NICE advice

Prontosan for acute and chronic wounds

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Prontosan. It is used to cleanse acute and chronic wounds.
- The **innovative aspects** are that this technology is the only solution or gel with the active ingredients polyhexamethylene biguanide and undecylenamidopropyl betaine, which the company claims help prepare the wound bed and prevent a biofilm forming.
- The intended **place in therapy** would be as an alternative to saline or water to cleanse wounds during dressing changes.
- The **main points from the evidence** summarised in this briefing are from 6 studies, 2 single-blind controlled trials, 2 retrospective reviews of patient data and 2 observational studies, including a total of 833 adults and children. They show that Prontosan is likely to be better than saline for treating acute and chronic wounds.
- **Key uncertainties** around the evidence or technology are that there is no evidence to show the effect of Prontosan on complete healing because of the short follow up in the studies.

- The **cost** of Prontosan is between £0.61 and £32.45 per unit (excluding VAT), depending on product type and quantity. The **resource impact** is to replace the cost of standard care, which is saline at £0.25 per 20 ml.

The technology

Prontosan (B Braun) is available as:

- Prontosan Wound Irrigation Solution
- Prontosan Wound Gel
- Prontosan Wound Gel X.

It is indicated for cleansing, decontaminating and moistening acute and chronic wounds and to prevent and remove biofilms. The solution and gels contain 2 active ingredients, an antimicrobial polyhexanide (polyhexamethylene biguanide [PHMB]), and a betaine surfactant (undecylenamidopropyl betaine). The company claims that PHMB and betaine disrupt and remove the biofilm from the wound bed, and cleanse and remove slough, devitalised tissue and other wound debris. Prontosan solution can be used for irrigation, or applied to gauze as a soak. The gels are applied to the wound bed during dressing changes after cleansing.

Innovations

The company says that Prontosan is the only wound cleansing solution or gel that contains the active ingredients polyhexamethylene biguanide and undecylenamidopropyl betaine. It claims that Prontosan removes and prevents a biofilm forming, and provides active wound cleansing, removing barriers to wound healing.

Current care pathway

Several indications can result in acutely infected or chronic non-healing wounds, such as surgical site infections, diabetic foot problems and pressure ulcers.

Care of acutely infected or chronic non-healing wounds aims to promote healing and minimise the risk of further complications. Saline or water are usually used to cleanse wounds. If the wound is suspected of being infected, a microbiological sample is usually taken and an antibiotic prescribed to treat the organism causing the infection. The wound is treated with regular cleansing and debridement, and then a dressing is applied. Care staff choose a dressing that promotes healing and

manages exudate on a case-by-case basis. Chronic non-healing wounds typically need more advanced dressings.

The following publications have been identified as relevant to this care pathway: NICE's guidelines on surgical site infections, diabetic foot problems and pressure ulcers.

Population, setting and intended user

Prontosan is for anyone with an acute or chronic wound.

It is applied by healthcare professionals in community and acute care settings, such as outpatient clinics, hospital inpatient care, GP surgeries, post-operative care and at the patient's home. Some basic training may be needed to use the technology.

Costs

Technology costs

The technology is available in several forms and quantities. The company has provided drug tariff prices for February 2020:

- Prontosan Wound Irrigation Solution: £4.96 for a 350-ml bottle (cost per dressing change £0.28 to £0.56); £14.72 for twenty-four 40-ml pods (61p each, single use).
- Prontosan Wound Gel X: £12.12 for a 50-g tube (cost per dressing change £1.21 to £3.03); £32.45 for a 250-g tube (cost per dressing change £1.30 to £3.25).
- Prontosan Wound Gel: £6.62 for a 30-ml bottle (cost per dressing change £1.66 to £3.31).

All Prontosan products except the single-use pods have an 8-week shelf life. The company notes that if an opened bottle or tube of Prontosan is used for subsequent dressing changes in the same patient it has the potential to reduce costs. The range in cost per dressing change is based on a range of volume use per wound dressing, depending on the size of wound. For each dressing change there are also costs for nurse time, basic dressings and a dressing pack (see the costs of standard care section for details).

