Introduction
Silver has considerable antimicrobial activity, even against many antibiotic-resistant strains of bacteria, and in recent years has increasingly been used in wound dressings to reduce bacterial bioburden. Silver may be incorporated into dressings in a number of different forms, most notably as elemental silver or in the ionic state. Ag⁺ is the ionic form, which has been demonstrated to have a broad antimicrobial effect. This document describes the mode of action, supporting evidence and practical application of a range of silver products (Askina® Calgitrol®), all of which contain ionic silver in the form of a patented silver alginate matrix.

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What is in the Askina® Calgitrol® range?
The Askina® Calgitrol® range comprises:
- Calgitrol® Ag
- Calgitrol® THIN
- Calgitrol® Paste.

Calgitrol® Ag
Calgitrol® Ag comprises two distinct layers. The primary wound contact layer is a patented silver alginate matrix that is laminated to a polyurethane foam layer. It has been shown that ionic silver is present in the dressing at a concentration of 141mg/100cm².

The matrix layer is a complex formulation that includes calcium and silver alginate combined with 10% bonded water. The primary function of the polyurethane foam layer is to increase the fluid handling capacity of the dressing and provide comfort.

Calgitrol® THIN
Calgitrol® THIN is composed of the same silver alginate matrix wound contact layer as Calgitrol® Ag. However, it does not have a polyurethane foam layer, making it much thinner while having the same antimicrobial efficacy as Calgitrol® Ag.

Calgitrol® THIN is identical on both sides of the dressing, with the ability to deliver ionic silver to a wound from both sides. It can be used to pack deep wounds, cavities or sinuses. In addition, the thinness of the dressing allows it to conform to irregularly shaped wounds or to wounds in awkward anatomical sites. Since the dressing is non-adhesive a secondary dressing is required to keep Calgitrol® THIN in place and to absorb exudate.

Calgitrol® Paste
Calgitrol® Paste is the newest product in the Calgitrol® range. It is an amorphous and homogeneous paste that conforms closely to the wound bed, helping to prevent any ‘dead spaces’ where bacteria may flourish. It is supplied sterile in a tube with a long cannula to aid application of the paste into tunnels, sinuses and awkward wound shapes. Calgitrol® Paste contains an average ionic silver concentration of 180mg/15g tube application.

How does Calgitrol® work?
The Calgitrol® range has been designed to deliver a controlled and sustained release of silver ions to the wound bed.

Silver ion release
When the Calgitrol® dressing or paste comes into contact with wound exudate, the fluid is absorbed into the alginate matrix. This is accompanied by a swelling and softening of the matrix, causing the silver and calcium alginate molecule to release the silver ions into the wound.

The dressings and paste retain a high concentration of silver ions within their molecular structure. As the silver ions at the wound bed surface are gradually depleted, further silver ions are drawn from within the dressing/paste. This leads to a constant diffusion of silver ions through the alginate matrix and into the wound bed, creating a steady state reaction where the concentration of silver in the wound bed is maintained by ongoing diffusion of silver ions through the alginate matrix.

Since the alginate matrix contains bonded water in its structure, wetting of the product prior to application is not necessary. In vitro experimentation has shown that the antimicrobial effect of Calgitrol® Ag commences within the first hour of dressing use due to the availability of ionic silver.

Antimicrobial effects of silver ions
While silver ions (Ag⁺) have long been known to have antimicrobial effects, silver in its elemental form (Ag⁰) does not. Silver ions have demonstrated a number of known bactericidal mechanisms. They:
- Disrupt the function of enzymes and proteins important for bacterial growth
- Directly damage the structure of the bacterial cell wall
- Interfere with bacterial DNA and RNA, so disrupting protein production and cell division

How much silver is released?
Diffusion of silver ions from the Calgitrol® Ag dressing has been shown in vitro to produce a steady state concentration of silver...
ions of about 60ppm (parts per million) over seven days (Figure 1)¹⁰; this data applies to all products in the Calgitrol® range. A minimum concentration of 20–40ppm has been suggested to be necessary for an antimicrobial effect¹¹,¹².

