and symptoms of infection.

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