Proposal for assessment of new health technologies

Important information – read this first!

- Submitted proposals for national health technologies (HTAs) will be published in full. If the proposer thinks there is information necessary for filling out the form, that should not be made public, please contact the secretariat (Nye Metoder) before submission.

  The proposer is aware that the form will be published in its entirety (tick): ☒

- Proposer has filled out point 19 below «Interests and, if any, conflicts of interest» (tick): ☒
- This form serves the purpose to submit proposals for health technology assessment (HTA) at the national level in Nye Metoder - the national system for managed introduction of new health technologies within the specialist health service in Norway. The form does not apply to proposals for research projects. A health technology assessment is a type of evidence review, and for this to be possible, documentation is required, e.g. from completed clinical trials. Lack of documentation may be one of the reasons why the Commissioning Forum (Bestillerforum RHF) does not assign a health technology assessment.
- If the proposal concerns a medical device, the proposer is familiar with the document «Guidance criteria for management of medical devices in the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway» (link) (tick): ☒

Contact information:

Name of the proposer (organization / institution / company / manufacturer)**:**

Willingsford Ltd.

Name of proposal contact:

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Date and locality:

August 21, 2024, Southampton, United Kingdom

1. Proposer's title on the proposal: *
   *This may be changed during the course of the process"

Amicapsil for treating wound infections and supporting tissue regeneration

2. Brief description of the health technology proposed to be considered:

Amicapsil (technical name MPPT or micropore particle technology) is a class IIb CE-marked medical device approved for the treatment of wounds. It acts via the wound microbiome using capillary-evaporation to support the immune response and can treat wound infections without the use of antimicrobials. It represents a first-in-class novel technology.

Four clinical trials have been conducted with Amicapsil, one 266-patient RCT comparing Amicapsil to antibiotics and antiseptics and three real-world-evidence (RWE) studies:

- The 266-patient RCT, which included several wound types, found that Amicapsil removes wound infections 60% quicker than gentamicin and iodine, and leads to a 50% quicker onset of tissue regeneration. Duration of hospital-stay was reduced by 31% by Amicapsil compared to gentamicin and 39% to iodine. In a subset of wounds (n=30/arm), consisting of dehisced surgical wounds and abscesses, wounds receiving Amicapsil reduced in surface area twice compared to gentamicin and iodine.
- An RWE study performed by an NHS hospital Trust in dehisced surgical wounds showed that MPPT results in an infection-free healing wound suitable for discharge in 4.0±0.9 days, i.e. exactly the same as in the clinical RCT mentioned above. The study reported: "*The wounds received between two and five applications [of Amicapsil] and it was well tolerated by all patients. Our standard treatment for these wounds would have been desloughing, typically using UrgoClean for 7 days or more, followed by NWPT for several weeks.*" Compared to historical data at the hospital, Amicapsil reduced the time to a healing wound suitable for discharge by 81% or more compared to NPWT, assuming 1 week with UrgoClean followed by 2 weeks or more with NPWT.
- Two RWE-studies have, using telemedicine in community care, evaluated Amicapsil in the treatment of acute and chronic pressure ulcers and soft tissue infection caused by an underlying osteomyelitis. One study was performed in collaboration with 2 spinal cord centres in the UK and the other was an independent patient-reported outcome study by the British Spinal Injuries Association. Both studies reported a 100% closure rate of acute and chronic pressure ulcers with Amicapsil. It was also found effective in controlling soft tissue infections caused by an underlying primary focus of infection, e.g. osteomyelitis. For acute pressure ulcers, per wound cost savings relative to SOC were 86% the first year and 100% subsequent years because the wounds closed.
- The studies found that Amicapsil is effective in immunocompetent and immunocompromised individuals, and it is not limited by antimicrobial resistance.
- O'Sullivan et al. (2020) highlights the use of Amicapsil in rehabilitation.
- No adverse events have been reported and it is classified as inherently safe.

To use Amicapsil, the wound is washed with clean water, the powder is applied to all wound surfaces that can be reached, and, if desired, the wound can be covered with a woven 100% natural cotton gauze swab. Due to its mode-of-action, the evaporation of air from the wound surface must be possible. If the wound surface is blocked, e.g. the patient sits on the wound, air can be supplied artificially using a small battery-operated pump. Off-loading is not required for healing, i.e. bed rest is not required; this is important in palliative care of wounds associated with osteomyelitis, as it allows the patient to lead an active life. Due to its ease-of-use, Amicapsil is suitable for telemedicine with the patient, family or carers being responsible for the daily dressing changes. This enables delivery of high-quality care in remote areas and frees up substantial nursing resources. It also provides independence to the patient.

