# External Assessment Centre report

## Title: Debrisoft monofilament debridement pad for the debridement of acute and chronic wounds


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### Declared interests of the authors

Description of any pecuniary relationship with sponsors, both personal and of the EAC. Please refer to NICE's Code of Practice for declaring and dealing with conflicts of interests.
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### Rider on responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

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### *Scope of the sponsor's submission*

The scope of the sponsor's submission mostly followed the statement of the NICE scope decision problem but with some omissions and additions. With regard to patients, adults with chronic wounds were evaluated but not children or acute wounds - the clinical evidence used for the cost model did not include these. Subgroups of open and closed wounds were not evaluated. The community setting was evaluated but the evidence for this was sparse. The intervention was Debrisoft and this was compared to hydrogel and gauze and the sponsor also added larvae, stating that the clinical evidence showed effective use of Debrisoft compared with larvae. Numerous outcomes were listed in the scope including time to wound healing, malodour, wound infections, quality of life and adverse events but the sponsor focused on time to debridement or debridement effectiveness, number of healthcare worker visits, number of dressings required and costs.

### *Summary of clinical evidence submitted by the sponsor*

No direct comparative evidence in the form of randomized or non-randomized controlled trials was available for Debrisoft compared to any of the three comparators. There were 51 items of clinical evidence included according to the PRISMA flow diagram and a large number of these were case reports and testimonials. There were seven studies submitted that had some comparative statements or numerical results of Debrisoft compared to another technology but it was mostly unclear as to the exact nature and timing of the comparator technology. The most convincing evidence was a study by Bahr et al 2010 which gave results for debridement efficacy and patient acceptability of Debrisoft compared to gauze, autolytic and sharp/surgical debridement. In the published journal article there were no details of the patients in the study but these were supplied by the sponsor. This study was used extensively by the sponsor in the cost model.

### *Summary critique of clinical evidence submitted by the sponsor*

The comparative evidence suggested that Debrisoft was associated with less pain, improved acceptability by patients, decreased time to treat, reduction in wound care visits, more removal of devitalized tissue and more effective debridement compared to standard treatment, previous methods (not specified), gauze, autolytic, enzymatic or sharp/scalpel debridement. There was no comparative evidence on larvae found. There was no useful evidence on the rate of wound healing or wound infections. There was no evidence on the average number of Debrisoft applications required to achieve complete debridement. None of the comparative studies mention that they were conducted solely in a community-based setting.

***Summary of economic evidence submitted by the sponsor***

The sponsor provided a simple cost model executed in Microsoft Excel. The analysis presented the costs and resource consequences of the use of Debrisoft in a community setting, and was compared with hydrogel, gauze and larvae. It was assumed that the aim of treatment is successful debridement of the wound. Separate analyses were conducted for applications in home and applications in a clinic setting. The analysis took an NHS perspective. It incorporated the costs of the technologies, supplementary technologies (such as dressings) and the costs of their application by a district nurse.

The analysis assumed a 'stopping rule' for Debrisoft, such that if the wound was not completely debrided after a maximum of three applications, patients would switch to an alternative technology (hydrogel).

Key clinical information used in the analysis was based on two studies: The case series by Bahr *et al* was used to inform the effectiveness of Debrisoft (1) and the VenUS II trial was used to inform the effectiveness of larvae and hydrogel (2). The number of applications of gauze to achieve debridement was based on assumptions.

The sponsor's base case analysis found that Debrisoft was less costly than all three comparators. The estimated average cost of £162, £351, £308, £330

and £83, £306, £165, £180 for Debrisoft, larvae, hydrogel and gauze for home and clinic settings respectively. In the sponsor's sensitivity analysis, Debrisoft remained cost-saving for clinical and home visit in all scenarios tested.

***Summary critique of economic evidence submitted by the sponsor***

The results of the sponsor's base case analysis were driven largely by the requirement for fewer appointments with Debrisoft compared to hydrogel and gauze in the analysis, and from cheaper product costs for Debrisoft relative to larvae. The EAC agrees with the sponsor's comment in the submission that the lack of information directly comparing gauze, hydrogel, larvae and Debrisoft is a key weakness. The EAC agrees that the lack of comparative results for Debrisoft with any of the comparators makes an assessment of the resource implications difficult as it is dependent on the relative effectiveness and number of applications required for each product. The EAC notes the implementation of the stopping rule after three applications of Debrisoft in the analysis. We understand that this reflects the design of the Bahr *et al* study, but it hinders comparison with the other technologies.

Another limitation of the analysis is the focus on time to debridement rather than wound healing. We note that other studies in this area have focused on wound healing rather than debridement, and consider this a more meaningful measure. In addition, the definition of the gauze comparator is unclear. We consider that the specification of the comparator for gauze reflects the use of gauze for 'wet-to-dry' debridement rather than for cleansing. Advice from NICE clinical experts suggests that there is variation in clinical practice with gauze in the UK.

Upon review of the sponsor's analysis, we identified some errors and noted some assumptions that we considered to be unlikely. In particular the implementation of the switching rule incorrectly omitted the costs of Debrisoft for a proportion of patients, and the unit costs of district nurse time were miscalculated. Also we noted that the analysis was based on loose larvae whereas bagged larvae are more common in UK clinical practice and

considered alternative assumptions for the amount time required for visits by district nurses.

### *External Assessment Centre commentary on the robustness of evidence submitted by the sponsor*

The clinical evidence is very limited in terms of patients included, interventions and comparators evaluated and outcomes measured. Most relevant studies are unpublished conference posters or testimonials and the published research is not of sufficient quality and does not measure the most useful clinical outcomes. So there is no good clinical evidence to suggest that Debrisoft is any better than any alternative technology, or to no debridement, in promoting wound healing or reducing wound infections. Because of this it is difficult to determine whether Debrisoft would actually be cheaper in NHS clinical practice in the community than any of the comparators when considering important clinical outcomes such as wound healing rates, or indeed the number of debridements needed.

### *Summary of any additional work carried out by the External Assessment Centre*

The EAC conducted additional searches in medical databases which found no new information on Debrisoft. The EAC contacted authors of case series reporting on Debrisoft by conference poster if they had any further information but little further useful information was obtained. The EAC reviewed the evidence on the effectiveness of debridement compared to no debridement for wound healing and found no conclusive evidence to demonstrate that debridement is more likely to result in wound healing. The EAC reviewed the best quality evidence on the effectiveness of methods of debridement other than Debrisoft and found two Cochrane reviews, another systematic review and a very large cohort study. The results of these are discussed in relation to the evaluation of Debrisoft.

In the cost model submitted by the sponsor, the EAC corrected the error detected in the cost model relating to the incorrect application of switching

(including the costs of Debrisoft applications for those people who switch to hydrogel) and corrected the estimates of district nurse time. Debrisoft remained cost saving compared to all three comparators but not by as much. The EAC made further amendments in the cost model to reflect the use of loose rather than bagged larvae, an increased amount of time per district nurse visit and cheaper unit costs for hydrogel and dressings. After all of these changes, Debrisoft was still cost saving compared to the three alternatives but not by as much.

The EAC conducted an exploratory analysis to examine the implications of switching to larvae or gauze, instead of hydrogel, following application of the stopping rule. In addition, we conducted a threshold analysis to assess the number of Debrisoft applications required to make it more expensive than the alternatives, keeping all other variables constant. We found that if more than nine applications of Debrisoft were required it would not be the most cost saving technology for wound debridement (assuming patients do not switch to an alternative debridement product).

# 1 Background

## *2.1 Overview and critique of sponsor's description of clinical context*

The clinical context is the care of wounds. Debridement is the removal of devitalised, contaminated or foreign material from the surface or acute or chronic wounds with the intension to expose healthy tissue. The description of the clinical context in the sponsor's submission is relatively brief and tended to favour the use of Debrisoft.

It is widely believed that wound healing is enhanced by the practice of debridement but there is little conclusive proof. See section 2.9 for a review of this. However, it seems to be accepted by most wound care professionals that debridement is mostly beneficial. The NICE clinical experts suggested the following comments:

"Whilst infection/bacterial proliferation/biofilm do inhibit healing I am not certain that devitalised tissue per se is always detrimental. Healing can occur happily beneath a dry escar of devitalised skin as long as there is no infection beneath it. Sometimes it is better to leave it intact rather than remove it as it can provide an effective barrier to infection for some time."

"Why do we debride a wound? To allow full assessment of the extent of the wound, to remove a potential source of infection and to allow the more rapid promotion of healthy granulation tissue. The decision to debride should only be taken as part of the overall management strategy and is the first stage in the process of moist wound healing. Some wounds the aim is to mummify the wound area whilst in others the margins between healthy tissue and non-viable tissue have not been defined and in these cases debridement should be avoided or delayed. "

"The word 'debridement' is misunderstood by different clinicians. It is the removal of devitalised tissue. Some clinicians view that as removal of all dead tissue, including slough, and others see it as the removal of necrotic (black) tissue through sharp or surgical debridement."

There are numerous methods of debridement. These have recently been summarised and compared in an European Wound Management Association (EMWA) debridement consensus document and relevant details summarised for this report (see Table 1)(3). This consensus document on debridement was sponsored by five different companies so is unlikely to be biased in favour of any one product. It attempts to give guidelines on debridement methods. In the NHS the current methods of debridement used are unclear. It is unclear whether this consensus document's recommendations are currently being followed.

**Table 1. Summary of debridement characteristics (3)**

| Debridement type | Relative speed of conduct | Advantages | Disadvantages | Who can do it. |
|---|---|---|---|---|
| Mechanical (Debrisoft or wet to dry) | Fastest | Claimed to be quick and easy, more effective, less pain. Patients can do it themselves under supervision. | Not useful if hard dry exudate, not suitable if wound painful, possible increased wound infection rates and risk of damage to healthy tissue | Generalist |
| Sharp | | Efficient in wounds with a solid layer of necrotic tissue | Risk of infection if sterile conditions not ensured | Skilled practitioner with specialist training |
| Larvae | Medium | Highly selective, reduced pain and malodour | May be painful, not suitable for bleeding wounds. Patients often not keen. | Generalist with minimal training |
| Autolytic or enzymatic | | Easy, little or no pain, no damage to healthy tissue | Risk of allergic reaction from dressings used, takes a long time to debride wound | Generalist |
| Surgical | Slowest | Efficient in wounds with a solid layer of necrotic tissue | Risk of removing healthy tissue, risk of infection if sterile conditions not met | Surgeon, podiatrists or specially trained nurse |

The Sponsor's submission did not include a survey of current debridement practice in the UK community. The NICE clinical experts did not give any clear opinion of which methods would be used most often in the community.

No published studies, audits or unpublished studies were found and there were no ongoing studies listed in the Current Controlled Trials Register.

The impact on leg ulcer wound healing of a variety of debridement methods has been systematically reviewed (4). Unfortunately this had a limited search of PubMed only so is likely to have missed relevant studies. The results were inconclusive as the comparators in the RCTs were not detailed and the relative effectiveness of the different types of debridement not evaluated. The recent US cohort study of a large number of patients with a variety of mainly chronic wounds (5) did not evaluate methods of debridement used in each patient or assess healing rates by debridement method. It is unclear whether the method of debridement will affect wound healing irrespective of the percentage of debridement achieved because of potential damage to the wound bed.

### *2.2 Overview of sponsor's description of ongoing studies*

There is one RCT listed in the submission that is ongoing:
*Clark M, Young T. A prospective, randomised controlled exploratory study comparing the debridement of sloughy venous leg ulcers undertaking either with a novel debriding agent (monofilament fibre pad) or autolytic debridement using wound dressings. On-going study (ISRCTN47349949).*
We have received the protocol for this RCT and it is labelled commercial-in-confidence. However, this RCT is listed on the Current Controlled Trials Register which is freely available and the details are taken from there.

The RCT PICOS are as follows:

- Patients – adults >18 yrs, male and female, leg ulcer no larger than 40cm2 of any aetiology and not older than 1 year. Leg ulcer to be at least 50% covered with devitalised tissue that is not fixed dry necrotic tissue or tenacious slough. Exclusions – malignant wound, pregnancy, various others.
- Intervention – Debrisoft
- Comparator – Autolytic debridement using wound dressings (hydrogel)

- Outcomes – primary – appearance of wound (from photos) and wound size within 14 days of treatment, secondary – changes in presence of hyperkeratosis, costs, patient and healthcare professional experience of debridement process. NB no mention of time to healing as an outcome measure, or wound infection rates.
- Study design – Open label RCT, no mention of blinding of outcome assessment. Sample size – 66 participants. No power calculation seen.

The RCT is running in the UK (Cardiff). The RCT end date 31/03/2013. Discussions with the sponsor in August 2013 indicated that recruitment was around half the target number so far and there were no useable outcomes as yet. We are not aware of any other ongoing comparative studies of Debrisoft.

## *2.3 Critique of sponsor's definition of the decision problem*

**Population**

The sponsor's definition of the decision problem is taken from the NICE final scope with variations from the scope and their justification. The population is adults and children with acute or chronic wounds.

The setting in the scope is debridement in a community-based setting. It is unclear whether the submission is focused on community-based debridement or not. The variation to the scope is that they have included a multi-disciplinary team including podiatrists and doctors, rather than limiting to nurses. The Submission states that "Clinical evidence shows that debridement is carried out by members of the multi-disciplinary team and not just nurses". It is unclear which evidence they were referring to. There was no published or unpublished evidence to show who does debridement in the UK in a community based setting so it is unclear whether this variation is justified or not.

**Intervention**

The intervention is the use of Debrisoft monofilament debridement pad (see Figure 1). It is a pad measuring 10cm x 10cm which has monofilament

polyester fibres projecting out on the wound contact surface, and feels soft and fleecy.

The SNOMED codes for this product were estimated to be Wound care (regime/ therapy) 22535800 and Special care of wound (regime/therapy) 42149003.

**Figure 1. Debrisoft pad**

There is a CE Mark on the product packaging. The submission included a UKAS Certificate of Registration (6639A – 01.09.2011), a certificate of quality assurance (Q1N 1109 45286 045 valid until 30.11.2014) and a Declaration of Conformity (KFE 0618 00, dated 09.12.2009). An email from the sponsor stated that 259 NHS CCG's and Health Boards have purchased Debrisoft through the prescription route in the past 24 months and 87 requisite points within hospital trusts purchasing Debrisoft at present.