Costs of standard care

The company says that the costs for treating uncomplicated chronic wounds with standard care per dressing change are:

- saline 25p per 20 ml
- 15 minutes of nursing time £6.50
- basic dressing 44p
- dressing pack 60p.

Chronic wound treatment is not a single treatment, it is a treatment process over a period of time. Wound care costs for 12 months range from £698 to £3,998 per person for a healed wound, to £1,719 to £5,976 per person for an unhealed wound (Guest et al. 2016; Andriessen and Eberlein 2008).

Unit costs and 12-month costs will vary depending on the wound, the extent of the intervention and the costs of the local provider.

The costs of standard care for treating acute wounds are uncertain and variable.

Resource consequences

The company says that Prontosan is used in around 60% of NHS trusts, and that usage varies between them, depending on local policy. Prontosan is often reserved for complex wounds.

According to the company, the technology costs more than standard care, however, it is expected that using this technology will release resources because acute and chronic wounds are likely to heal more quickly.

Prontosan will be used instead of saline or water to cleanse wounds. This is unlikely to cause a substantial change in care facilities and infrastructure. Prontosan will need to be made available during dressing change. The company says that brief training may be needed for some staff but will probably be unnecessary in staff who are already trained in cleansing with saline or water.

Regulatory information

Prontosan is a CE marked class III medical device.

Equality considerations

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

Older people, people with diabetes and people with restricted mobility are more likely to have chronic or non-healing wounds. Age and disability are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six studies including 833 people are summarised in this briefing.

The included studies are:

- a single-blind randomised controlled trial comparing Prontosan and saline in vascular leg ulcers and pressure ulcers
- a single-blind prospective controlled trial comparing Prontosan and saline in venous leg ulcers
- a retrospective review of data on the use of the Prontosan range in children with burns
- an observational study describing the use of Prontosan solution to debride chronic wounds
- a multicentre observational study on the use of Prontosan in people of all ages with chronic wounds
- a retrospective record review comparing Prontosan with saline and Ringers solution.

There are other studies published on Prontosan that have not been reviewed in this briefing. The 6 most relevant studies for the NHS have been selected.

The clinical evidence, and its strengths and limitations, is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The 3 comparative studies showed that using Prontosan could improve chronic wound healing. One of these studies reported improved pain scores and wound odour control for Prontosan compared with saline solution. Another of the studies followed wounds for 6 months and recorded total healing in most wounds. In this study wounds that were treated with Prontosan healed significantly more quickly.

Bellingeri et al. (2016)

Study size, design and location

289 people with chronic wounds (vascular leg ulcers and pressure ulcers) in a single-blind randomised controlled trial. Location: Italy.

Intervention and comparator(s)

Prontosan solution and saline.

Key outcomes

Wounds were assessed using the Bates-Jensen wound assessment tool (BWAT) on day 0, day 7, day 14, day 21 and day 28. Outcomes were analysed using a 2-tailed student's t-test. There were statistically significant improvements in outcomes for wounds cleansed with Prontosan between day 0 and day 28: BWAT total score, p=0.0248; BWAT inflammation, p=0.03; BWAT wound size reduction, p=0.049; and granulation tissue improvement, p=0.43. There was no significant difference in pain between the 2 groups.

Strengths and limitations

The study participants had a mixed aetiology of chronic wounds; however, they were similar in terms of demographics, clinical status and wound characteristics.

Romanelli et al. (2010)

Study size, design and location

40 people with chronic venous leg ulcers in a single-blind prospective controlled trial. Location: Italy.

Intervention and comparator(s)

Prontosan solution and saline. Both groups also had standard wound care of polyurethane foam and compression bandaging.

Key outcomes

Baseline pH on the wound surface (median range) in both groups was 8.9 (range 0.6). After 4 weeks of treatment, wound surface pH was 7.0 (range 0.3) in the Prontosan group. This was significantly lower ($p<0.05$) than the wound surface pH in the saline group in week 4. There was no significant reduction in wound size from baseline to the end of the study period in either of the groups. Patient-reported visual analogue scale pain scores were significantly improved ($p<0.05$) in the Prontosan group in week 4 of treatment. The authors also noted that wound odour was better controlled in the Prontosan group and that bacterial burden was lower.