**How does Calgitrol® differ from other silver dressings?**

**Antibacterial efficacy**

Calgitrol® products contain a higher concentration of silver than most other silver dressings² (range from 546 to 1.6mg/100cm²). In a review of ten different silver dressings, Calgitrol® Ag displayed the highest performance in a range of in vitro tests of antimicrobial efficacy³. The authors concluded that this was due to the high levels of ionic silver in the dressing and the steady release of ions over time.

In vitro tests have confirmed that Calgitrol® Ag is active against a broad range of microorganisms, including the bacteria MRSA (methicillin-resistant Staphylococcus aureus) and Pseudomonas aeruginosa, and the yeast Candida albicans⁴,⁵,⁶.

**Ionic silver**

A number of silver-containing dressings require activation with water or saline prior to use for the release of silver ions to occur⁷. The Calgitrol® range contains silver in the ionic form, which is readily available due to the presence of bonded water and does not require activation with water or saline. From the first contact with the wound bed, silver ions are available and able to exert antibacterial action⁸.

**Moist wound environment**

Wounds produce varying levels of exudate. A dressing applied to a wound needs to be appropriately absorbent so that it prevents exudate leakage and avoids the need for frequent dressing changes. Some moisture in the wound bed is desirable to produce the moist wound environment that is needed to assist with the healing process. A balance is therefore required between absorbency of exudate and the maintenance of a moist wound environment.

Calgitrol® Ag includes a polyurethane foam backing that assists with fluid absorption, making the dressing suitable for moderately to highly exuding wounds. Absorption of exudate will also help to protect periwound skin from maceration. When compared with several other silver dressings, in vitro tests showed Calgitrol® Ag to have high moisture absorbency and to perform well in terms of moisture management⁹.

**Safety**

The Calgitrol® range delivers a steady release of silver ions to the wound bed over time. This avoids the too rapid release or 'dumping' of large amounts of silver, which may cause staining of the wound or periwound area.

An in vitro study of the biocompatibility of fibroblast cells and Calgitrol® Ag found no evidence that the dressing caused cell lysis or cytotoxicity¹°. In an animal study that used Calgitrol® Ag on a full thickness wound, serum silver levels were measured at day 1, 3 and 7 after dressing application. The highest serum level of silver found was 0.008ppm and was on day 7¹¹.

Animal studies have also shown that Calgitrol® Ag is associated with blood silver levels well below those known to induce hepatotoxicity and agrina-like symptoms¹²,¹³,¹⁴. A further study has found that Calgitrol® Ag does not cause skin discolouration, erythema or oedema¹⁵.

**When should Calgitrol® be used?**

Calgitrol® Ag and Calgitrol® THIN and Calgitrol® Paste are indicated for use in infected or critically colonised wounds, including:

- Category/Stage I-IV pressure ulcers
- Venous and arterial leg ulcers
- Second degree burns
- Donor sites

**Contraindications**

Calgitrol® dressings should not be used:

- If the patient has a known sensitivity to silver or alginates
- If the presence of metals is contraindicated, eg MRI scanning
- On wounds that have occurred as a result of syphilis, tuberculosis or deep fungal infection
- On third degree burns
- If the dressing packaging has been opened or damaged in anyway.

At present there are no contraindications for the use of silver dressings in paediatrics. To avoid inappropriate treatment, it is recommended that the manufacturer’s instructions are followed, together with best practice guidelines for wound management.
Step-by-step guide to application

The characteristics of the wound will guide which product to use (Table 1). Prior to application of the dressings or paste, cleanse the wound according to the local wound care protocol and wound type.

If a biofilm is suspected, the wound may be cleansed using a polyhexamethylene biguanide (PHMB) solution for 10–15 minutes prior to dressing application (eg Prontosan®). Prontosan® Gel X can also be applied to the wound bed for 1–2 days to help prevent biofilm reformation10.

Calgitrol® Ag

Select the appropriate size of dressing to completely cover the wound surface, extending 2–3cm beyond the wound edge. If necessary, several dressings can be overlapped to cover a large area

Apply the Calgitrol® Ag (the dark grey surface) touching the wound. No activation of the dressing is required.