**Comparator(s)**

The comparators in the scope are hydrogel or other autolytic dressing and cleansing with gauze. There is no mention of using gauze for debridement (wet to dry debridement which is also done with gauze and can cause some confusion as it is not the same as cleansing with gauze). The sponsor added the use of larvae as a comparator, justified in the submission as follows: "Clinical evidence for Debrisoft shows effective use of Debrisoft compared with larvae". It was unclear as to which comparative evidence they were referring to. They also stated at the face to face meeting that they wished to compare Debrisoft to larvae in the economic model. Larvae can be used loose or in bags. Loose larvae tend to be cheaper whereas bagged larvae tend to be easier to use. Very little evidence was submitted on the effectiveness of any of the comparators. The sponsor did not provide much in the way of comparative evidence of Debrisoft versus any of the comparators. Such that was found is evaluated in the sections below. There was no evidence given in the submission to demonstrate which debridement methods are currently being used in a community-based setting.

**Outcomes**

There are a large number of outcomes listed in the final scope and these are reproduced in the submission. Listed outcomes include time to healing, wound infections and quality of life. The clinical outcomes that would better have been used in the submission are healing rates or time to healing because these are the most important outcomes from a patient's perspective. Most of the good quality published evaluations of debridement use one of these two outcomes (2, 4, 5). Generic quality of life measures such as EQ-5D would also have been useful, as would wound infection rates, as infections are one of the main causes of subsequent amputations. The submission focuses on surrogate outcomes only such as visual assessment of wound, debridement efficacy and acceptability of debridement to the patient and healthcare professional, rather than using the sponsor's statement of the decision problem with the long list of outcome measures. Mean number of debridements to achieve wound healing would also have been useful. It is

unclear whether there is good correlation between time to debridement and time to wound healing.

### Cost analysis

The sponsor's cost analysis covers some of the criteria in the final scope but not all. There are also some additions and some points are unclear. These are summarised in Table 2.

**Table 2. Cost analysis summary**

| Criteria | Included from scope | Not included from scope | In addition to scope | Unclear |
|---|---|---|---|---|
| Patients | Adults, chronic wounds, | Children, acute wounds, | | Open or closed wounds (because no subgroup analysis) |
| Setting | Community setting (because it doesn't consider hospital costs) | | | |
| Intervention | Debrisoft | | | |
| Comparator | Hydrogel, gauze | | Larvae | Whether the gauze debridement is wet to dry or whether it is wet cleansing with gauze |
| Outcomes | Time to debride, duration, number and frequency of visits by healthcare workers, numbers of dressings required, type of dressing, costs, | Quality of life, pain and discomfort, malodour, time to healing, wound infections, need to refer to specialist care, need to switch to sharp debridement, adverse events | | |

### Subgroups

The subgroups to be considered in the final scope were patients with wounds where the skin could be intact (such as lymphoedema or hyperkeratotic skin) or not intact (open wounds including haematoma). The clinical information

presented included some case reports and case series on both subgroups. The model did not evaluate these or any other subgroups.

**Special considerations, including issues related to equality**

The special considerations mentioned in the scope include people with chronic wounds, diabetic foot ulcers and spinal injury pressure sores being protected as having a disability under the Equality Act 2010. No new equalities issues have been identified by the sponsor or by the EAC regarding to the population or the assessment. The submission states 'There are no equality issues relating to the population for which Debrisoft is intended'.

# 2 Clinical evidence

## *2.1 Critique of the sponsor's search strategy*

The sponsor's search strategy was adequate to find all relevant published studies on Debrisoft. Additional searches revealed no new useful information (see Appendix 1). A request to ten authors of posters where there was numerical information included on the posters (marked with an asterisk on Table 29 and Table 30) revealed no further useful information. Four poster authors responded directly and the company responded to two others.

## *2.2 Critique of the sponsor's study selection*

The study selection consisted of including any studies on Debrisoft, without any limitation on whether the study designs could demonstrate the claimed benefits of Debrisoft compared to the comparators listed in the final scope or compared to larvae. Therefore a large number of studies that have been described by the sponsor do not provide any evidence on comparative effectiveness although they do describe settings in which Debrisoft has been used. These studies are not considered further in the main body of this report but are listed and described briefly in Appendix 2.

## *2.3 Included and excluded studies*

According to the PRISMA flow diagram in the submission, the sponsor included 51 studies in the qualitative synthesis. However, many of these were single case studies or testimonials, some within longer documents. The

sponsor's submission included the following pieces of evidence for the clinical effectiveness:

- Journal articles (n=8)
- Posters (n=28)
- Advertising reports sponsored by the company that include several case studies (n=2)

The sponsor's submission states that there are 18 studies with information on historical comparators. It is unclear which of the included studies these are as there are no references with this statement.

There are seven comparative studies that were included in the sponsor's submission that have been evaluated in this report:

1. Bahr S, Mustafi N, Hattig P, Piatkowski A, Mosti G, Reimann K, et al. Clinical efficacy of a new monofilament fibre-containing wound debridement product. J Wound Care. 2011;20(5):242-8.(1)
2. Callaghan R, Stephen-Haynes J. Changing the face of debridement in pressure ulcers. Poster presentation, EPUAP Conference Cardiff, September 2012. (6)
3. Collarte A. Evaluation of a new debridement method for sloughy wounds and hyperkaratotic skin for a non-specialist setting, Poster Presentation at EWMA Conference, Brussels - May 2011(7)
4. Johnson S, Collarte A, Lara L, Alberto A. A multi-centre observational study examining the effects of a mechanical debridement system. Journal of Community Nursing. 2012;26(6):43-6(8)
5. Mustafi N et al. Clinical efficacy of a monofilament fibre containing wound debridement product evaluated in a multicentre real life study, CPC, January 2011(9)
6. Pietroletti R, Capriotti I, Di Nardo R, Muscioli P, Gonzalez M, Ermolli P. Economical comparison between three different types of debridement (autolytic and enzymatic vs mechanical debridement with polyester fibres) Poster presentation, Wounds UK, Harrogate November 2012(10)
7. Wiser M. A monofilament debridement product - Is it a new support for debridement? Poster presentation, EWMA Conference, Vienna - May 2012(11)

There were no additional relevant studies found from the searches (see Appendix 1 for details of the searches conducted.

### *2.4 Overview of methodologies of all included studies*

Please see Table 3 for the main description of the comparative studies. All information is likely to be generalizable to the UK but it is unclear whether it would be appropriate to a community setting. Bahr et al (2010)(1) was the main study which provided much of the evidence for the clinical effectiveness that subsequently was used in the sponsor's cost model. This study did not evaluate time to healing or healing rates. It did not evaluate wound infections. It also gave no details on study participants (age, gender, wound nature or size). It graded debridement into three classes:

- Class A – Wound bed covered with slough and some black necrotic plaques, and the skin around the wound is covered with scales, dried exudate and hyperkeratotic tissue
- Class B – Wound bed covered with slough and some scales and dried exudate on peri-wound skin
- Class C – less than 20% slough on wound bed and peri-wound skin clean.

In answer to questions further information was obtained on the background characteristics of the Bahr 2010 study, which were used in Table 9.

The other published journal article, by Johnson et al (2012)(8), had some information about participants that Debrisoft was used on but very little information about the comparison. Results were given in tabular form only. The remaining comparator studies were conference posters (7, 9-12) and gave very little information about methods and results. For example, Callaghan 2012(12) assessed location of pressure ulcers, pain during and after treatment, reduction in wound care visits and categorisation of the ulcer but there was no information at all about the 12 patients in the study. Mustafi 2011(9) gave no details of patients in the poster itself but further information was sent by the sponsor in the form of an unpublished report. This has been used in Table 3, Table 4 and Table 5.

**Table 3. Characteristics of included studies**

| Study (Country) (Conflicts of Interest - CoI) | Study design | Debrisoft patient characteristics, numbers | Control patient characteristics, numbers , comparator treatment used | Age, demographic character-istics | Outcomes |
|---|---|---|---|---|---|
| Bahr 2010 (Germany, Austria, Italy) (company sponsored)(1) | Case series with retrospective controls from same centres, not matched | N=60 enrolled, 57 evaluated. 54 had 1 wound, 3 had 2 wounds, acute and chronic combined | N=NG, wound types NG<br>1. autolytic with hydrogel<br>2. mechanical with wet gauze<br>3. surgical | Age 68.3 (SD 14.5, 42-91), 45% female, wound size 60.4cm$^2$ (SD 104.8) duration 5.2 months (SD 2.3) | Vs 1,2,3 duration of debridement procedure, user satisfaction graph, debridement efficacy<br>Vs 1 user satisfaction, debridement efficacy, time to complete debridement |
| Callaghan 2012 (UK) (company sponsored)(12) | Case series with a comparison | N=12, pressure ulcers, characteristics NG | N=NG, patient selection unclear | NG | Reduction in wound care visits |
| Collarte 2012 England) (company sponsored)(7) | Case series with a comparison, not matched | Characteristics NG, n=10 | Patient selection unclear, n=NG<br>'standard best practice including autolytic debridement' | NG | Time to treat |
| Johnson et al 2012 (UK) (NG)(8) | Case series, historical comparison on same patients | Hospital and community, n=20,<br>10 chronic leg ulcers, 10 chronic wounds including diabetic, ischaemic, leg ulcers | Same.<br>"previous methods" unspecified | NG | Debridement performance<br>Skin condition compared to previous hyperkeratotic method |

| Study (Country) (Conflicts of Interest - CoI) | Study design | Debrisoft patient characteristics, numbers | Control patient characteristics, numbers , comparator treatment used | Age, demographic character-istics | Outcomes |
|---|---|---|---|---|---|
| Mustafi 2011 (Germany) (company sponsored)(9) | Case series with a comparison, not matched | Lymphoedema – acute and chronic wounds, N=60 | Characteristics NG N=NG | 42 women, 18 men, mean age 69.3 years (SD 14.54, range 48-94) | Time to debridement |
| Pietroletti 2012 (Italy) (company sponsored)(10) | Case series, retrospective comparison, non-matched | Characteristics NG N=27 | Characteristics NG N=25 'autolytic or enzymatic' | NG | % debridement at first use |
| Wiser 2012 (France) (company sponsored) (11) | Case series with retrospective comparison of 'similar patient group' non-matched | 15 patients with venous leg ulcers or diabetic foot ulcers | Characteristics NG, N=NG 'saline soaks' | NG | Pain tolerance, Discomfort, |

### *2.5 Overview and critique of the sponsor's critical appraisal*

The sponsor submission critically appraised five of the studies – Haemmerle et al 2011(13), Bahr et al 2010(1), Stephen-Haynes 2012(14), Gray et al 2011(15) and Johnson et al 2012(8). It is unclear why these five were chosen. It states that the reason was that these were case series with multiple patients but there were 17 case series with multiple patients submitted. The five were critically appraised using a checklist for case series and were all found to be generally of low quality. It is unclear whether this was used in their conclusions about the nature of the evidence and its believability.

### *2.6 Results*

The results of the comparative studies compared to the claims of benefits for Debrisoft given in the final scope and by comparator are shown in Table 4, Table 5 and Table 6. Table 4 lists each study that reports any comparative results on each of the claimed benefits. Table 5 gives the comparative information when it was given as qualitative statements only. Table 6 gives any comparative numerical information given, including p values of statistical comparisons. None of these studies mention that they were conducted in a community-based setting.

The comparative evidence suggested that Debrisoft was associated with less pain, improved acceptability by patients, decreased time to treat, reduction in wound care visits, more removal of devitalized tissue and more effective debridement compared to standard treatment, previous methods (not specified), gauze, autolytic, enzymatic or sharp/scalpel debridement. There was no comparative evidence on larvae found.

It can be seen that there is no comparative information on most of the claimed benefits, particularly healing rates, compared to the comparators listed in the scope and to larvae. There was no useful evidence on the rate of wound healing or wound infections.

In answers to questions about the evidence base the sponsor stated that:

"the complete healing outcome would bring in all sorts of confounding variables and the comparison of the benefits between debriding alternatives would be lost in the impact of the variables to complete wound healing, ie the physiology of the patient, background disease, effect of arterial status etc." Also "The evidence base is not sufficient at this time to allow a meaningful analysis of costs or time to complete healing with debrisoft compared with other debridement methods in scope (hydrogel or other autolytic dressing, and cleansing with gauze)"

With regard to the required number of Debrisoft applications required to achieve complete debridement, there was no evidence found in any of the 51 studies submitted by the sponsor. In response to a question about this, the sponsor's response was:
"we do not know the mean number of applications required with Debrisoft to achieve complete debridement in all patients".

**Table 4. Table of evidence regarding claimed benefit and comparators to Debrisoft**

| Claimed benefit | 'Standard treatment' or previous methods not specified (actual comparator description) | Gauze (mechanical debridement wet gauze) | Autolytic | Enzymatic | Sharp/ scalpel | Larvae |
|---|---|---|---|---|---|---|
| Reduction in pain | Wiser 2012 (saline soaks)(11) | - | - | - | - | - |
| Improved acceptability | Wiser 2012 (saline soaks)(11) | Bahr 2010(1) | Bahr 2010(1) | - | - | - |
| Faster treatment and healing | Collarte 2012 (standard treatment)(7) | - | Bahr 2010(1) | - | - | - |
| Reduced risks of trauma to healthy tissue, and of bleeding | (skin condition) Johnson 2012 (8) | - | - | - | - | - |
| Reduced time and resources needed | Callaghan 2012 (unclear)(12) | Mustafi 2011(9) | Bahr 2010(1) | - | Mustafi 2011(9) | - |
| Lower costs and shorter waiting times | | - | - | - | - | - |
| More effective debridement | Collarte 2012 (standard treatment) (7), Johnson 2012 (previous methods)(8) Wiser 2012 (saline soaks)(11) | - | Bahr 2010(1) Pietroletti 2012(10) | Bahr 2010 (1) Pietroletti 2012(10) | - | - |
| Improved patient concordance | | - | - | - | - | - |
| Avoidance of on-going costs relating to specialist methods of debridement | | - | - | - | - | - |