Strengths and limitations

The study was partially funded by the company, and one of the authors has received payment for clinical consultation. The people included in each arm of the study had no statistically significant differences in age, mean disease duration, mean wound size or pain score at the start of the study. The study follow up was only 4 weeks, which is unlikely to be long enough to show any differences in wound healing. The study results are presented in graphs only; however, it seems the differences between the 2 groups were not significant until week 4 of the study.

Ciprandi et al. (2018)

Study size, design and location

198 children with burns in a retrospective data review. Location: UK, Italy, Russia, Germany and Belgium.

Intervention and comparator(s)

Prontosan solution and gels, no comparator.

Key outcomes

The data review was intended to collect data on the safety of using the Prontosan range on children with burns in routine clinical practice. Of the 198 records reviewed, adverse events were reported in 5 children (3 cases of itching, 1 rash and 1 case of hypergranulating tissue). All adverse events resolved and healed well. No severe adverse events were recorded. 11 children (5.5%) developed clinical signs of infection, which was mostly found to be Staphylococcus aureus when tested.

Strengths and limitations

Because this study is not comparative it is not possible to draw any conclusions about whether Prontosan is more effective than other treatments for burn wound cleansing and moistening. However, because 80% of the children included in the study were under 4 years old, this study provides useful safety data for a patient population less reported on in research.

Ricci (2018)

Study size, design and location

70 people with chronic wounds (older than 6 weeks) in an observational study. Location: Italy.

Intervention and comparator(s)

Prontosan solution; treatment was given in 2 regimens: group A (40 people) was treated with a single application of Prontosan for different time durations (2, 5, 10 and 15 minutes) and group B (30 people) was treated with Prontosan for 10 minutes, daily, during dressing changes for 14 days.

Key outcomes

In group A, there were no changes after the 2-minute and 5-minute applications. At 10 minutes there was improvement in 4 out of 10 wounds and at 15 minutes there was improvement in 5 out of 10 wounds. In group B, after 14 days of treatment, 73% of wounds were cleaned and debrided. People in group B reported a reduction in pain. Peri-wound skin was improved in 29 out of 30 people in group B. One person in group B had tissue deterioration due to maceration.

Strengths and limitations

Because this study is not comparative it is not possible to draw any conclusions about whether Prontosan is more effective than other treatments for debriding chronic wounds. It is not clear what types of chronic wounds were included in the study. The follow-up period of 14 days is not

long enough to show the effect of Prontosan on wound healing. However, it should be noted that all wounds had been present for 6 weeks before the study, and had not responded to standard treatment in this time. The study results suggest that Prontosan should be applied for at least 10 minutes to effectively remove residue and debride chronic wounds.

Durante et al. (2014)

Study size, design and location

124 adults and children with chronic wounds in a multicentre observational study. Location: Italy.

Intervention and comparator(s)

Prontosan wound gel, no comparator.

Key outcomes

Wound size and pain decreased significantly ($p<0.001$) from baseline to the end of the study. Wound size decreased in length (-17.5; range 21.4 cm), width (-15.5; range 21.1 cm) and area (-8.3; range 16.7 cm^2). Pain in adults was measured using the visual analogue scale, and reduced by -4.67 (range 2.7). In children under 3 years the face, legs, activity, cry, consolability scale was used, which changed by less than 1 (range 4). Overall, 90% of wounds reduced in size and 80% of people reported a reduction in pain compared with the baseline visit. 75% of wounds reached complete skin integrity by the end of the study. Exudate also reduced: at the baseline visit 15% of wounds had no exudate, and this increased to 74% by the end of the study. The authors also noted that dressing changes were required less frequently at the final visit compared with the baseline visit.