Calgitrol® THIN

Once removed from the outer package, the dressing can be cut to size before removal of the protective layers. The dressing should overlap the wound margins by 2–3cm

Remove one of the protective layers and apply the exposed face of the dressing to the wound. No activation of the dressing is required (Figure 2)

Following application of the dressing, remove the second protective layer and apply an absorbent secondary dressing

To pack deeper wounds and tunnels, Calgitrol® THIN can be rolled and inserted into the wound. Calgitrol® THIN can also be used for the wounds in difficult-to-dress locations, where a good conformability is needed (eg on the heel, elbow, or shoulder).

Calgitrol® Paste

Shake the package to ensure the paste is well mixed

Apply a thick layer to the wound and cover with a suitable secondary dressing (eg Askina® SilNet), which will keep the paste in close contact with the wound. In the case of a diabetic foot ulcer a film dressing may be also used.

How often should Calgitrol® be changed?
The frequency of dressing changes depends on the level of exudate. This will be indicated by whether the dressing has reached saturation. Dressing changes should be performed when the dressing has reached its absorbent capacity or the matrix has completely gelled. Daily dressing changes may be required initially for infected wounds if exudate levels are particularly high. In a moderately exuding wound this may be reduced to every 2–3 days.

Calgitrol® Ag may be left in place for up to seven days. Calgitrol® Paste should be changed after each dressing change, which may be daily or up to every three days depending on the condition of the wound.

How should Calgitrol® be removed?
To remove Calgitrol® Ag gently lift it from the wound. If the dressing sticks to the wound bed, a cleansing solution will aid removal. After dressing removal, thoroughly cleanse the wound to remove any dressing residue.

Calgitrol® THIN will dissolve within 2–3 days of application into a dark coloured paste, which can be removed easily by washing the wound with sterile saline or an appropriate wound irrigation solution.

Calgitrol® Paste is removed by thoroughly cleansing the wound. Any patches of paste that have dried out may also be removed in this way.

When should Calgitrol® be discontinued?
The wound should be reviewed regularly and the dressing discontinued when exudate levels are minimal and/or an alternative dressing regimen is indicated. If there is evidence of infection, treatment with systemic antibiotics should be considered.
Use of Calgitrol® Ag in burns patients
Partial thickness burn wounds are challenging to manage. Significant associated problems that may precede wound infection include high levels of exudation, pain and delayed wound healing, which result in high resource usage.

Dressings used on partial thickness burns need to reduce the risk of wound infection and also manage exudate while keeping the wound moist. Calgitrol® dressings are non-adherent and may be removed in one piece without attachment to the wound bed. This can help to minimise trauma and pain at dressing changes.

A study of 65 outpatients with partial thickness burns (less than 24 hours post injury and a total body surface area of less than 15%) were randomised to treatment with Calgitrol® Ag (n=30) or 1% silver sulfadiazine (n=35). The patients treated with Calgitrol® Ag required significantly fewer dressing changes (p<0.02), significantly less nursing time (p<0.02), healed significantly faster (7 vs 14 days) and had significantly lower pain scores (p<0.02) compared to patients treated with silver sulfadiazine.

A study of patients with deep burns undergoing late necrectomy showed that by day 18 the microbiological burden in the wounds of patients treated with Calgitrol® Ag was reduced to a greater extent than that of patients treated with antiseptic ointment. Wound preparation for split skin grafting was significantly shorter for patients treated with Calgitrol® Ag than it was for those treated with the antiseptic ointment.

Use of Calgitrol® in chronic wounds
All wounds contain some bacteria and most heal without problems. However, bacteria in large numbers and/or of a particular type can delay wound healing and cause considerable morbidity and mortality. Early intervention using topical antimicrobial dressings containing silver can be used to reduce the bioburden of critically colonised or locally infected wounds. They may also help the healing of the ulcer and reduce the risk of amputation (eg diabetic foot ulcer). Calgitrol® dressings provide a sustained, controlled release of silver ions to the wound bed, which may provide superior antimicrobial activity, with the regression of clinical signs seen in wounds within two weeks.