**Table 5. Quotes of results of debrisoft compared to comparator where numerical results not given**

| Claimed benefit | 'Standard treatment' or previous methods not specified (actual comparator description) | Gauze (mechanical debridement wet gauze) | Autolytic | Enzym -atic | Sharp/ scalpel | Larvae |
|---|---|---|---|---|---|---|
| Reduction in pain | 'reported pain less' Wiser 2012 (saline soaks)(11) | - | - | - | - | - |
| Improved acceptability | 'better tolerated' Wiser 2012 (saline soaks)(11) | | | - | | - |
| Faster treatment and healing (a) | 'decreased time to treat' Collarte 2012 (standard treatment)(7) | - | 'autolytic took significantly longer | - | - | - |
| Reduced risks of trauma to healthy tissue, and of bleeding | | - | - | - | - | - |
| Reduced time and resources needed | 'reduction in woundcare visits' Callaghan 2012 (comparator unclear)(12) | 'significant differences' | - | - | 'significant differences' | - |
| Lower costs and shorter waiting times | | - | 'not as expensive in comparison to other current debridement methods' Pietroletti 2012(10) | | - | - |

| Claimed benefit | 'Standard treatment' or previous methods not specified (actual comparator description) | Gauze (mechanical debridement wet gauze) | Autolytic | Enzym -atic | Sharp/ scalpel | Larvae |
|---|---|---|---|---|---|---|
| More effective debridement | 'removing more devitalised tissue and hyperkeratosis more quickly' Collarte 2012 (standard treatment)(7) 'effective debridement, better than with soaks' Wiser 2012(11) | - | Debrisoft 'mean of 92% of debrided wound bed whereas 2 uses of autolytic debridement gives mean of 38.4%' 'autolytic would need to be used 8-10 times to give the same results' Pietroletti 2012(10) | | - | - |
| Improved patient concordance | | - | - | - | - | - |
| Avoidance of on-going costs relating to specialist methods of debridement | | - | - | - | - | - |

**Table 6. numerical results of debrisoft compared to comparator**

| Claimed benefit | Debrisoft | 'Standard treatment' or previous methods not specified (actual comparator description) | Gauze (mechanical debridement wet gauze) | Autolytic | Enzym-atic | Sharp/ scalpel | Larvae |
|---|---|---|---|---|---|---|---|
| Reduction in pain | - | - | - | - | - | - | - |
| Improved acceptability (User mean score) Bahr 2010(1) | 2.29 (SD 0.57) | - | 2.49 (SD 0.67) | | - | | - |
| Faster treatment Bahr 2010(1) | Shorter | - | Longer (p<0.05) | Longer (p<0.05) | - | Longer (p<0.05) | - |
| Faster healing | - | - | - | - | - | - | - |
| Reduced risks of trauma to healthy tissue, and of bleeding Johnson 2012(8) | - | Skin condition compared to previous hyperkeratosis method very good n=1, good n=1, much better n=6, N/A n=12. | - | - | - | - | - |
| Reduced time and resources needed | - | - | - | - | - | - | - |
| Lower costs and shorter waiting times | - | - | - | - | - | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| More effective debridement Bahr 2010(1) | 1.98 (SD 0.68) | 2.62 (SD 0.47) all debridement options | - | 2.54 (0.72) hydrogel | - | - | - |
| More effective debridement Johnson 2012(8) | | Performance compared to previous method very good n=3, good 5, much better n=8, N/A n=4 | - | - | - | - | - |
| Improved patient concordance | | | - | - | - | - | - |
| Avoidance of on-going costs relating to specialist methods of debridement | | | - | - | - | - | - |

## 2.7 Description of the adverse events reported by the sponsor

Potential adverse events from Debrisoft include increased wound infections, slower healing time and increased pain compared to other debridement techniques.

The sponsor's submission states in section 6.7.1 that it will discuss the adverse events found in the studies included in the economic evidence rather than in the clinical effectiveness evidence. However, some of the evidence for both parts are mentioned in the adverse events section. Also it states that Bahr 2010(1) is not a comparative study in section 6.7.2 yet in table B6 it mentions that Bahr 2010(1) has historical comparators. The adverse events discussed are pain and discomfort, bleeding and anxiety. Also that debridement should not be used on ischaemic limbs. There was no mention of whether Debrisoft increases wound infections or not.

No comparative results on adverse events were presented by the sponsor. It is currently unclear if use of Debrisoft is associated with higher rates of wound infections than the comparators of gauze, hydrogel or larvae. It is also unclear if use of Debrisoft is associated with higher or lower rates of pain to the patient than the comparators of gauze, hydrogel or larvae. The NICE expert advisors have not voiced a clear opinion about adverse events with the use of Debrisoft compared to the comparators of gauze, hydrogel or larvae.

The case studies and series described in Appendix 2 did not report any serious unexpected events.

## 2.8 Description and critique of evidence synthesis and meta-analysis carried out by the sponsor

No evidence synthesis or meta-analysis was conducted by the sponsor. None would be appropriate, given the evidence submitted.

## 2.9 Additional work carried out by the External Assessment Centre in relation to clinical evidence

1. Searches in Medline and Web of Science using the keyword Debrisoft yielded one reference (Bahr 2011)(1) already included in submission. Searches in Embase yielded 4 references, 3 were already in submission and one was in a German publication (16) which was unobtainable.
2. The EAC asked the poster authors of any of the posters with numerical results for any additional material they had in any language that might assist the evaluation. No useful information was forthcoming.
3. An early HTA found no RCTs comparing debridement to no debridement in chronic wounds (17) but a more recent review on debridement methods has shown there may be some RCTs (4) but the descriptions of the primary study control groups in this review are unclear. A recent Cochrane review on debridement in diabetic foot ulcers has claimed that direct evidence on debridement versus no debridement is lacking (18). There have been no large, good quality RCTs of debridement versus no debridement in any acute or chronic wounds so whether it is beneficial or not in acute or chronic wounds is unclear. RCTs found include one on surgical debridement in chronic venous ulcers which showed that 16% of 28 ulcers had complete healing in the debridement group compared to 4.3% of 27 ulcers in the control group (19). Another on surgical debridement (20) found that 21/22 (95%) ulcers treated with surgical debridement had completely healed within 6 months, compared to 19/24 (79%) in the conservative care group. An early RCT on debridement versus no debridement in acute wounds (gunshot) found that slightly more patients in the debridement group (4/89) got wound infections that those in the control group (2/74) (21). A recent US cohort study of a large number of patients with a variety of mainly chronic wounds found that those wounds receiving more frequent debridement had faster healing rates on average (5). However the results may be confounded by a variety of factors such as patient characteristics, nursing care experienced and debridement methods used.
4. However, with regard to effectiveness of debridement, there does exist good comparative evidence on the comparators – for example:

There is a large cohort study published recently of 312,744 wounds (154,664 patients, median age 69 years) looking at frequency of debridement and time to heal (5). The debridement methods included autolytic, enzymatic, mechanical, surgical and biosurgical (larvae). The wound types were a wide variety of chronic wounds. The study found that more debridements per wound resulted in faster healing times. Unfortunately there was no analysis of wound healing rates by debridement method. There was insufficient time in the evaluation to merit asking for this additional analysis to be conducted.

A Cochrane review of debridement of diabetic foot ulcers (18) included RCTs on larvae compared with hydrogel (22) and hydrogel compared with gauze/standard care (23-25). A Cochrane review of debridement of surgical wounds (26) included RCTs of hydrogel compared to gauze (27, 28).

### *2.10 Conclusions on the clinical evidence*

There is no good comparative evidence to support the sponsor's claimed benefits of Debrisoft compared to any of the comparators listed in the final scope, and to larvae, in a community-based setting for the most important outcome measures of healing rates, time to healing and wound infections. There is very limited comparative evidence on surrogate outcomes such as debridement effectiveness and time to treat. There is no comparative evidence at all on a number of the claimed benefits such as reduced risks of trauma to healthy tissue, reduced time and resources needed patient concordance and avoidance of ongoing costs. The quality of the evidence precluded the use of indirect comparison and mixed treatment methods for determining relative effectiveness and safety.

# 3 Economic evidence

## *3.1 Published economic evidence*

### Critique of the sponsor's search strategy

The search strategy looked for published economic evaluations of debridement in Medline Embase, NHSEED and Econlit. There was no mention of strategies looking for unpublished or grey literature economic evaluations. However, on the PRISMA diagram they mention that they found four publications from bibliography and grey literature searching.

### Critique of the sponsors study selection

The inclusion criteria were

- Patients – wounds associated with any condition in patients of any age, gender or race
- Intervention – not specified
- Comparators – autolytic debridement, hydrogel or hydrocolloid, larval debridement, biosurgery or maggot therapy, mechanical debridement (gauze swabs – method not specified).
- Outcomes – numerous outcomes specified including type of wound and cost

The inclusion criteria were appropriate except that they restricted the studies to English Language only, yet the parent company to Activa Healthcare (Lohmann and Rauscher GmbH) is German, so one might have anticipated economic evaluations in the German healthcare setting.

The outcomes listed in the selection criteria table are much more detailed than one would have expected if they were actually being used as selection criteria. It is more likely that the papers were obtained using patient and comparator criteria and then the outcomes in those papers were listed in this table (Table C1 of the submission).

### Included and excluded studies

There were 16 studies included in the review of economic studies, from 19 publications: the Venus II trial had four publications(2, 29-31). All were fully published journal articles or HTA reports. There was one non-English

language study excluded. We have asked for this paper or its reference to be sent to us by the sponsor but we cannot confirm if the correct paper was subsequently provided. A paper in Turkish was sent to us but this was not an economic study (32).

The literature review reported results from three types of study: cost studies, resource use studies and studies showing the time to debridement. The studies showing only time to debridement were appraised by the EAC but were not economic studies and did not provide relevant information to inform the cost analysis. They are described and reasons given in Appendix 3. The only study from the sponsor's literature review of economic studies that was referenced in their independent economic analysis is the VenUS II trial by Soares et al. (29)

There were two posters with cost evidence that were sent to us by the sponsor in the clinical effectiveness submission (Pietroletti 2012(10) and Hawkins 2012(33)) but these were not discussed in the systematic review of economic evidence. Hawkins (2012)(33) compares the cost of debridement with larvae to Debrisoft but there are so few details about the methods that it was not found to be useful. Pietroletti (2012)(10) compares the costs of 5 episodes of enzymatic (171 Euros), and autolytic debridement (151 Euros) to one episode of Debrisoft (35 Euros) debridement. It is unclear why only one Debrisoft debridement was used. If five episodes had been used in this study the cost would have been 175 Euros – slightly more expensive than the other debridement methods. This poster is also discussed in the clinical effectiveness section of this report as it does have some comparative clinical evidence. No further information was available for either of these posters.

**Overview of methodologies of all included economic studies**

The EAC reviewed 10 of the studies included in the sponsor's submission (**Error! Reference source not found.**). Eight are cost studies; of which two of hem also report information of resource use. The other two papers are not strictly economic analyses but report information on resource use to debride wounds.

**Table 7: Included economic studies**

| Study (country) | Patient numbers | Type of study | Comparators | Economic Outcome |
|---|---|---|---|---|
| Wayman 2000 (UK)(34) | 12 | Randomised controlled trial | Hydrogel dressing<br>Larval therapy | Number of nursing visits required and the costs of nursing time and dressing to achieve debridement or one month of treatment |
| Harding 2000 (UK)(35) | - | Cost effectiveness study | Gauze<br>Granuflex<br>Comfeel | Calculation of comparative costs in £ sterling for three different treatment protocols for each wound type |
| Thomas 2006 UK(36) | - | Review study | Autolytic debridement<br>Maggots | Total cost of managing chronic wounds in UK |
| Mulder 1995 (USA)(37) | 17 | Retrospective analysis | Hypertonic saline hydrogel<br>Saline moistened gauze | Total cost of product and nursing time involved with wound care |
| Woo 2013 (Canada)(38) | hypothetical | Cost analysis | Sharp debridement<br>Autolytic debridement (hydrogel)<br>Enzymatic debridement<br>Biological debridement (Larvae)<br>Mechanical debridement (Gauze) | Cost associated with the various debridement methods available to achieve a clean wound base for healing |

| Study (country) | Patient numbers | Type of study | Comparators | Economic Outcome |
|---|---|---|---|---|
| Mosher 1999 (USA)(39) | - | Cost effectiveness study | Autolysis<br>Wet-to-dry dressing<br>Collagenase<br>Fibrinolysin | Cost-effectiveness of each debridement methods |
| Soares 2009 (UK)(29) | 267 | Cost-effectiveness study | Bagged larvae<br>Loose larvae<br>Hydrogel | Cost effectiveness outcome are expressed in terms of incremetal cost per ulcer-free day and incremental costs per quality adjusted life years |
| Waycaster 2013 (USA)(40) | - | Cost effectiveness study | Collagenase dressing<br>Hydrogel dressing | Direct medical costs of care to the long-term facility |
| Gilead 2012 (Israel)(41) | 435 | Observational study | Maggot debridement (no comparators) | Number of treatments and duration of treatments |
| Milne 2010 (USA) (42) | 14 | Randomised controlled trial | Hydrogel<br>Collagenase | Time to complete necrotic tissue debridement in institutionalized adults with pressure ulcers |

Cost and resource use studies included in the analysis are summarised below.

- Soares (2009)(29): This was a UK-based RCT funded by the NIHR HTA programme. It compared the effectiveness and cost-effectiveness of bagged larvae, loose larvae and hydrogel in patients with venous or mixed venous and arterial leg ulcers. Healing was the primary endpoint for the VenUS II trial. There were no statistically significant differences for this measure between the treatment groups; however significant differences in the time to debridement were reported (time to debridement with loose larvae was shorter). Information on resource use was collected from questionnaires completed by nurses and patients. The following was collected: cost of debriding agents, duration and costs of health care consultations, and nature and costs of compression therapy. Health benefit was measured in terms of ulcer-free days and quality adjusted life years (QALYs). Estimates of expected cost and benefit were reported for larval therapy and hydrogel. Descriptive measures of costs and health benefits for each of the three trial arms were presented. A sensitivity analysis was conducted to assess the impact on the results of using nurse reported data on consultation rather than patient reported data. The analysis indicates that larval therapy cost, on average, £97.60 more per participant per year than treatment with hydrogel.
- Wayman (2000)(34): in this randomised controlled trial larval debridement was compared with hydrogel dressing in the treatment of necrotic ulcer. The end point of the study was debridement of the ulcer or month's treatment, whichever was sooner. Only costs of nurse time and debrider were included in the analysis.
- Harding (2000)(35): the authors developed a model to compare the three comparators, which was populated with information derived from published clinical trial and from multinational studies on chronic venous

leg ulcers and pressure sores. Three protocols of care were designed using available information and compared.

- Thomas (2006)(36): the purpose of this review study was to calculate the cost savings that might be achieved when using maggot debridement therapy instead of autolytic debridement. Inputs were obtained from the available literature on different types of debridement techniques. The results suggest that the more widespread use of maggots would bring significant clinical benefits to patients and potential financial benefits to the NHS.
- Woo (2013)(38): the cost analysis was based on expert opinions on a hypothetical patient with a chronic wound that required debridement. The size of the wound was assumed to be 10cm X 10cm. Direct and indirect cost associated with wound debridement were estimated in the analysis including health care personnel, supplies, complications associated with the treatment, operating room, transportation and out-of-pocket expenses.
- Mosher (1999)(39): A decision-tree model was constructed to examine clinical outcomes and costs of four debridement protocols. Inputs for the model was derived from a literature review of the MEDLINE database from the years 1985 to 1995. The analysis was conducted from the payer's perspective (Medicare), hence, only direct costs were considered.
- Mulder (1995)(37): this retrospective analysis aimed t to compare the costs of hydrogel and secondary dressing with saline moistened gauze as debriding agents for dry eschar. The efficacy of hydrogel was published in a separate study (43). Cost of materials used and time required to change dressing were included in the analysis. Results suggest that hydrogel is a more cost effective than gauze in debriding wounds.
- Waycaster (2013)(40): A 3-stage Markov model was used to determine the expected costs and outcomes of wound care for collagenase and hydrogel dressings. Outcome results used in the analysis were taken

from a randomized clinical trial that directly compared collagenase and hydrogel dressings.