Amicapsil does not contain antimicrobials and will not contribute to antimicrobial resistance and climate change. The ingredients are readily biological recyclable. It will reduce clinical waste substantially, which typically include plastics, chemicals and silicones.

3. Brief description of current standard of care (SOC) (Which health technology (ies) are currently used. What is the status of the technology (ies)? Whether it provides curative treatment, life extension, etc.)
Will the proposed technology replace or be a supplement to today's SOC?

Current standard care of infected, also referred to as critically colonised, wounds as well as draining fistulas, e.g. caused by an underlying osteomyelitis, is primarily based on antimicrobials. However, a large number of studies, including treatment guidelines by regulatory bodies, question the efficacy of antimicrobials, i.e. antibiotic and antiseptic, in the treatment of infected wounds, ulcers and burns:

- NICE guidance (NICE, 2014) on the treatment of pressure ulcers states that systemic antibiotics, topical antimicrobials, and negative pressure wound therapy (NPWT) should not be used for treating pressure ulcers.
- The US FDA in 2016 concluded that dressings containing antibiotics and antiseptics are ineffective in treating wound infections and in supporting healing (FDA, 2016).
- Westby et al. (2017) concluded in a Cochrane meta-analysis of 39 studies that: "*we are unable to determine which dressings or topical agents are the most likely to heal pressure ulcers, and it is generally unclear whether the treatments examined are more effective than saline gauze.*"
- Hussey et al. (2019) concluded: "*This paper suggests that in the last 20 years there has been a large increase in the use of antimicrobial wound dressings despite a lack of research evidence to support their routine use. Expenditure [to the NHS] on antimicrobial wound dressings has risen by over £28 million between 1997 and 2016.*"
- The US FDA (Verma et al., 2022) in April 2022, following a 2-year analysis of the wound area, concluded that wounds not healing spontaneously constitute an **unmet medical need** due to lack of effective treatments.

The consensus is, therefore, that existing treatments for wound infections are ineffective and there is consequently no *recommended* standard care approach. Furthermore, in addition to lack of efficacy, antibiotics and antiseptics are both associated with a large number of adverse effects:

- Damage to commensal microbes, which are required for healing (Wang et al., 2021).
- Development of antimicrobial resistance, i.e. both antibiotics and antiseptics.
- Tissue and cell toxicity, including cell types required for healing and immune cells.
- In adults, antibiotics increase the risk of cancer, diabetes, asthma, miscarriage, and in children born to a mother treated with antibiotics during pregnancy antibiotics increase the risk of long-term health implications such as genital, ophthalmic, and oral and maxillo-facial malformations, as well as epilepsy and cerebral palsy. Antibiotics administered to babies and infants increase the risk of cognitive impairment, affecting functional and immune development, atopic dermatitis, inflammatory bowel disease (IBD), coeliac disease, necrotizing enterocolitis (NEC), autoimmune autistic disorder (AAD) and attention deficit hyperactivity disorder (ADHD). In later life, these babies and infants are at elevated risk of developing asthma, allergy, and obesity.
- Environmental damage, including substantial contributions to climate change.

Amicapsil would replace the use of antimicrobials in wound care. The Amicapsil wound treatment procedures are comparable to existing treatments and its adoption would not require any organizational changes, investments in equipment etc.

4. This proposal concerns:	Yes	No
A brand new and innovative health technology	☒	☐
Anew application, or a new indication for an established method	☐	☒
A comparison between several methods	☒	☐
A technology that is already in use	☒	☐
If yes – technology used in clinical practice	☒	☐
If yes – technology used in research/clinical trials	☒	☐
A re-evaluation of technology used in clinical practice	☐	☒
The technology is relevant for disinvestment	☐	☒

Amicapsil is based on the novel micropore-particle-technology or MPPT and is first-in-class. MPPT uses capillary-evaporation to control the moisture level on the wound surface. These micro-pumping effects in parallel remove microbial toxins and enzymes and disrupts the structure of biofilm. This removes the inhibition of the immune cells, and they are now able to regain control of the wound to remove the infection.