Strengths and limitations

Because this study is not comparative it is not possible to draw any conclusions about whether Prontosan is more effective than other treatments for chronic wounds. The reported reductions in wound size have very large standard errors, which do not seem to support the statistical significance reported. The study recruited people of all ages (from 4 days to 91 years old) with mixed wound aetiology, which may have contributed to the uncertainty in the results.

Andriessena and Eberlein (2008)

Study size, design and location

112 adults with venous leg ulcers in a retrospective review of records. Location: Netherlands.

Intervention and comparator(s)

Prontosan solution compared with saline or Ringers solution.

Key outcomes

The wounds treated with Prontosan had a higher chance of completely healing after 6 months (97% compared with 89%), and mean time to healing was significantly faster in the Prontosan group (3.31 months compared with 4.42 months; p<0.0001). There were fewer infections in the Prontosan group (2 out of 59 [3%]) than in the control group (7 out of 53 [13%]). The authors noted that wound cleansing with Prontosan was more effective than wound cleansing with saline or Ringers solution and that it improved the condition of the local wound environment.

Strengths and limitations

This study followed patient records for 6 months, which was long enough to observe the total healing of most included wounds. The authors noted that all people included in the study also received standardised compression therapy using bandaging to improve venous flow, speeding up wound healing.

Sustainability

The company claims that using Prontosan will reduce the number of dressings and nurse visits needed because of faster healing. The containers, shipping carton and cardboard packing that contain the gel can be recycled. There is no published evidence to support these claims.

Recent and ongoing studies

None.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 3 experts were familiar with and had used this technology before.

Level of innovation

Two experts agreed that Prontosan is an innovative technology. One expert did not think that Prontosan was an innovative technology compared with other irrigation and cleansing solutions, however, they did note that education to cleanse and soak wounds was a novel approach. All experts agreed that Prontosan is the only wound solution or gel containing polyhexamethylene biguanide.

Potential patient impact

Two clinical experts said that using Prontosan could lead to reduced wound infections. One said that Prontosan could be used to reduce surgical site infections and improve quality of life and outcomes after surgery. One expert said that Prontosan can interrupt and dissolve biofilm formation and prevent reformation as well as remove non-viable tissue and foreign bodies from the wound bed. One expert said that Prontosan did not sting patients when applied.

All experts agreed that Prontosan would benefit people with chronic wounds. One expert clarified that this includes wounds over 14 days old. One expert said that using Prontosan after surgery could help surgical wounds heal and prevent infection. Two experts said that Prontosan may also benefit people who have risk factors for poor healing.

Potential system impact

All experts said that using Prontosan has the potential to improve healing but 1 noted that the evidence for this is currently limited. Two experts said that Prontosan has potential to improve healing outcomes and reduce the risk of hospital-acquired infections after surgery. This could lead to reductions in the need for antibiotics, wound dressing changes, wound swabs and laboratory time and hospital readmissions.

The experts said that using Prontosan costs slightly more than standard care but expect that it would save costs in the long term because of the reduced need for further treatment.

The clinical experts said that using Prontosan instead of other wound cleansers (saline) would not require any major change to services. One expert noted that the company recommends a longer 'soak-time' for Prontosan, which requires brief staff training.

General comments

One clinical expert said that, in their experience, using Prontosan has reduced biofilm formation and incidence of infection. The expert also said that Prontosan effectively removed debris from the wound bed, leading to a colour change that indicates a healthier wound bed and improved healing.

Expert commentators

The following clinicians contributed to this briefing:

- Tracy Vernon, lead nurse, Skin Integrity, Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust. Is on the Coloplast Advisory Board and the Urgo Advisory Board. Has been provided with Prontosan free of charge for the purposes of a trust-wide clinical evaluation from B Braun. Sponsorship at European Wound Management Association conference by B Braun.
- Mark Collier, nurse consultant and associate lecturer tissue viability, private healthcare provider with links to University of Hertfordshire and Lincoln. Has been provided with Prontosan free of charge for the purposes of an independent evaluation and has received payment from B Braun to take part in focus groups.
- Denise Woodd, independent clinical nurse specialist wound care and leg ulcers with links to NHS Portsmouth and Solent NHS Trust.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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