- Gilead (2012)(41): Non-comparative retrospective study. Information on the number of treatment and on the duration of visit was collected from 435 patients with chronic wounds treated with maggot debridement in 16 centres in Israel.
- Milne (2010)(42): The objective of this study was to identify the time to complete necrotic tissue debridement with collagenase compared to hydrogel in institutionalized adults with pressure ulcers. 27 patients were randomised to one of the two arms.

Comparative cost results for the included cost studies are in Table 8. Where costs were given in currencies other than GB Sterling, they were converted using the currently available exchange rates in order to make comparisons across studies. Calculated GB Sterling amounts are given in brackets, using the exchange rates of USA $= 0.641 and CAN $= 0.61. It can be seen that there is variation on whether larvae or hydrogel is cheaper.

**Table 8: Cost results from the systematic review**

| Author | Time horizon | Resource/cost included | Cost | | | |
|---|---|---|---|---|---|---|
| | | | Debrisoft | Hydrogel | Larvae | Gauze |
| Wayman (2000)(34)<br>UK | Time to achieve the debridement or one month of treatment | Number of nursing visits required and the costs of nursing time and dressing to achieve debridement or one month of treatment | N/A | £1,054 | £492 | N/A |
| Harding (2000)(35)<br>UK | 12 weeks | Dressing and nurse time costs, wound cleansing and debridement, the use of fillers, and compression. | N/A | N/A | £541 | N/A |
| Thomas (2006)(36)<br>UK | Annual | Total UK management cost | Not clear | Not clear | Not clear | Not clear |
| Mulder (1995)(37)<br>USA | Not clear | Dressing and nursing time | N/A | $193.93 (£124.22) | N/A | $182.47 (£116.93) |
| Woo (2013)(38)<br>Canada | Time to clean wound bed | Direct and indirect costs: health care personnel, supplies, complications associated with the treatment, operating room, transportation and out-of-pocket expenses | N/A | CAN $1504 (£918) | CAN $2150 (£1313) | CAN $1840 (£1123) |
| Mosher (1999)(39)<br>USA | Not clear | Costs for physician visit, diagnostic tests, and inpatient days | N/A | $920.73 (£589.8) | N/A | $1008.72 (£646.41) |
| VENUS II trial(29)<br>UK | 12 months | NHS perspective: costs of contacts with nurses and doctors at home, clinic, and hospital | N/A | £1,596 | £1,696 | N/A |
| Waycaster (2013)(40)<br>USA | 1 year | Direct medical costs of care to the long-term care facility: nursing time, dressings, wound care kits | N/A | $5480 (£3510) | N/A | N/A |

**Overview and critique of the sponsor's critical appraisal for each study**

Although the systematic review identified 16 studies, only 8 were quality assessed by the sponsor using the BMJ guidelines(44). As these studies were not used in the economic analysis they are not discussed further here. However, from the quality assessment VENUS II (Soares et al)(29) provided the most detail on methods and results of the analysis.

**Does the sponsor's review of economic evidence draw conclusions from the data available?**

Although the systematic review identified 16 studies, only one was used in the economic evaluation (the Venus II trial)(29). For the remainder, the characteristics of each study were tabulated, but no conclusions or interpretations of the results of the studies were provided in the sponsor's submission.

None of the identified studies provide evidence on the costs or cost-effectiveness of Debrisoft. The study by Soares et al(29), reporting the cost-effectiveness results from the VenUS II trial, is the most relevant to the analysis. It was a well-conducted study and resource-use results were prospectively collected. It was also relatively recently conducted and was from a UK perspective.

## *3.2 De novo cost analysis*

**Overview**

The sponsor provided a simple cost model executed in Microsoft Excel. The analysis presents the costs and resource-consequences of the use of Debrisoft in a community setting, and is compared with hydrogel, gauze and larvae. Separate analyses are conducted for applications in the home and applications in a clinic setting. The analysis takes an NHS perspective. It incorporates the costs of the technologies, supplementary technologies (such as dressings) and the costs of their application by a District Nurse.

The analysis assumes a ‘stopping rule’ for Debrisoft, such that if the wound is not completely debrided after a maximum of three applications, patients will switch to an alternative technology (hydrogel).

Key clinical information used in the analysis are based on two studies: The study by Bahr *et al* is used to inform the effectiveness of Debrisoft (1) and the VenUS II trial is used to inform the effectiveness of larvae and hydrogel (2). The effectiveness of gauze is based on assumptions made by the sponsor.

**Patients**

The sponsor states that patients included in the analysis are adults and children requiring debridement of an acute or chronic wound by a nurse in the community setting. Patients can be treated by district nurse at home (including residential or nursing home), or in a community-based clinic. Patients treated in hospital are excluded from the analysis and this is consistent with the scope issued by NICE.

We note that the scope and the sponsor’s submission refer to treatment of both adults and children; both documents also refer to the debridement of chronic and acute wounds. A single cost analysis is provided in the sponsor’s submission to account for all debridement; no distinction is made between adults and children, or between acute and chronic wounds. The clinical evidence used in the cost analysis is drawn from the debridement of chronic wounds in adult populations. We therefore consider the cost analysis to reflect the debridement of chronic wounds in adults.

**Technology and comparators**

The technology used in the de novo cost analysis is Debrisoft as a single-use pad to debride acute and chronic wounds.

The sponsor includes the two comparators listed in the scope issued by NICE:

- Hydrogel or other autolytic dressing;

- Cleansing with gauze.

In addition, the sponsor's cost analysis also includes larvae debridement as a comparator. The sponsor states that use of larvae is an appropriate comparator for sloughy wounds as it is used in the UK by nurses in the community. Two types of larvae are described in the submission: loose and bagged. However, in the economic analysis the sponsor included only loose larvae.

Advice from the NICE clinical advisor is that larvae are used in clinical practice in the UK and would be an appropriate comparator; however this would most likely be bagged larvae rather than loose. The inclusion of loose larvae in the sponsor's cost analysis is likely to bias against Debrisoft as bagged larvae tend to be more expensive than loose larvae. We explored the impact of this in supplementary analyses conducted by the EAC.

We note that the comparison with gauze included within the analysis is based on *debridement* with gauze, rather than *cleansing* with gauze. Debridement with gauze (also referred to as 'wet-to-dry' debridement) is reflected in the analysis with a visit to apply the gauze, and a separate visit where debridement takes place by removing the gauze. We consulted the NICE clinical advisors on which is the most appropriate comparator. There was some disagreement between centres about how gauze is used, and we concluded that there is variation in clinical practice in the use of gauze in the UK.

**Model structure**

The model is described in the submission as a cost-consequence analysis. It presents the costs and resource consequences of the technologies and is therefore consistent with the MTEP methods guide (45). The clinical pathway included in the model involves:

- an assessment of the skin and wound by a District Nurse

- ordering the debridement agent if not available to the District Nurse immediately

- application of the debridement agent by a District Nurse

- re-assessment of the wound. One or more further applications of the debridement products until debridement is judged to be complete.

Overall, the EAC considers this general reflection of the pathway of care to be appropriate.

The sponsor states that the time horizon reflects the time necessary to complete debridement of the wound; hence, it varies between comparators. The EAC considers this timeframe to be appropriate if only concerned with debridement; however we consider that time to wound healing would be a more appropriate time horizon to judge the costs and resource-consequences of the products. This would be a more meaningful outcome for patients and could reflect that patients may require multiple debridement rather than just one successful debridement. In addition, we note that the clinical information used in the cost analysis is derived from studies where complete debridement of all patients was not observed (discussed further below).

The analysis assumes a 'stopping rule' for Debrisoft, such that if the wound is not completely debrided after a maximum of three applications, patients will switch to debridement with hydrogel. No switching to alternative debridement products is included for the three comparators. This assumption reflects the design of the Bahr et al study. In this study all patients received a maximum of three applications of Debrisoft. We queried with the NICE clinical experts whether a maximum of three applications of Debrisoft and whether switching to hydrogel was plausible. The advice from one clinical expert was that the choice of debridement product would depend on the type and position of the wound and the reason for debridement. One of the clinical experts further advised that 2-3 applications of Debrisoft would be required to debride a hard eschar, and 1 application for a sloughy wound. The EAC note that the trial protocol for the ongoing trial of Debrisoft also specifies a maximum number of

3 applications for Debrisoft and a maximum number of three applications for hydrogel. The results of this trial will therefore offer no further information on the average number of applications for debridement or wound healing.

Two possible scenarios are considered in the model: if the patient is seen at home or in a community based clinic. Both scenarios are presented for each comparator and analysed as two separate analyses. This implicitly assumes that the choice of technology is not affected by where the patient is treated (and vice versa).

The key assumptions in the sponsor's model are noted below.

- The maximum number of applications of Debrisoft is three.
- Patients whose wounds are not fully debrided after three applications of Debrisoft are then treated with hydrogel.
- No patients treated with hydrogel, gauze or larvae switch to an alternative debridement agent
- All treatments are provided by a District Nurse and each visit takes 15 minutes.
- No adverse events that require treatment with NHS resources are associated with any of the debridement agents.
- Treatment is based on a wound size of 10cm by 10cm
- Hyodrogel and Debrisoft must be pre-ordered for use in a home setting but are available immediately in a clinic setting. Larvae must be pre-ordered for use in home or clinic settings. Pre-ordering requires an extra appointment with the nurse for a return visit to apply the treatment. Gauze does not require pre-ordering in any setting.
- Following treatment with hydrogel, gauze and larvae, an additional nurse appointment is required to assess the success of debridement. For Debrisoft this assessment occurs immediately after application within the same nurse appointment.

## Clinical parameters and variables

Clinical parameters in the model were obtained from a variety of sources, and are outlined in section 8.2.5 of the sponsor's submission.

*Number of treatment applications*

A key driver of the cost analysis is the number of applications required to achieve complete debridement for each product. In the absence of comparative results for Debrisoft with the other products, the sponsor based the number of applications on two key sources of clinical information, supplemented by assumptions.

The mean number of applications of larvae and hydrogel are based on the VenUS II trial (2, 29). The primary outcome of this study was wound healing. In the trial the number of applications was measured over the period of one year of follow-up. Debridement continued until full debridement or until the discontinuation of debridement treatment as the debridement phase.

The mean (SD) number of applications of loose and bagged larvae were 1.44 (1.22) and 1.46 (1.06) respectively. The sponsor used the average of all larvae in the analysis (1.45)(29). For hydrogel a mean (SD) of 9.2 (27.78) applications was reported (29) and used in the sponsor's analysis. The sponsor reported a lack of relevant sources of information on the likely number of applications required for gauze and assumed an average of 12 applications would be required to achieve debridement.

The information on Debrisoft came from the study by Bahr *et al.(1)* This reported that 77% of wounds treated with Debrisoft were completely debrided after three applications at 12 days of follow-up (1). Patients in the study by Bahr et al(1) received a maximum of three applications, and the mean number of Debrisoft applications to debridement (or healing) comparable to the results from the VenUS II study(29) were not available.

In addition, we note that the statistic of 77% complete debridement is taken from the 'Discussion' section of the paper by Bahr *et al*, and is not reported

within the ‘Results’ section of the paper. The primary outcome in the study by Bahr et al was debridement efficacy expressed as three grades of debridement (see Section 2.4 for further details). The authors report that after three applications of Debrisoft 47% of wounds were identified as class A; 25% as class B; 7% as class C; and 21% had re-epithelialised (1). We requested information from the sponsor as to whether this outcome was pre-specified in the analysis plan for the trial. They responded that the primary endpoint was debridement efficacy at days 0, 4 and 8. They further stated that in the Result section of the paper the proportion achieving debridement at 8 days was reported, which accounts for only 28% of patients. In referring to the two sets of results (reported in the results and discussions section) the sponsor further noted *“The two parameters, “complete debridement” and “proportion of each class of wound” could not be correlated to difference in their endpoint.”*

The lack of information from a direct comparison or network meta-analysis means that the comparison of number of applications for each of the products is likely to be biased. It is difficult to judge the likely impact of that bias on the results. We have attempted to examine the characteristics of the patients’ and their wounds included in the two studies; however very little information is available in the reported publication by Bahr et al(1) . We requested additional information from the sponsor on patient and wound characteristics at baseline and these are reported in Table 9 below. The population in the Bahr study were slightly younger than in the VenUS II trial , but had larger wounds to debride.

**Table 9. Baseline characteristics for the clinical studies used in the cost analysis**

| Characteristics | VENUS II(2) | Bahr 2010(1) |
|---|---|---|
| Population | 267 | 57 |
| Age (SD) | 74 (12.6) | 68 (14.5) |
| Type of wound | Venous or mixed venous and arterial ulcers with at least 25% coverage of slough or necrotic tissue | Chronic wound |
| Median size of wound (range) cm^2 | 13.2 (0.6-197.9) | 17.4(1.94-391) |
| Duration of wound (months) | Median 7<br>Range: 1-372 | Mean 5.2<br>SD:2.3 |

In the cost model it was assumed that patients not completely debrided after three applications of Debrisoft would be switched to debridement with hydrogel. These patients are then assumed to receive the same number of applications of hydrogel as for patients treated with hydrogel initially (9.2 applications). The EAC considers this to be a conservative assumption as it implies that initial debridement with Debrisoft had no impact at all.

For larvae, hydrogel and gauze it was assumed that all wounds are fully debrided after the mean number of applications (see Table 11). From the reported Kaplan-Meier curves of the VenUS II trial, it appears that the probability of debriding at the end of the study (320 days follow-up) was approximately 0.975 with larvae and 0.78 with hydrogel. After the mean length of treatment the probability of debriding was 0.46 for larvae (length of treatment 12-13 days) and 0.34 for hydrogel (length of treatment 43 days). (2)

*Time to debridement*

Information on the time to debridement is provided in the sponsor's submission and included in Table 10 below for completeness; however, these results are not used within the cost model because they use the number of applications instead and this is correlated to time to debridement.