Data in a preclinical wound healing model support this mode-of-action, where MPPT 48 hours after start of use led to a 107% (2.1-fold) increase in the overall number of immune cells in the wound, including a 24.8-fold increase in the number of macrophages and a 7.2-fold increase in lymphocytes compared to gentamicin and untreated controls (Sams-Dodd and Sams-Dodd 2018). The gentamicin and untreated control groups were similar to each other. Wound colonisation in terms of number of bacteria was similar in the MPPT and untreated control groups, demonstrating that MPPT is not an antimicrobial, whereas gentamicin, as expected, reduced the bacterial count.

5. This health technology involves (Multiple ticks are possible)

Pharmaceutical	☐
Medical device/IVD medical device that is CE-marked*	☒

CE-marked medical device, Class IIb, approved as a treatment for wounds

Medical device/IVD medical device that is not CE-marked	☐
Procedure	☐
Screening	☐
Highly specialized services / national offers	☐
Organization of the health services	☐
Other (describe)	☐

NA

6. Application of the technology:

Prevention	☒
Assessment and diagnostics	☐
Treatment	☒
Rehabilitation	☒
Specialist health care	☒
Primary health care	☒

Amicapsil removes wound infection and supports tissue regeneration in immunocompetent and immunocompromised individuals. It can be used on all types of wounds and dermatological lesions, including soft tissue infection caused by an underlying primary focus of infection, e.g. osteomyelitis. It is not limited by antimicrobial resistance. It is suitable for telemedicine and selfcare.

Amicapsil can be used in primary and secondary care and most patients discharged from hospital will be able to continue treatment at home. Substantial in-house experience is available in rehabilitation, e.g. persons with spinal cord injury.

7. Responsibility for funding

	Yes	No
Is the specialized health service responsible for financing the technology today?	☐	☒
May the specialized health service become responsible for funding the health technology?	☒	☐

Amicapsil is not currently used in Norway, but its adoption would offer substantial patient benefits as well as savings and freeing up resources in the healthcare system.

8. Is the technology mentioned in the national guidelines or action programs prepared by the Norwegian Directorate of Health?

Yes	No
☐	☒

No

9. Does the technology involve the use of radiation (ionizing/ non- ionizing)?

Yes	No
☐	☒

No

10. Which discipline(s) does the health technology apply to, and which patients are affected? (Could the health technology also affect other groups (e.g. health personnel or relatives)?)

The intended use of Amicapsil is the treatment of wounds, ulcers and burns and dermatological lesions. It is effective on infections by resistant strains and will not contribute to new resistance. It is suitable for immunocompetent and immunocompromised individuals, e.g. persons with spinal cord injury, and it is suitable for self-care and can be delivered using telemedicine. It is not associated with any health risks to patients or healthcare personnel.

11. Which aspects are relevant to the assessment? (Multiple ticks are possible)

Clinical efficacy	☒
Safety/adverse effects	☒
Costs/resource use	☒
Cost-effectiveness	☒
Organizational consequences	☐
Ethical	☐
Legal	☐

12. Please suggest the main scope/objective for the health technology assessment, as well as secondary scopes/objectives (in compliance with question 10). For those familiar with "PICO" (Patient, Intervention, Comparator, Outcome) – please include tentative suggestions for PICO.

As outlined above, a body of evidence demonstrates that antimicrobials are ineffective in treating wounds. ICH E10 guidance states that clinical trials cannot include placebo or comparators if these are known to expose the participants to increased risk of death or irreversible morbidity. Therefore, once an RCT had demonstrated superiority of Amicapsil to antibiotics and antiseptics in the treatment of wounds, comparators could no longer be included in the trials. Please see Supplement 5 in Sams-Dodd et al. (2024) for a discussion of the topic. An HTA needs to take these regulatory restrictions into consideration. However, the use of single-arm trials, using historic data or published data on other treatments for comparison, have become increasingly common and accepted, e.g. NICE (2022) characterize a non-interventional single-arm study with comparison to published evidence on comparators as Real-World-Evidence.

In relation to PICO-criteria, an HTA could focus on the following:

Patients: Immunocompetent or immunocompromised patients with wounds, e.g. dehisced surgical wounds and pressure ulcers; and patients with soft tissue infection caused by osteomyelitis, who either are scheduled for surgery or require long-term palliative care due to the osteomyelitis being inoperable.

Intervention: Treatment with Amicapsil vs. SOC.

Comparators: Standard wound care for infected/critically colonized wounds, i.e. antibiotics and antiseptics. Published studies on Amicapsil include an RCT comparing Amicapsil to gentamicin (antibiotic) and iodine (antiseptic); and 3 RWE-studies comparing Amicapsil to historic hospital data or to published data in community care. Information on treatments received by the participants prior to changing to Amicapsil is also available in many cases, offering information on the treatment that were ineffective, i.e. a cross-over design.