Cost benefits
The low frequency of dressing changes has many advantages for the patient and the clinical team. For burns patients, dressing changes are more comfortable and so the need for general anaesthesia, and the associated costs and risks, is reduced. Recently, it has been suggested that the use of a silver alginate dressing and appropriate wound cleansing every three days is cheaper than daily wound care with silver sulfadiazine ointment combined with an absorbent dressing.

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Calgitrol® Ag in the management of a second degree burn case study
A 33-year-old male patient suffered partial thickness burns to 22% of his body surface in a gas leak accident. The burns affected his face, both arms and both legs (Figure 1).

Calgitrol® Ag was selected for treatment of the wounds on his legs due to the risk of infection and also because it was necessary to use a dressing that could manage moderate exudate (Figure 2). The patient was treated as an outpatient, which significantly reduced his anxiety. The dressings were changed every three days in the clinic and covered using a gauze fluff roll. The wounds were completely epithelialised 18 days after the injury (Figure 3). During the first three days of treatment using an alternative dressing, the patient’s pain score was 8–9. His pain score reduced to 2–3 when using Calgitrol® Ag.

Figure 1: Lower leg burns on presentation
Figure 2: Lower leg burns treated with Calgitrol® Ag
Figure 3: Complete epithelialisation three weeks after injury
Calgitrol® Paste in a pressure ulcer case study

An 85-year-old lady presented with a Category/Stage IV pressure ulcer to the sacrum, which developed following confinement to bed while in a nursing home. The pressure ulcer had been present for approximately six weeks (Figure 1). There were clinical signs of infection and the patient complained of pain.

Calgitrol® Paste was applied to provide a dressing with a good contact with the wound surface and to support autolytic debridement (Figure 2). This was covered with an absorbent secondary dressing. The wound dressing was changed daily or whenever the patient had been incontinent. Significant improvement was seen after two weeks, with removal of 90% of the necrotic tissue after four weeks. At this time, granulation tissue was observed with a reduction in the overall wound size (Figure 3).

References
4. BBraun 2011. Askina Calgitrol® Ag/Askina Calgitrol™ THIN Ionic silver alginate dressings. BBraun Hospicare Ltd. Available at: http://tinyurl.com/2zwrwv
Table 2 Summary of evidence for Calgitrol® Ag