**Table 10: Reported time to debridement**

| Treatment | Duration (days) | Source |
|---|---|---|
| Larvae | 12-13 | Soares M (2009)(29) |
| Hydrogel | 43 | Soares M (2009)(29) |
| Gauze | 28 | Conservative assumption |
| Debrisoft | 12 | Bahr S (2011)(1) |

**Table 11: Summary of key inputs for the sponsor's economic model**

| Variables | Value | Source |
|---|---|---|
| Larvae number of applications | 1.45 | Soares M (2009)(29) |
| Hydrogel number of applications | 9.2 | Soares M (2009)(29) |
| Gauze number of applications | 12 | Assumption |
| Debrisoft number of applications | 3 | Bahr S (2011)(1) |
| Efficacy of Debrisoft after 3 applications | 0.77 | Bahr S (2011)(1) |
| Treatment if Debrisoft fails after 3 applications | Hydrogel | Assumption |
| Time per visit (minutes) | 15 | Assumption |

## Resource identification, measurement and valuation

Resource use in the community setting was derived from searches of the clinical and economic literature in conjunction with the expert opinions of four experienced tissue viability nurses from the UK. The following resources are included in the analysis:

- District nurse home visit
- District nurse clinic visit
- Debrider Gauze
- Debrider Hydrogel

- Debrider Larvae
- Debrider Debrisoft
- Cover dressing: Film and Absorbent dressing pad
- Dressing pack

The valuation of resource use was reported as obtained from published sources where possible. Costs were expressed in 2012-2013 GB pounds sterling.

*Debridement products*

The amount of each product required is assumed to be based on the number of applications required and the amount of product for each application. It is assumed that the amount of product required is to debride a wound of 10cm by 10cm. This information is summarized in Table 12.

Device costs are taken from the British National Formulary (BNF) 2013 . The unit costs of larvae are not listed in the BNF and were provided directly to the sponsor by one of the suppliers (46).

**Table 12: Amount and unit cost of each debridement product**

| Parameter | No. of application to complete debridement | Source | Cost per pack | No of units per pack | Unit | Cost per applic-ation | Source |
|---|---|---|---|---|---|---|---|
| Debrisoft | 3 | Bahr S (2010)(1) | £6.19 | 1 | 10cm X 10cm dressing | £6.19 | BNF 2013 (A5.5.3) |
| Loose Larvae | 1.45 | Soares M (2009)(29) | £175.00 | 300 | 10cm X 10cm dressing | £175.00 | Biomonde personal communication (2013) |
| Bagged Larvae | 1.45 | Soares M (2009)(29) | £295.00 | 400 | 10cm X 10cm dressing | £295.00 | Biomonde personal communication (2013) |
| Hydrogel | 9.2 | Soares M (2009)(29) | £2.03 | 1 | 15g or 10cm x 10cm sheet | £2.03 | BNF 2013 (median price) A5.2.1 |
| Gauze | 12 | Conservative assumption based on clinical opinion | £0.39 | 5 | 7.5cm x 7.5cm dressing | £0.39 | BNF 2013 (A5.7.2) |

The costs of larvae included in the analysis are based on the costs of loose larvae. Advice from a NICE clinical advisor is that bagged larvae would be used in UK clinical practice. This would have the effect of making larvae more expensive relative to Debrisoft. We have considered this in supplementary analyses conducted by the EAC.

We note that the costs of larvae differ substantially from those reported in the VenUS II study (29). Soares *et al* obtained unit costs (reported as prices in 2006) directly from larvae suppliers and noted unit costs for loose larvae as £58 per 300 maggots plus £16.50 delivery (sources: LarvE, Zoobiotic) and for bagged larvae as £98.79 per 300 maggots plus £20.89 delivery (sources: Biobag, Biomonde)(29). The EAC has checked the current prices of larvae. We note that one of the companies cited in the paper by Soares *et al* (Zoobiotic) has since been taken over by the other company (Biomonde). The EAC confirms that the unit costs of larvae reported in the sponsor's submission are as advertised on the larvae suppliers website (46) .

From the initial submission it was unclear whether the unit costs of larvae included delivery costs. We clarified with this with sponsor who confirmed that packaging and delivery costs are included within these unit costs.

*Supplementary products*

For all debridement products, a sterile dressing pack is used at each visit (£0.60 per pack).

When Hydrogel is applied on the wound a secondary, non-absorbent dressing is needed (film dressing). It is assumed in the cost analysis that this cost would be incurred for each appointment (£1.02 per dressing). Larvae and Gauze just need the application of absorbent dressing pads and these costs (£0.17 per dressing) are assumed to apply for each visit. The sponsor states that Debrisoft does not require any applications of secondary dressings and therefore no additional dressing costs are included.

The EAC consider that the additional film and absorbent dressings would not be required prior to debridement, specifically at the first appointment if the

debridement product has to be ordered. The sponsor included the cost of film for all appointments in the hydrogel group and absorbent dressings for all appointments in the larvae group. The EAC has assessed the impact of this in their supplementary analyses.

*Nurse visits and application of debridement products*

The number of nurse visits is assumed to depend on the product and its availability at the moment of the first visit. This in turn depends on whether the patient is seen at home, or in a community based clinic.

The model assumes that gauze is available immediately in both home and clinic settings. Debrisoft and hyodrogel must be pre-ordered for use in a home setting but are available immediately in a clinic setting. Larvae must be pre-ordered for use in home or clinic settings. This results in an extra appointment with the nurse for these treatments as there is an initial appointment to assess the wound and order the product, then another appointment to apply the treatment.

It is assumed within the cost model that an additional nurse appointment is required to assess the success of debridement following treatment with hydrogel, gauze and larvae. For Debrisoft, the model reflects that the nurse can assess the success of debridement immediately following application within the same nurse appointment.

A summary of the number of visits required for each treatment is provided in Table 13. It is assumed that each health care contact is with a District Nurse and takes 15 minutes. Travel time is included for home visits. District Nurse costs are stated as taken from Table 10.1 reporting costs of a Community Nurse with qualifications from the Unit Costs of Health and Social Care compiled by the PSSRU (2012)(47). The estimates provided by the sponsor are £24.25 for a home visit and £12.75 for a clinic visit.

The EAC considers that a miscalculation has occurred in the estimation of District Nurse costs. The PSSRU reports the costs of a Community Nurse with and without qualifications, with the former provided as an additional figure in

parenthesis in the PSSRU report. The costs given for home visits include travel costs; no estimate of home visits without travel cost is provided. We believe that the sponsor has incorrectly interpreted the figures in/out of parenthesis as the costs with/without travel. We have clarified this with researchers at PSSRU who confirmed that our interpretation is correct.

The PSSRU estimated cost of one hour of patient contact time is £58 for a Community Nurse with qualifications, and £70 per hour of home visit, including travel time, for a Community Nurse with qualifications.(47) Therefore the cost for 15 minutes of qualified Community Nurse time would be £14.50 for a clinic visit and £17.50 for a home visit. We have incorporated these unit costs in the supplementary analyses conducted by the EAC.

**Table 13: Assumption regarding number of visits for application of debridement and assessment of wounds**

| Treatment | Location | First application | Subsequent applications |
|---|---|---|---|
| Larvae | Home | **3 visits**<br>1. Assess and order treatment<br>2. Apply treatment<br>3. Re-assess and reorder if needed | **2 visits**<br>1. Apply treatment<br>2. Re-assess and reorder if needed |
| Larvae | Clinic | **3 visits**<br>1. Assess and order treatment<br>2. Apply treatment<br>3. Re-assess and reorder if needed | **2 visits**<br>1. Apply treatment<br>2. Re-assess and reorder if needed |
| Hydrogel | Home | **3 visits**<br>1. Assess and order treatment<br>2. Apply treatment<br>3. Re-assess and reorder if needed | **1 visit**<br>1. Reassess and reapply |
| Hydrogel | Clinic | **2 visits**<br>1. Assess and apply treatment<br>2. Re-assess and reapply if needed | **1 visit**<br>1. Reassess and reapply |
| Gauze | Home | **2 visits**<br>1. Assess and apply treatment<br>2. Re-assess and reapply if needed | **1 visit**<br>1. Reassess and reapply |
| Gauze | Clinic | **2 visits**<br>1. Assess and apply treatment<br>2. Re-assess and reapply if needed | **1 visit**<br>1. Reassess and reapply |
| Debrisoft | Home | **1 visit**<br>1. Assess and apply treatment. Re-assess debridement | **1 visit**<br>1. Reassess and reapply |
| Debrisoft | Clinic | **1 visit**<br>1. Assess and apply treatment. Re-assess debridement | **1 visit**<br>1. Reassess and reapply |

We consulted with the NICE clinical experts on the assumptions regarding the number of healthcare contacts required for each type of debridement but we did not receive useful information on this.

We note that the time taken per visit is very different from that reported in the VenUS II study (29). In VenUS II results on the length of clinic and home visits were recorded by nurses prospectively. Soares *et al* report that the average duration of clinic visits to be 22 minutes and for home visits 40 minutes (29). We have assessed the impact of this in supplementary analyses conducted by the EAC. We also consulted with the NICE clinical experts regarding the assumption of each healthcare contact taking place with a District Nurse and lasting for 15 minutes but no clear confirmation was provided.

**Technology and comparators' costs from the sponsor's submission**

**Debrisoft (home visit) - £161.77**

- 4 District nurse visits (DN visit cost £24.25 + 1 Dressing pack £0.6) – £99.40
- 3 Applications - £18.57
- Cost to debride with Debrisoft (77% of patients) - £117.97
- Cost to debride with Hydrogel (23% of patients) - £308.42

**Debrisoft (clinic visit) - £83.14**

- 3 District nurse visits (DN visit cost £12.75 + 1 Dressing pack £0.6) - £40.05
- 3 Applications - £18.57
- Cost to debride with Debrisoft (77% of patients) - £58.62
- Cost to debride with Hydrogel (23% of patients) - £165.25

**Hydrogel (home visit) - £308.42**

- 11.2 District nurse visits (DN home visit cost £24.25 + 1 Dressing pack £0.6 + secondary dressing £1.02) - £289.74
- 9.2 Applications - £18.68

**Hydrogel (clinic visit) - £165.25**

- 10.2 District nurse visits (DN visit cost £12.75 + 1 Dressing pack £0.60 + secondary dressing £1.02) - £146.57
- 9.2 Applications - £18.68

**Gauze (home visit) - £329.94**

- 13 District nurse visits (DN home visit cost £24.25 + 1 Dressing pack £0.60 + Secondary dressing £0.17) – £325.26
- 12 Applications - £4.68

**Gauze (Clinic visit) - £180.44**

- 13 District nurse visits (DN clinic visit cost £12.75 + 1 Dressing pack £0.60 + Secondary dressing £0.17) – 175.76
- 12 Applications - £4.68

**Larvae (home visit) - £351.33**

- 3.9 District nurse visits (DN home visit cost £24.25 + Dressing pack £0.60 + Secondary dressing £0.17) – £97.58
- 1.45 Applications – 253.75

**Larvae (clinical visit) - £306.48**

- 3.9 District nurse visits (DN clinic visit cost £12.75 + 1 Dressing pack £0.60 + Secondary dressing £0.17) – 52.73
- 1.45 Applications - £253.75

## Sensitivity analysis

The submission included details of deterministic sensitivity analysis and scenario analysis conducted to explore uncertainty around model parameters and the effect that this has on the incremental cost of Debrisoft. No probabilistic analyses were presented.

The number of debridement applications and the number of district nurse visits were increased and decreased by 20%, owing to the absence of consistent information about the likely variation in mean values. Additional sensitivity analyses were conducted on unit costs and product prices, considering an increase and decrease of 20%.

The cost of debrider gauze, debrider hydrogel, cover dressing, and dressing pack were omitted from the sensitivity analysis. This choice was justified on the grounds that the costs are marginal and would not have a significant impact on the results of the model.

A multi-way scenario sensitivity analysis was conducted on two parameters: probability that Debrisoft will debride wound after 3 applications and the number of district nurse visits (hydrogel) in clinic.

## *3.3 Results of de novo cost analysis*

### Base-case analysis results

Results as reported from the sponsor's submission base-case model are shown in Table 14 and Table 15 below. These results suggest that Debrisoft is cost saving in both contexts (clinical and home visits). The EAC confirm that results in the submission match the output of the submitted model.

**Table 14: Sponsor's submission base case-result (home visit)**

| Intervention | Debrisoft | Gauze | Hydrogel | Larvae |
|---|---|---|---|---|
| **Mean cost per patient (£)** | 162 | 330 | 308 | 351 |
| **Debrisoft incremental cost (£)** | | -168 | -147 | -190 |

**Table 15: Sponsor's submission base case result (clinic visit)**

| Intervention | Debrisoft | Gauze | Hydrogel | Larvae |
|---|---|---|---|---|
| **Mean cost per patient (£)** | 83 | 180 | 165 | 306 |
| **Debrisoft incremental cost (£)** | | -97 | -82 | -223 |

### Sensitivity analysis results

The sponsor varied the number of nurse visits, duration of nurse visits, unit costs and product prices (larvae and Debrisoft only) by an increase and decrease of 20%. In the multi way scenario-based sensitivity analysis, the sponsor varied simultaneously the percentage of wounds completely debrided after three application of Debrisoft and the number of nurse visits for hydrogel in clinic.

Results of the sponsor's sensitivity analysis as reported in their submission are shown in Table 16 and Table 17 below:

Debrisoft remained cost-saving for clinical and home visit in all scenarios tested.