Outcome: The primary outcome parameters should be safety, and for wounds closure rate, and for draining fistulas control of soft tissue infection. Secondary outcome measures could be: time to closure, per wound costs (consumables and bed-days), use of nursing resources, patient independence, and environmental aspects, e.g. CO_2e emission and clinical waste.

13. Please give a brief explanation of why it is important that the health technology assessment proposed should be conducted.

Amicapsil represents a fundamentally different approach to the treatment of wounds as it acts via the skin and wound microbiomes instead of using antimicrobial properties. Studies show that the adoption of new technologies into healthcare practice can take many years, i.e. an average of 17 years. Therefore, to accelerate the adoption of this new technology to the benefits of patients, the healthcare system, and the environment, the performance of an HTA is essential.

14. Please comment on the technology that is proposed to be assessed with regard to the following points:

The severity of the disease/condition the health technology targets

Amicapsil is suitable for treating wound infections and supporting tissue regeneration in any type of wound, ulcer and burn, which can range in severity from a simple blister to life threatening wounds and being acute and chronic. Amicapsil has demonstrated efficacy on treatment-resistant infections. Amicapsil can furthermore remove soft tissue infection resulting from the presence of osteomyelitis, thereby improving patient well-being, ability to avoid bed rest, and reducing the risk for sepsis.

Expected effect

For wounds, the expected outcome is full closure. Time to closure can be affected by co-morbidities, e.g. diabetes and medication that interferes with healing.

For draining fistulas, resulting from an underlying primary infection such as osteomyelitis or an anal fistula and which may look like a wound from the outside, Amicapsil can control the frequently occurring soft tissue infection and can reduce the fistula to a narrow, non-infected canal. It will not close the fistula, i.e. allowing the continued escape of infectious debris. In several individuals, who experienced frequent episode of septicaemia due to the associated soft tissue infection, the use of Amicapsil essentially stopped these occurrences, which often resulted in emergency hospitalisation.

Amicapsil can be used preventively on surgical wounds post-surgery to reduce the risk of infection and it can be used to remove soft tissue infection prior to surgery, allowing surgery to take place in non-infected tissue, which will improve the success rate. For example, in connection with surgery for osteomyelitis, the prior removal of soft tissue infection and the regeneration of tissue will reduce the risk of reinfection and non-healing and it will minimize the amount of tissue that needs to be removed.

Safety

No adverse events have been observed with Amicapsil/MPPT (Bilyayeva et al., 2017, 2014; Lovgren et al., 2018; O'Sullivan et al., 2020; Ryan, 2017; Sams-Dodd et al., 2024; Sams-Dodd and Sams-Dodd, 2020, 2018; Smith and Ridler, 2024), including after daily application for more than 4 years directly onto muscle and bone. MPPT is classified as inherently safe based on ISO 13485:2016; ISO 14971:2019; and ICE 62366-1:2015/A1:2020.

MPPT only contains natural non-toxic ingredients that are readily biologically recyclable, and all packaging is either natural (and readily biodegradable) or recyclable. No antimicrobials, chemicals, plastics, or silicones are used in the treatment process. The only non-recyclable component used is the tape used to fasten a cotton gauze pad over the wound. MPPT will not contribute to AMR, environmental pollution, or climate change.

Total number of patients in Norway the health technology is applicable to

For pressure ulcers, Norwegian data indicate a prevalence of 5% to 48% in hospitals and between 10 and 33% in community care (https://www.helsebiblioteket.no/innhold/omsorgsbiblioteket/oppsummeringer/forebygging-av-trykksar), resulting in 30,000 new pressure ulcers annually of which 1000 patients die (https://www.smartcarecluster.no/aktuelt/2018/12/tidewave-r-d-og-trykks%C3%A5rspesialist-tester-venderegime).

For surgical site infections, data from 2005-2010 have shown a prevalence of 1.5 to 2.1% in hospitals in Norway but this was before the increase in antimicrobial resistance. More recent data from the UK (2017-2022) indicate a prevalence of 11% (Guest et al. 2023).