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<thead>
<tr>
<th>Reference</th>
<th>Title</th>
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<td>In vitro studies</td>
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<td>Thomas S, McCubbin P. J Wound Care 2003; 12(8): 305-8.</td>
<td>Antimicrobial properties of ten silver-containing dressings</td>
<td>In vitro</td>
<td>To test 10 silver-containing dressings for the ability to produce sufficiently high concentrations of silver ions for antimicrobial efficacy</td>
<td>Calgitrol® Ag was shown to have sustained antimicrobial activity over two or more days Calgitrol® Ag was active within the first two hours of application, had no risk of transmission of microorganisms, and had best overall performance score</td>
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<td>Aramwit P; et al. Int J Molec Sci 2010; 11: 2864-74</td>
<td>Evaluation of the antimicrobial effectiveness and moisture binding properties of wound dressings</td>
<td>In vitro</td>
<td>To investigate the antimicrobial efficacy and moisture penetration of five commercially available wound dressings</td>
<td>Calgitrol® Ag and ACTICOATTM had the largest zone of inhibition, possibly due to the highest concentrations of silver All dressings, except Bactigras®, showed bactericidal activity, achieving a four log reduction in E.coli Calgitrol® Ag maintained the best environment within the wound with regards to moisture</td>
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<td>Clinical studies</td>
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<td>Ricci E, et al. Acta Vulnologica 2007; 5(3): 105-11</td>
<td>Askina® Calgitrol® Ag: clinical use of an advanced ionic silver dressing</td>
<td>Open ended, non-controlled, non-randomised cohort study (n=37)</td>
<td>To determine the clinical efficacy of Calgitrol® Ag on patients with infected or critically colonised wounds; patients who required systemic antibiotics were not included in the study</td>
<td>Clinical signs of infection were alleviated in 34/37 (&gt;90%) cases within the two week test period. No allergic reactions to the dressing occurred</td>
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<td>Costa L, Linhares V. Proceedings EWMA Conference 2008 (Lisbon)</td>
<td>Second-degree burn in a diabetic – application of a silver alginate dressing</td>
<td>Case study with photo control</td>
<td>To evaluate the use of Calgitrol® Ag in a diabetic patient with a second degree burn on the arm</td>
<td>Complete healing in two weeks with a good aesthetic and functional result</td>
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<tr>
<td>Goeman C, et al. Poster presentation. EWMA Conference 2008 (Lisbon)</td>
<td>Dressing changes every 3 days: fiction or reality?</td>
<td>Case study with photo control</td>
<td>To examine whether the use of a silver alginate foam dressing with a change every 3 days is cost-effective</td>
<td>The use of silver alginate foam dressing with a renewal every 3 days is cheaper than a daily wound care with silver sulfadiazine ointment combined with an absorbent dressing</td>
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<td>Durante CM. Proceedings WUWHS Conference 2008 (Toronto)</td>
<td>Clinical effectiveness of a polyurethane foam covered with a layer of calcium alginate and ionic silver</td>
<td>Prospective, open label (n=20)</td>
<td>To evaluate the clinical efficacy of Calgitrol® Ag in controlling the microbial development and managing the exudate</td>
<td>The use of Calgitrol® Ag lead to a decrease in the bacterial count and improvement of the local wound condition. There was an absence of local and systemic complications No loss of absorption power under compression was found</td>
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<td>Trial C, et al. J Wound Care 2010; 19(1)</td>
<td>Assessment of the antimicrobial effectiveness of a new silver alginate wound dressing: a RCT</td>
<td>Prospective, open-label, randomised controlled trial (n=42)</td>
<td>To compare the efficacy and tolerability of Calgitrol® Ag against Algosterrer®(a silver-free alginate dressing)</td>
<td>Calgitrol® Ag dressing had superior antimicrobial effect to Algosterrer® The two dressings were similar in terms of reduction of local infection, local tolerance, acceptability and usefulness</td>
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<tr>
<td>Opasonon et al. Int Wound J 2010; 7(6): 467-71</td>
<td>Clinical effectiveness of silver alginate dressing in outpatient management of partial-thickness burns</td>
<td>Prospective, descriptive study (n=65)</td>
<td>To compare the efficacy of the Calgitrol® Ag dressing and 1% silver sulfadiazine in patients with partial-thickness burn wounds</td>
<td>Average pain scores were lower (p&lt;0.002) in the Calgitrol® Ag group compared to the 1% silver sulfadiazine group. The Calgitrol® group also had fewer dressing changes (p&lt;0.002), decreased nursing time (p&lt;0.02) and shorter healing time (7 vs 14 days in controls)</td>
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<tr>
<td>Chmyrev IV. Proceedings EWMA Conference 2011 (Brussels)</td>
<td>Use of silver containing wound dressings after late necrectomy in the patients with deep burns</td>
<td>Cohort, prospective control (anti-septic ointment and polyurethane film) n=26 vs Calgitrol® Ag n= 22</td>
<td>To compare the use of bandages plus anti-septic ointment and polyurethane film (control) with Calgitrol® Ag in patients with deep burns undergoing late necrectomy</td>
<td>By day 18 bacterial load was lower in Calgitrol® Ag treated patients than in the control group. Wound preparation for split skin grafting was significantly shorter for patients treated with Calgitrol® Ag (p=0.05)</td>
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Summary

Askina® Calgitrol® is an appropriate dressing range for patients with wounds showing signs of infection or at increased risk of infection, that have moderate to high exudate levels or are difficult to dress. Calgitrol® products contain a higher concentration of silver than most other silver dressings and this is in the ionic form. The immediate availability and sustained release of silver ions make it an effective product range that is designed to maintain ongoing antimicrobial action for up to seven days.

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