**Table 16: Sponsor's submission sensitivity analysis results**

| Variable | Debrisoft incremental cost using (-20% of base case values) | | | | | | Debrisoft incremental cost using (+20% of base case values) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Gauze | | Hydrogel | | Larvae | | Gauze | | Hydrogel | | Larvae | |
| | Home | Clinic | Home | Clinic | Home | Clinic | Home | Clinic | Home | Clinic | Home | Clinic |
| No Application Larvae | -£168 | -£97 | -£147 | -£82 | -£139 | -£173 | -£168 | -£97 | -£147 | -£82 | -£240 | -£274 |
| No Application Hydrogel | -£169 | -£98 | -£144 | -£79 | -£190 | -£224 | -£167 | -£96 | -£150 | -£85 | -£189 | -£223 |
| No Application Debrisoft | -£171 | -£100 | -£150 | -£85 | £192 | -£226 | -£165 | -£94 | -£144 | -£79 | -£187 | -£221 |
| No Application Gauze | -£167 | -£96 | -£147 | -£82 | £190 | -£223 | -£169 | -£98 | -£147 | -£82 | -£190 | -£223 |
| No of nurse visit Larve | -£168 | -£97 | -£147 | -£82 | £170 | -£213 | -£168 | -£97 | -£147 | -£82 | -£209 | -£234 |
| No of nurse visit Hydrogel - home | -£182 | -£97 | -£102 | -£82 | £203 | -£223 | -£155 | -£97 | -£191 | -£82 | -£176 | -£223 |
| No of nurse visit Hydrogel - clinic | -£168 | -£104 | -£147 | -£60 | £190 | -£230 | -£168 | -£91 | -£147 | -£105 | -£190 | -£217 |
| No of nurse visit Gauze | -£103 | -£62 | -£147 | -£82 | £190 | -£223 | -£233 | -£132 | -£147 | -£82 | -£190 | -£223 |
| No of nurse visit Debrisoft - home | -£184 | -£97 | -£162 | -£82 | £205 | -£223 | -£153 | -£97 | -£131 | -£82 | -£174 | -£223 |
| No of nurse visit Debrisoft - clinic | -£168 | -£104 | -£147 | -£88 | £190 | -£230 | -£168 | -£91 | -£147 | -£76 | -£190 | -£217 |
| Nurse time - home | -£133 | -£97 | -£120 | -£82 | £198 | -£223 | -£204 | -£97 | -£174 | -£82 | -£181 | -£223 |
| Nurse time - clinic | -£168 | -£76 | -£147 | -£68 | £190 | -£225 | -£168 | -£119 | -£147 | -£96 | -£190 | -£221 |
| Debrider larvae (loose) | -£168 | -£97 | -£147 | -£82 | £139 | -£173 | -£168 | -£97 | -£147 | -£82 | -£240 | -£274 |
| Debrider Debrisoft | -£171 | -£100 | -£150 | -£85 | £192 | -£226 | -£165 | -£94 | -£144 | -£79 | -£187 | -£221 |

**Table 17: Sponsor's submission multi-way scenario analysis results**

| Variable | Probability debrisoft debride the wound | Nuber of nurse visits Hydrogel -clinic | Gauze | | Hydrogel | | Larvae | |
|---|---|---|---|---|---|---|---|---|
| | | | Home | Clinic | Home | Clinic | Home | Clinic |
| Base case | 77% | 10.2 | | -£97 | | -£82 | | -£223 |
| Scenario 1 | 77% | 5 | -£168 | -£114 | -£147 | -£25 | -£190 | -£241 |
| Scenario 2 | 77% | 12 | | -£91 | | -£102 | | -£217 |
| Scenario 3 | 50% | 5 | | -£106 | | -£16 | | -£232 |
| Scenario 4 | 50% | 10.2 | -£117 | -£69 | -£95 | -£53 | -£138 | -£195 |
| Scenario 5 | 50% | 12 | | -£56 | | -£66 | | -£182 |
| Scenario 6 | 90% | 5 | | -£119 | | -£29 | | -£245 |
| Scenario 7 | 90% | 10.2 | -£193 | -£111 | -£171 | -£96 | -£214 | -£237 |
| Scenario 8 | 90% | 12 | | -£109 | | -£119 | | -£235 |

## Subgroup analysis

The scope specified that subgroups defined according to whether wounds are open or closed should be considered. The sponsor did not provide an analysis of these subgroups. The key consideration for a subgroup analysis is whether the number of applications used differs for open compared to closed wounds. The clinical evidence does not have any comparative information on which to base a subgroup analysis of this type; however we note that comparative information is also not available for the main analysis.

## Model validation

The sponsor noted that the model was validated with the clinical experts outlined in Section 8.2.5. of the submission. Several tests, listed in section 8.7.1 of the submission, were undertaken for testing the technical validity of the model.

The EAC also undertook a check of the model inputs and calculation. Upon review of the analyses the EAC found an error in the calculations of the total cost of Debrisoft. It is stated in the submission that the cost analysis assumes that, in the Debrisoft group, all patients receive a maximum of three applications of Debrisoft. The wounds of 77% of these patients are fully debrided and require no further debridement, the remaining 23% are assumed to then receive hydrogel. The model submitted by the sponsor calculates that

77% of patients received Debrisoft and the 23% of patients received Hydrogel. Therefore the cost of Debrisoft applications (including product, District nurse visits etc) for the 23% of people who switch has been incorrectly omitted from the analysis. We queried this with the sponsor who agreed that their original calculation was incorrect. We have corrected this in our supplementary analysis presented below.

The error identified for the base case analysis and described above also applies to all of the sensitivity analyses. In addition, errors in the sensitivity analyses are also noted. It is assumed that a 20% increase/decrease in the number of applications increases/decreases the frequency of nurse contacts OR the amount of debridement product required, but never both together because a visit from a nurse would be associated with use of a debridement product. The EAC considers this to be inappropriate. Furthermore, the 20% increase/decrease is also applied to Debrisoft. This implies that all patients receive a *maximum* (note not mean) number of application of 2.4 or 3.6, which is not possible. This error has been further considered in the EAC's analysis presented below.

### *3.4 Interpretation of economic evidence*

The sponsor concluded that Debrisoft is cost saving for use in the debridement of wounds compared to larvae, gauze and hydrogel. This result is driven largely by the requirement for fewer appointments with Debrisoft compared to hydrogel and gauze in the analysis, and from cheaper product costs for Debrisoft relative to larvae. The sponsor notes in the submission that the lack of information directly comparing gauze, hydrogel, larvae and Debrisoft is a key weakness. The EAC agrees that the lack of comparative information for Debrisoft with any of the comparators makes an assessment of the resource implications difficult as it is dependent on the relative effectiveness and number of applications required for each product. In addition, there are some assumptions and estimates in the analysis that the EAC consider to be incorrect or unlikely including the error in implementing the switching rule, the unit costs of a district nurse, the time spent by the district nurse, the use of loose larvae and the cost of hydrogel and dressings.

These are explored in the supplementary analysis conducted by the EAC and are reported below.

## *3.5 Additional work undertaken by the External Assessment Centre in relation to economic evidence*

### *Corrected sponsor's base case*

The EAC corrected the error detected in the cost model relating to the incorrect application of switching (including the costs of Debrisoft applications for those people who switch to hydrogel). The corrected results for the sponsor's base-case are provided in Table 18 and Table 19. These reduce the cost savings of Debrisoft compared to the three comparators.

**Table 18: Corrected base case result (home visits)**

| Intervention | Debrisoft | Gauze | Hydrogel | Larvae |
|---|---|---|---|---|
| **Mean cost per patient (£)** | 189 | 330 | 308 | 351 |
| **Debrisoft incremental cost (£)** | | -141 | -120 | -162 |

**Table 19: Corrected base case result (clinic visits)**

| Intervention | Debrisoft | Gauze | Hydrogel | Larvae |
|---|---|---|---|---|
| **Mean cost per patient (£)** | 97 | 180 | 165 | 306 |
| **Debrisoft incremental cost (£)** | | -84 | -69 | -210 |

### Corrected sponsor's sensitivity analysis

The EAC corrected the sponsor's sensitivity and scenario analysis based on the corrected error detected in the cost model relating to the incorrect application of switching. Results obtained from the increment and decrease in number of applications also include a corresponding variation in the number of district nurse visit. The results of this analysis are reported in Table 20 and Table 21. Debrisoft remained cost-saving for clinic and home visits in all scenarios tested but not by as much as in the sponsor's submission.

**Table 20: Corrected sensitivity analysis results**

| | Values | Hydrogel - home | Gauze - home | Larvae - home | Hydrogel - clinic | Gauze - clinic | Larvae - clinic |
|---|---|---|---|---|---|---|---|
| **Base case (77% correction)** | | **-£120** | **-£141** | **-£162** | **-£69** | **-£84** | **-£210** |
| | | | | | | | |
| Number of applications - Larvae | 1.2 | -£120 | -£141 | -£97 | -£69 | -£84 | -£151 |
| | 1.7 | -£120 | -£141 | -£228 | -£69 | -£84 | -£268 |
| Number of applications - hydrogel | 7.4 | -£80 | -£153 | -£178 | -£34 | -£91 | -£133 |
| | 11.0 | -£159 | -£129 | -£156 | -£75 | -£77 | -£111 |
| Number of applications - Debrisoft | 2.4 | -£138 | £160 | £181 | -£80 | -£96 | -£222 |
| | 3.6 | -£101 | £122 | £144 | -£57 | -£72 | -£198 |
| Number of applications - Gauze | 9.6 | -£120 | -£80 | -£162 | -£69 | -£50 | -£210 |
| | 14.4 | -£120 | -£202 | -£162 | -£69 | -£117 | -£210 |
| Nurse cost per visit home | 19.4 | -£97 | -£110 | -£175 | -£69 | -£84 | -£210 |
| | 29.1 | -£142 | -£172 | -£175 | -£69 | -£84 | -£210 |
| Nurse cost per visit clinic | 10.2 | -£120 | -£141 | -£162 | -£56 | -£64 | -£214 |
| | 15.3 | -£120 | -£141 | -£162 | -£81 | -£103 | -£206 |
| Debrider larvae (loose) | 140 | -£120 | -£141 | -£112 | -£69 | -£84 | -£159 |
| | 210 | -£120 | -£141 | -£213 | -£69 | -£84 | -£261 |
| Debrider Debrisoft | 5 | -£123 | -£145 | -£166 | -£72 | -£88 | -£214 |
| | 7.4 | -£116 | -£137 | -£159 | -£65 | -£80 | -£206 |

**Table 21: Corrected scenario analysis results**

| Variable | Probability debrisoft debride the wound | Number of nurse visits hydrogel - clinic | Gauze | | Hydrogel | | Larvae | |
|---|---|---|---|---|---|---|---|---|
| | | | Home | Clinic | Home | Clinic | Home | Clinic |
| Base case | 77% | 10.2 | | -£84 | | -£69 | | -£210 |
| Scenario 1 | 77% | 5 | -£84 | -£103 | -£69 | -£47 | -£210 | -£229 |
| Scenario 2 | 77% | 12 | | -£78 | | -£198 | | -£203 |
| Scenario 3 | 50% | 5 | | -£82 | | -£10 | | -£208 |
| Scenario 4 | 50% | 10.2 | -£58 | -£39 | -£36 | -£24 | -£79 | -£165 |
| Scenario 5 | 50% | 12 | | -£26 | | -£108 | | -£150 |
| Scenario 6 | 90% | 5 | | -£114 | | -£65 | | -£240 |
| Scenario 7 | 90% | 10.2 | -£181 | -£105 | -£160 | -£90 | -£203 | -£231 |
| Scenario 8 | 90% | 12 | | -£103 | | -£241 | | -£228 |

*EAC additional analysis*

The EAC conducted a number of supplementary analyses to test the robustness of the results to a number of key assumptions. These are described below. We have tested the impact of each amendment individually and cumulatively on the results of the cost analysis.

*Unit cost of a District Nurse*

As described above, the average cost of a District nurse appointment was incorrectly calculated in the cost model. We have amended this and included District Nurse costs of £70 per hour for home visits and £58 per hour for clinic appointments (47). This is based on costs reported for the costs of a Community Nurse with qualifications from the Unit Costs of Health and Social Care compiled by the PSSRU (2012) (47).

*Type of larvae*

Type of larvae The NICE clinical advisor confirmed that bagged larvae are used in the UK rather than loose. We have updated the unit costs to reflect a unit cost of bagged larvae of £295 (46).

*Inclusion of additional dressings*

In addition to the dressing pack included for all visits, the sponsor included cost of additional film or absorbent dressings for gauze, hydrogel and larvae. These were included for all visits, but the EAC considers that they would not be required if the product was not applied during the visit (i.e. if the nurse has to order the debridement product and make return visit to apply it). The costs of the dressing associated with these visits were removed from the analysis.

*Length of district nurse contact.*

In the base case analysis it was assumed that the length of a district nurse contact is 15 minutes. This was based on an assumption in the sponsor's submission. However we used evidence from the VenUS II trial in sensitivity analyses so we tested this assumption by assuming that all district nurse

contacts would take 22 minutes in clinic and 40 minutes at home, based on the time taken for dressing applications reported by Soares et al(29).

*Cost of hydrogel, gauze and dressings.*

There are many different unit costs listed in the BNF for some resources, including hydrogel, gauze and dressings. The sponsor's basecase uses the median price from each category. The EAC considers that the cheapest option should be used in practice and have included this is the analysis.

The results of this analysis (individually and cumulatively) are shown in Table 22 below. These results suggest that Debrisoft, after applying all changes cumulatively, is even more cost saving than in the sponsor's base case.

This is mainly due to the longer length of district nurse contact and the higher cost of bagged larvae.

**Table 22: EAC base case results: (individually and cumulatively)**

| | Individual impact | | | | | | Comulative impact | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Home visit | | | Clinic visit | | | Home visit | | | Clinic visit | | |
| | Hydrogel | Gauze | Larvae | Hydrogel | Gauze | Larvae | Hydrogel | Gauze | Larvae | Hydrogel | Gauze | Larvae |
| Sponsor base case | -£147 | -£168 | -£190 | -£82 | -£97 | -£223 | | | | | | |
| A 100% receive Debrisoft | -£120 | -£141 | -£162 | -£69 | -£84 | -£210 | -£120 | -£141 | -£162 | -£69 | -£84 | -£210 |
| B Nurse cost per hour: £ 70 | | | | | | | | | | | | |
| Nurse cost per visit home (15 mins): £17.5 | | | | | | | | | | | | |
| Nurse cost per visit clinic (15 mins) : £14.5 | -£109 | -£119 | -£201 | -£92 | -£112 | -£222 | -£88 | -£98 | -£180 | -£77 | -£97 | -£207 |
| C Bagged larvae instead of Loose larvae | -£147 | -£168 | -£364 | -£82 | -£97 | -£397 | -£88 | -£98 | -£354 | -£77 | -£97 | -£381 |
| D Dressing adjustment | -£146 | -£170 | -£192 | -£82 | -£99 | -£225 | -£88 | -£98 | -£355 | -£76 | -£97 | -£381 |
| E Nurse time (Soares) | -£288 | -£355 | -£145 | -£115 | -£147 | -£219 | -£222 | -£285 | -£276 | -£109 | -£149 | -£372 |
| F Cheapest alternative | -£135 | -£172 | -£193 | -£71 | -£101 | -£227 | -£211 | -£288 | -£280 | -£99 | -£152 | -£375 |
| Comulative base case results | | | | | | | **-£211** | **-£288** | **-£280** | **-£99** | **-£152** | **-£375** |

The EAC re-ran the sponsor's sensitivity and scenario analyses based on the base case results reported in Table 22. Additional parameters and variations were considered in the analyses. These parameters and variations include:

- Duration of nurse visit (home and clinic)
- Number of hydrogel nurse clinic and home visit in the scenario analysis (variation in number of nurse home visit was not included in the sponsor's analysis)

Results of these analyses are listed in Table 23 and Table 24.

**Table 23: EAC sensitivity analysis**

| | Values | Hydrogel - home | Gauze - home | Larvae - home | Hydrogel - clinic | Gauze - clinic | Larvae - clinic |
|---|---|---|---|---|---|---|---|
| EAC Base case | | -£211 | -£288 | -£280 | -£99 | -£152 | -£375 |
| Number of applications - Larvae | 1.2 | -£211 | -£288 | -£167 | -£99 | -£152 | -£276 |
| | 1.7 | -£211 | -£288 | -£393 | -£99 | -£152 | -£473 |
| Number of applications - hydrogel | 7.4 | -£143 | -£309 | -£301 | -£66 | -£145 | -£204 |
| | 11.0 | -£281 | -£268 | -£259 | -£132 | -£142 | -£164 |
| Number of applications - Debrisoft | 2.4 | -£265 | -£342 | -£333 | -£127 | -£180 | -£403 |
| | 3.6 | -£158 | -£235 | -£226 | -£71 | -£124 | -£347 |
| Number of applications - Gauze | 9.6 | -£211 | -£174 | -£280 | -£99 | -£98 | -£375 |
| | 14.4 | -£211 | -£403 | -£280 | -£99 | -£206 | -£375 |
| Nurse cost per visit home | 56 | -£255 | -£348 | -£255 | -£99 | -£152 | -£375 |
| | 37.37 | -£168 | -£229 | -£305 | -£99 | -£152 | -£375 |
| Nurse cost per visit clinic | 25.52 | -£211 | -£288 | -£280 | -£119 | -£185 | -£369 |
| | 17.02 | -£211 | -£288 | -£280 | -£78 | -£120 | -£381 |
| Debrider larvae (loose) | 236 | -£211 | -£288 | -£194 | -£99 | -£152 | -£289 |
| | 354 | -£211 | -£288 | -£365 | -£99 | -£152 | -£460 |
| Debrider Debrisoft | 5 | -£215 | -£292 | -£283 | -£103 | -£156 | -£378 |
| | 7.4 | -£208 | -£285 | -£276 | -£95 | -£148 | -£371 |
| Nurse time - home visit | 32 | -£168 | -£228 | -£305 | -£99 | -£152 | -£375 |
| | 48 | -£255 | -£348 | -£255 | -£99 | -£152 | -£375 |
| Nurse time - clinic visit | 46 | -£211 | -£288 | -£280 | -£71 | -£108 | -£383 |
| | 24 | -£211 | -£288 | -£280 | -£108 | -£167 | -£372 |

**Table 24: EAC scenario analysis**

| Variable | Probability debrisoft debride the wound | Number of nurse visits hydrogel - clinic/home | Gauze | | Hydrogel | | Larvae | |
|---|---|---|---|---|---|---|---|---|
| | | | Home | Clinic | Home | Clinic | Home | Clinic |
| Base case | 77% | 11.2/10.2 | -£288 | -£152 | -£211 | -£99 | -£280 | -£375 |
| Scenario 1 | 77% | 5 | -£358 | -£180 | **£22** | -£5 | -£349 | -£403 |
| Scenario 2 | 77% | 7 | -£336 | -£169 | -£53 | -£41 | -£327 | -£392 |
| Scenario 3 | 77% | 12 | -£279 | -£143 | -£242 | -£131 | -£271 | -£365 |
| Scenario 4 | 77% | 15 | -£246 | -£126 | -£354 | -£567 | -£237 | -£349 |
| Scenario 5 | 50% | 5 | -£293 | -£149 | **£87** | **£26** | -£284 | -£372 |
| Scenario 6 | 50% | 7 | -£244 | -£126 | **£38** | **£3** | -£235 | -£348 |
| Scenario 7 | 50% | 11.2/10.2 | -£141 | -£88 | -£64 | -£35 | -£133 | -£311 |
| Scenario 8 | 50% | 12 | -£122 | -£68 | -£84 | -£56 | -£113 | -£289 |
| Scenario 9 | 50% | 15 | -£49 | -£32 | -£157 | -£91 | -£40 | -£254 |
| Scenario 10 | 90% | 5 | -£389 | -£195 | -£10 | -£20 | -£381 | -£418 |
| Scenario 11 | 90% | 7 | -£380 | -£191 | -£97 | -£62 | -£371 | -£413 |
| Scenario 12 | 90% | 11.2/10.2 | -£359 | -£183 | -£282 | -£130 | -£351 | -£406 |
| Scenario 13 | 90% | 12 | -£355 | -£179 | -£317 | -£168 | -£347 | -£401 |
| Scenario 14 | 90% | 15 | -£341 | -£172 | -£449 | -£231 | -£332 | -£394 |

In addition to the analyses reported above, the EAC conducted additional exploratory analyses to assess the possible impact of (i) switching to bagged larvae or to gauze and (ii) different numbers of applications of Debrisoft.

*Switching analysis*

The sponsor's analysis assumed that all patients would switch to hydrogel if Debrisoft had not fully debrided the wound after three applications. The EAC investigated the impact of this assumption by analysing scenarios where if Debrisoft does not completely debride the wound after three applications, patients will switch to either gauze or bagged larvae. These patients are then assumed to receive the same number of applications of gauze or larvae as for patients treated with them initially (12 and 1.45 respectively). The analysis starts from the EAC's cumulative base case results shown in the last row of Table 22. Results of this analysis are presented in Table 25Table 26.

**Table 25: Sensitivity analysis - switching to bagged larvae**

| | Saline & gauze | | Hydrogel | | Bagged Larvae | | Debrisoft | |
|---|---|---|---|---|---|---|---|---|
| | Home | Clinic | Home | Clinic | Home | Clinic | Home | Clinic |
| Cost of debridement | £348 | £431 | £309 | £347 | £531 | £556 | £246 | £244 |
| Debrisoft incremental cost | -£103 | -£187 | -£63 | -£103 | -£285 | -£311 | | |

**Table 26: Sensitivity analysis - switching to gauze**

| | Saline & gauze | | Hydrogel | | Bagged Larvae | | Debrisoft | |
|---|---|---|---|---|---|---|---|---|
| | Home | Clinic | Home | Clinic | Home | Clinic | Home | Clinic |
| Cost of debridement | £348 | £431 | £309 | £347 | £531 | £556 | £204 | £215 |
| Debrisoft incremental cost | -£145 | -£215 | -£105 | -£132 | -£327 | -£340 | | |

These results suggest that Debrisoft also remains cost-saving when patients, after three unsuccessful applications, have been switched to a more expensive comparator than hydrogel, such as bagged larvae.

*Debrisoft applications/ efficacy*

The EAC conducted a threshold additional analysis to identify the number of Debrisoft applications required to make is more expensive than hydrogel in two different scenarios: switching to hydrogel or carrying on only with Debrisoft until the wound is completely debrided. In both cases the starting point for the analysis is the EAC's cumulative base case results shown in the last row of Table 22. All other variables are held constant apart from the number of Debrisoft applications (which in turn changes to the total amount of Debrisoft product, district nurse costs etc).

Results of this analysis are reported in Table 27 and Table 28 below.

**Table 27: Threshold analysis assuming patients switching to hydrogel after a given number of Debrisoft application**

| Debrisoft applications | Incremental cost | |
|---|---|---|
| | Home | Clinic |
| 3 | -£211 | -£99 |
| 4 | -£158 | -£71 |
| 5 | -£104 | -£43 |
| 6 | -£51 | -£15 |
| 7 | £2 | £13 |

**Table 28: Threshold analysis assuming patients do not switch to alternative debridement**

| Debrisoft applications | Incremental cost | |
|---|---|---|
| | Home | Clinic |
| 3 | -£377 | -£153 |
| 4 | -£283 | -£125 |
| 5 | -£230 | -£97 |
| 6 | -£176 | -£69 |
| 7 | -£123 | -£41 |
| 8 | -£69 | -£13 |
| 9 | -£16 | £15 |
| 9.2 | -£5 | £20 |
| 10 | £38 | £43 |

Results from the first scenario (patients switch to hydrogel after a certain number of Debrisoft applications) show that Debrisoft is no longer cost-saving if after seven applications the wound is not completely debrided, requiring patient to be switched to hydrogel.

If switching is not included (Table 28), then Debrisoft is no longer cost saving if nine applications are required per patient.

## *3.6 Conclusions on the economic evidence*

Most of the analyses show that Debrisoft is likely to be cost saving relative to hydrogel, gauze or larvae for the debridement of wounds. This is driven by the cheaper debridement product costs when compared to larvae, and a fewer number of applications required compared to hydrogel and gauze.

Unfortunately there are no comparative results to make a robust assessment of whether the number of applications required to debride the wound would be less with Debrisoft compared to hydrogel or gauze. It is very difficult to make a qualitative assessment of the relative difference in the plausible number of applications required for each product due to very different study designs and a lack of comparable statistics (specifically an average number of applications required to debride a wound). In the absence of robust evidence on this measure we have conducted a threshold analysis. This shows that if less than

seven applications of Debrisoft are required on average, then it is likely to be cost saving. Note that the cohort study of frequency of debridements and time to healing (5)(Wilcox 2013) showed that the median number of debridements was two, with a range of 1-138.

All of the analyses focus on a time to debridement. We note that other studies in this area have focussed on wound healing rather than debridement. We also note that whilst differences were found in the time to debridement for alternative products in the VenUS II study, no statistically significant differences were found in the primary outcome measure of wound healing. The estimated costs the alternative debridement products were much higher in this study. This is due to the longer period of follow-up (one year) and that hospital costs were also included. In all of the analyses presented here, hospital costs and the treatment of adverse effects are not included. If they were included we could expect the overall cost of Debrisoft (and the other products) to be much higher.

# 4 Conclusions

There is insufficient robust evidence to demonstrate that Debrisoft is clinically more effective than other methods of wound debridement, in particular with regard to rates of wound healing and wound infections. It would be better to measure outcomes to wound healing because this is a clinically much more important outcome and there does not appear to be a strong correlation between achieving complete debridement and subsequent wound healing. In the VenUS II trial a significant difference in debridement was found but no difference in time to healing.

If the decision is only concerned with debridement efficiency Debrisoft may be cheaper overall compared to larvae and hydrogel and debridement with gauze (which apparently is not used in UK, according to NICE clinical experts). This does not take into account adverse events, hospital visits etc, and only focuses on short term follow up of time to debridement completion.

There is no information on debridement methods currently being used by nurses or other health professionals in the community in the UK.

# 5 Implications for research

A randomised controlled trial of Debrisoft compared to normal current practice in the community is needed. We suggest that follow up should be to wound healing. Outcomes would also include wound infections, costs and quality of life. It would require that the number of applications of the debridement technique would need to reflect the number of application required in clinical practice, rather than have the trial restricted to a fixed number. The RCT that is currently ongoing is not helpful in this respect.

An audit of current debridement practice in community health practice in the UK would be very helpful.

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68. Stephen-Haynes J. The role of an active debridement system in assisting the experiences clinician to undertake an assessment and determine appropriate wound management objectives. Poster presentation, EWMA Conference; ViennaMay 2012.
69. Stoffels I, Dissemond J, Klode J. Fireworks with after effects - Successful use of a polyester monofilament fibre product for the removal of embedded explosive residue. Poster presentation, EWMA Conference; ViennaMay 2012.
70. Van Dam R. The effective management of a patient with a grade four sacral pressure ulcer. Poster presentation, Wounds UK Conference; HarrogateNov 2012.
71. Van Dam R, Alblas J, van den Wijngaard A, Andriessen A. Complex Cae series of frail elderly patients with stagnating lacerations treated with collagen dressing in a nursing home setting. Poster presentation, EWMA Conference; ViennaMay 2012.
72. van Zweeden JM. Aspecial case: How lower limb amputation was prevented. Poster presentation, EWMA Conference; ViennaMay 2012.
73. Weindorf M, Dissemond J. Wound debridement with a new debrider: A case report series about dermatologic patients with chronic painful ulcerations of differing aetiology. Poster presentation, EWMA Conference; ViennaMay 2012.
74. Wilson N. Reducing the cost od debridement - a case study. Poster presentation, TVS Conference; KetteringApril 2013.
75. Lok C, Paul C, Amblard P, Bessis D, Debure C, Faivre B, et al. EMLA cream as a topical anesthetic for the repeated mechanical debridement of venous leg ulcers: a double-blind, placebo-controlled study. J Am Acad Dermatol. 1999;40(2 Pt 1):208-13.
76. Groenewald JH. An evaluation of dextranomer as a cleansing agent in the treatment of the post-phlebitic stasis ulcer. SAMJ, S Afr med j. 1980;57(20):809-15.
77. Jiang KC, Luo N, Chen YC, Wang AP. Use of maggot debridement therapy for tropical diabetic hand syndrome. Journal of Wound Care. 2013;22(5):244-7.

78. Sherman RA. Maggot versus conservative debridement therapy for the treatment of pressure ulcers. Wound Repair Regen. 2002;10(4):208-14.
79. Opletalova K, Blaizot X, Mourgeon B, Chene Y, Creveuil C, Combemale P, et al. Maggot therapy for wound debridement: a randomized multicenter trial. Arch Dermatol. 2012;148(4):432-8.

**Appendix 1. Additional searches**

Medline 1946-present. 8th August 2013

| | | |
|---|---|---|
| 1 | debrisoft.mp. | 1 |
| 2 | Debridement/ | 11837 |
| 3 | limit 2 to "therapy (maximizes sensitivity)" | 5897 |
| 4 | monofilament.mp. | 1766 |
| 5 | 2 and 4 | 9 |
| 6 | Randomized Controlled Trials as Topic/ or RCT.mp.Multimedia | 105392 |
| 7 | 2 and 6 | 98 |

Embase 1980-present 8th August 2013

| | | |
|---|---|---|
| 1 | debrisoft.mp. | 4 |
| 2 | debridement/ or debridement.mp | 30978 |
| 3 | limit 2 to "therapy (maximizes sensitivity)" | 9302 |
| 4 | monofilament.mp. | 2383 |
| 5 | 2 and 4 | 30 |
| 6 | limit 2 to randomized controlled trial | 810 |

CAB abstracts 1984–present 8th aug 2013

| | | |
|---|---|---|
| 1 | debrisoft.mp. | 0 |
| 2 | debridement/ or debridement.mp | 1517 |
| 3 | monofilament.mp. | 257 |
| 4 | 2 and 4 | 0 |

Web of Science – 8th August 2013
Search Debrisoft – 1 reference
Search Debridement AND wound AND RCT – 5 refs
Search debridement AND wound AND random* - 306 refs

**Appendix 2. List of studies with no comparisons considered by the EAC, with reasons why not included in main effectiveness section of the report**

The following studies were appraised but were in vitro evaluations so could not be used to demonstrate the claimed clinical benefits of Debrisoft compared to any comparators:

(a). Westgate, S.J. And Cutting, K.F. A novel treatment method for the removal of biofilm material, Poster presentation, EWMA Conference, Vienna - May 2012
(b). Wiegand C, Reddersen K, Abel M, Ruth P, Hipler U.-C. Poster Presentation, Wounds UK Conference, Harrogate - November 2012

The following studies were appraised but did not provide comparative information and so could not be used to demonstrate the claimed benefits of Debrisoft compared to any comparators. They also did not have any useful information for the model, such as mean number of debridements with Debrisoft per person. They were either case reports or case series with few patients. Gray 2011 discussed the clinical characteristics of specific wounds which had hyperkeratosis, haematomas and slough but there was very little information given about the patients and no summary results so no conclusions can be drawn about the effectiveness of Debrisoft. Skovgaard-Holm 2012 was a conference poster and further information on the study (a report and a short journal article, both in Danish) was obtained from the author. There was some numerical information in these but it did not make sense, for example percentages in one pie chart summed to 40% only. There was information on pain but no summary statistics. The remaining studies were single case studies only.

(c). Gray D, Cooper P, Russell F, Stringfellow S. Assessing the clinical performance of a new selective mechanical wound debridement product. Wounds UK. 2011, 7(3): 42-6
(d). McGrath A. The management of a patient with chronic oedema: a case study. British Journal of Community Nursing. 2013:S12-9.
(e). Skovgaard-Holm H, Simonsen H (2012) Evaluation of a new polyester monofilament debridement pad* from both patients and homecare nurses point of view, Poster presentation, EWMA Conference, Vienna - May 2012
(f). Stephen-Haynes J, Callaghan R. A New Debridement Technique tested on Pressure Ulcers. Wounds UK. 2012, 8(3 Suppl): S6-S11.
(g). Whitaker JC. Self-Management in combating chronic skin disorders. Journal of Lymphoedema. 2012, 7(1): 46-50.
(h). Young T. Safe debridement in the community setting. Wounds Essentials. 2012. 2:82-89.

**Table 29. Characteristics of non-comparative studies**

| Study (Country) | Study design | Debrisoft patient numbers | Patient characteristics, | Age, demographic characteristics | Outcomes |
|---|---|---|---|---|---|
| Gray 2011 (UK)(15) | Case series | 18 | Ng | Ng | No numerical results |
| McGrath 2013 (UK)(48) | Case study | 1 | Leg oedema | 35yrs, male | No numerical results |
| *Skovgaard-Holm 2012 (UK)(49) | Case series | 10 | Ng | Ng | Pain graph |
| Stephen-Haynes 2012 (UK)(14) | Case studies | 2 | Pressure ulcers | 74, 82yrs, female | No numerical results |
| Whitaker 2012 (UK)(50) | Case study | 1 | Leg ulcer | Female | No numerical results |
| Young 2012 (UK)(51) | Case studies | 2 | Small ulcer, haematoma | Female | No numerical results |

The following studies were appraised but had no comparative information so could not be used to demonstrate the claimed benefits of Debrisoft compared to any comparators. They were either case reports or case series with few patients. Most were available only as conference posters. Also they were all sponsored by Activa Healthcare or its parent company Lohmann & Rauscher.

Studies in the table with asterisks are those where further information was sought from the study authors because more than case studies were presented and there was the potential for some useful summary information to be obtained.

Dam 2012(52) presented no information on the age or gender of the 29 study patients in the poster itself. Additional information from the author was an abstract by Fogh 2013 which had no further details of the study.

Haemmerle 2011(13) did give information of the study participants but no summary results of the debridement process apart for very general statements. Request for further information generated no further information

Johnson 2011(53) was authored by one of the NICE clinical experts. The poster has summary information about the 10 patients in the case series and healing rates from a mixed set of wound types. Of the ten patients, one died, seven wounds healed and two had ongoing wounds. No additional information was sent by the author. The study was felt to be too small to give useful rates of healing with Debrisoft if it was to be compared to another case series using a different debridement method.

Rieke 2012(54) was described as a cohort study but the follow up length was unclear but was longer than 4 weeks. There is summary information about patients and their diabetic foot ulcers and the ulcer condition after treatment in terms of red, yellow and black tissue only. Further information on this study from the Sponsor was that the study was stopped due to organisational reasons and that further results are not available.

Sewell 2012(55) was on 11 patients with acute wounds – gravel rash and gave pain score results. Further information sent by the author gave qualitative results on use of debrisoft and pain scores per patient.

Van den Wijngaard 2012(56) was the largest case series by far but there was no information about the patients in the study from the poster. There was no further information available.

(i). Alblas J, Klicks R.J. Andriessen A. A special case: treatment of a patient with necrotizing fasciitis. Poster Wounds UK Harrogate, 12-14 Nov 2012.

(j). Alblas J, Klicks R.J. Clinical efficacy of a monofilament fibre wound debridement product for trauma wounds and bites, Poster presentation, EWMA Conference, Vienna - May 2012

(k). Amesz S, Alice van den Wijngaard, Palliative care of a critically ill patient after vulvar carcinoma radiation treatment – a case study, Poster presentation, Wounds UK, Harrogate November 2012

(l). Dam W, Winther C, Rasmussen S. A new effective method for debridement of chronic wounds based on polyester monofilament fibre technology, Poster presentation, EWMA Conference, Vienna - May 2012

(m). Denyer J. The use of debridement pads in the management of children with severe Epidermolysis Bullosa, Poster presentation EWMA 2013 (NOT YET PUBLISHED)

(n). Flinton R. A new solution to an old problem - an innovative active debridement system, Poster Presentation, Wounds UK Conference, Harrogate - November 2011

(o). Fumarola S. The effect of a new debridement technique on patient wellbeing. Wounds UK. 2012, 8(4): 84-89.

(p). Haemmerle G, Duelli H, Abel M, Strohal R. The wound debrider: a new monofilament fibre technology: results of a pilot study. Poster EWMA Brussels, 25-27 May 2011
(q). Johnson S. A 10 Patient evaluation of a new active debridement system, Poster Presentation, Wounds UK Conference, Harrogate - November 2011
(r). Lloyd-Jones M, Parry-Ellis R. An evaluation of the role of an active debridement* system within a First Dressing Initiative, Poster Presentation, Wounds UK Conference, Harrogate - November 2012
(s). Makanin AJ, Slavnika IA, Rubanov LN, Chernov AA. Early surgical intervention for a patient with a severe electric burn of the skull, Poster presentation, EWMA Conference, Vienna - May 2012
(t). Prouvost L. A monofilament product as an alternative to mechanical debridement of the wound bed and periwound skin, Poster presentation, EWMA Conference, Vienna - May 2012
(u). Sewell D. Rash Decisions – A new solution to the management of 'gravel rash', Poster Presentation, Wounds UK Conference, Harrogate - November 2012
(v). Rieke F. A cohort study on the treatment of diabetic foot ulcer patients using a monofilament debrider and a collagen dressing, Poster presentation, EWMA Conference, Vienna - May 2012
(w). Smith J (ed) Debrisoft: Revolutionising debridement. MA Healthcare Ltd, London 2011.
(x). Smith J (ed). The missing link. The key to improved wound assessment. MA Healthcare Ltd, London 2012.
(y). Stephen-Haynes J. The role of an active debridement system in assisting the experienced clinician to undertake an assessment and determine appropriate wound management objectives. Poster presentation, EWMA Conference, Vienna – May 2012
(z). Stoffels I , Dissemond J, Klode J. Fireworks with after effects - Successful use of a polyester monofilament fibre product for the removal of embedded explosive residue, Poster presentation, EWMA Conference, Vienna - May 2012
(aa). van Dam R. The effective management of a patient with a grade four sacral pressure ulcer, Poster presentation, Wounds UK, Harrogate November 2012
(ab). van Dam R, Alblas J, van den Wijngaard A, Andriessen A(2012) Complex Case series of frail elderly patients with stagnating lacerations treated with a collagen dressing in a nursing home setting, Poster presentation, EWMA Conference, Vienna - May 2012
(ac). van den Wijngaard A, Andriessen A. Clinical efficacy of a monofilament fiber debridement product evaluated in patients with skin lesions, scales, rhagades and hyperkeratosis. Poster EWMA Vienna, Austria, 23-25 May 2012
(ad). van Zweeden J M. A special case: How lower limb amputation was prevented, Poster presentation, EWMA Conference, Vienna - May 2012
(ae). Weindorf M, Dissemond J. Wound debridement with a new debrider: A case report series about dermatologic patients with chronic painful ulcerations of differing aetiology, Poster presentation, EWMA Conference, Vienna - May 2012
(af). Wilson N. Reducing the cost of debridement – a case study, Poster Presentation at TVS Conference, Kettering. April 2013

**Table 30. Characteristics of company sponsored studies with no comparison information**

| Study (Country) | Study design | Debrisoft patient numbers | Patient characteristics, | Age, demographic characteristics | Outcomes |
|---|---|---|---|---|---|
| Alblas 2012 (NL)(57) | Case study | 1 | Buttock wound | 63, male | No numerical results |
| Alblas 2012 (NL)(58) | Case studies | 4 | Trauma wounds | 61, 62, 87, 89 yrs, 2 female, 2 male | No numerical results |
| Amesz 2012 (NL)(59) | Case study | 1 | Vulval cancer | 52 yrs, female | No numerical results |
| *Dam 2012 (NL)(52) | Case series | 29 | Chronic wounds (venous, arterial, pyoderma gangrenosum, vasculitis, traumatic | Ng | Fibrin reduction in wound, proportion given pain relief, proportion with keratosis removed |
| Denyer 2013 (UK)(60) | Case study | 1 | Child with epidermolysis bullosa | Female | No numerical results |
| Flinton 2011 (UK)(61) | Case study | 1 | Venous leg ulcer | 81 yrs, female | No numerical results |
| Fumarola 2012 (UK)(62) | Case study | 1 | Necrotising infection | 62 yrs, male | No numerical results |
| *Haemmerle 2011 (Austria, Germany)(13) | Case series | 11 | Mixed, arterial, venous, diabetic ulcers | 55-90 yrs, 5 female, 6 male | No numerical results |
| *Johnson 2011 (UK)(53) | Case series | 10 | Mixed venous, neuroischaemic, neuropathis, leg and foot ulcers, amputation | 60-75yrs, 6 female, 4 male | Healing rates |
| Lloyd-Jones 2012 (UK)(63) | Case series | 16 nurse evaluations | - | - | No numerical results |
| Makanin 2012 (Austria) (64) | Case study | 1 | Skull electric burn | Male | No numerical results |
| Prouvost 2012 (France)(65) | Case series | 4 | Chronic leg wounds | 65-80 yrs, 2 female, 2 male | No numerical results |

| Study (Country) | Study design | Debrisoft patient numbers | Patient characteristics, | Age, demographic characteristics | Outcomes |
|---|---|---|---|---|---|
| *Rieke 2012 (NL)(54) | Cohort | 25 | Diabetic foot ulcers, mean duration 10.7 (SD 14.5) months, mean size 7.2 (SD 6.1) $cm^2$ | 6.3 (SD 14.5, 23-87), 9 female, 16 male, | Ulcer condition before and after (red, yellow and black tissue) |
| *Sewell 2012 (UK)(55) | Case series | 11 | Gravel rash from motorcycle accidents | 2 female, 9 male | Pain scores |
| Smith 2011 (UK)(66) | Case studies | 5 | Chronic leg ulcers | 48-92 yrs, 4 female, 1 male. | No numerical results |
| Smith 2012 (UK)(67) | Case study | 1 | Chronic leg ulcer | 77 yrs, female | No numerical results |
| Stephens-Haynes 2012 (UK) (68) | Case studies | 2 | Haematoma, foot ulcer | 2 female | Pain score, treatment time |
| Stoffels 2012 (Germany)(69) | Case study | 1 | Firework burn and residue on face | 17 yrs, male | No numerical results |
| van Dam 2012 (NL)(70) | Case study | 1 | Sacral pressure sore | 78 yrs, male | No numerical results |
| *van Dam 2012 (NL)(71) | Case series | 10 | Skin lacerations | 76 (62-100), 8 female, 2 male | Wound healing rates |
| *van den Wijngaard 2012 (NL)(56) | Case studies | 2 | Chronic leg wounds | 61-80 yrs, 1 female, 1 male | No numerical results |
| | *Case series | 120 | Ng | Ng | Efficacy of debridement |
| van Zweeden (2012 (NL)(72) | Case study | 1 | Chronic leg wound | 66 yrs, female | No numerical results |
| Weindorf 2012 (Germany)(73) | Case series | 5 | Chronic leg wounds | Ng | Pain before and during treatment |
| Wilson 2013 (UK)(74) | Case study | 1 | Chronic leg wound | 75 yrs, female | No numerical results |

**Appendix 3. Appraisal of studies from the sponsor's economic literature review not included in the main report**

| Study (country) | Patient numbers | Type of study | Population | Comparators | Outcome | Assessment |
|---|---|---|---|---|---|---|
| Lok 1999 (France)(75) | 97 | Double-blind placebo-controlled study | Patients with venous leg ulcer | EMLA cream as a topical anaesthetic for the repeated mechanical treatment<br>Placebo | Number of debridement required to obtain a clean ulcer<br>Pain during debridement<br>Safety of debridement | No economic evidence<br>Comparators not completely related to those proposed in the scope |
| Groenewald 1980 (South Africa)(76) | 100 | Single blind randomised trial | Patients with post-phlebitic stasis ulcer | Dextranomer<br>Current treatment | Cleansing and healing time | No economic evidence<br>Comparators not completely related to those proposed in the scope |
| Jiang 2013 (China)(77) | 1 | Case report | Diabetic patients with infectious hand ulceration | Initial surgical debridement<br>Maggots | Time to debridement<br>Tolerability | No economic evidence<br>No proper comparative study<br>Wound type not included in the scope |
| Sherman 2002 (USA)(78) | 103 | Cohort study | Patients with pressure ulcer | Maggots<br>Not clear | Time to debridement<br>Amount of necrotic tissue | No proper comparative study<br>No economic data |
| Opletalova 2012 (France)(79) | 119 | Randomised multicentre trial | Patients with non-healing, sloughing wound on the lower limb | Bagged larvae<br>Surgical debridement | Percentage of slough in wounds at day 15 | No economic evidence |