Consequences for resource use in the public health service

The introduction of Amicapsil will free-up considerable resources in the public health service as a higher percentage of wounds would heal to closure, substantially quicker, and allowing many patients to be responsible for own care. For example, for acute infected grade 3 pressure ulcers, treated using telemedicine, the healing rate was 100% with Amicapsil in 1.6 months compared to only 15% healing within the first year with SOC, requiring an average of 8.2 months to close. Calculated reductions in costs and nurse visits per acute pressure ulcer the first year are 86%. Please see Sams-Dodd et al. (2024), Supplement 6.

Generally, the quicker treatment is initiated, the quicker the healing, the less Amicapsil will be required, and the less severe the long-term implications will be. For example, persons with spinal cord injury, who develop a grade 4 pressure ulcer, i.e. down to muscle, will on average develop osteomyelitis after 4 months unless the wound and the associated soft tissue infection is treated in time. Once osteomyelitis is present in this immunocompromised population, the prospects are poor (see Russell et al. 2020), and the condition will be associated with considerable costs. Data from the US suggest that pressure ulcers and their implications are responsible for over 25% of the total healthcare costs associated with spinal cord injury. Early intervention using Amicapsil to treat new wounds will be able to avoid a large percentage of these costs.

Need for revision of existing national guidelines or preparation of new guidelines

Amicapsil can readily be incorporated into existing wound care routines. The main change will be replacing the use of current standard care approaches with Amicapsil.

15. Please provide references to documentation of the health technology's effect and safety (i.e. previous technology assessments). (Up to 10 key references can be provided, please do not send attachments in this step of the process):

Bilyayeva O, Neshta VV, Golub A, Sams-Dodd F. Effects of SertaSil on wound healing in the rat. J Wound Care. (2014) 23:410–6. doi: 10.12968/jowc. 2014.23.8.410

Bilyayeva O, Neshta V, Golub A, Sams-Dodd F. Comparative clinical study of the wound healing effects of a novel micropore particle technology: effects on wounds, venous leg ulcers, and diabetic foot ulcers. Wounds. (2017) 29:1–9.

Ryan E. The use of a micropore particle technology in the treatment of acute wounds. J Wound Care. (2017) 26:404–13. doi: 10.12968/jowc.2017.26.7.404

Sams-Dodd J, Sams-Dodd F. Time to abandon antimicrobial approaches in wound healing: a paradigm shift. Wounds. (2018) 30:345–52.

Lovgren M-L, Wernham A, James M, Martin-Clavijo A. Pyoderma gangrenosum ulcers treated with novel micropore particle technology. BrJDermatol. (2018) 179:152.

Sams-Dodd J, Sams-Dodd F. Micropore particle technology promotes wound healing, whereas Polyhexamethylene biguanide causes tissue degeneration: a case report. Wounds. (2020) 32:E6–E10.

O'Sullivan O, Hayton L, Findlay-Cooper K, Phillip R. Novel micropore particle technology for spinal cord injury chronic wound healing: A new paradigm? BMJ Mil Health. (2020) 169:184–7. doi: 10.1136/bmjmilitary-2020-001509

Sams-Dodd J, Belci M, Bandi S, Smith D, Sams-Dodd F. Stable closure of acute and chronic wounds and pressure ulcers and control of draining fistulas from osteomyelitis in persons with spinal cord injuries: non-interventional study of MPPT passive immunotherapy delivered via telemedicine in community care. Front Med (Lausanne). 2024 Jan 5;10:1279100. doi: 10.3389/fmed.2023.1279100. PMID: 38249963; PMCID: PMC10797031.

Smith D. and Ridler (2024). Survey of user-experiences in the spinal cord injured-community with MPPT for treating wounds and pressure ulcers and for controlling soft tissue infection caused by osteomyelitis. Frontiers in Rehabilitation Sciences, 5: 10.3389/fresc.2024.1386518.

16. Please provide the name of the marketing authorization holder/manufacturer/supplier of the health technology (if applicable/available):

Willingsford Ltd., Southampton, United Kingdom

17. Marketing Authorization Status (MA) or CE-marking: When is MA or CE- marking expected? If possible, provide the time of planned marketing:

Amicapsil has been CE-marked since 2016.

18. Additional relevant information (up to 300 words.)

The Directors of Willingsford are Danish and understand Norwegian. We can therefore support the introduction of Amicapsil in Norway. Also, we have very substantial experiences in the use of Amicapsil across wound types as well as supporting treatment via telemedicine.

19. Interests and potential conflicts of interests

Please describe the proposer's relationships or activities that may affect, be influenced by, or be perceived by others to be important for further management of the health technology that is proposed assessed. (E.g. proposer has financial interests in the matter. Proposer has or has had assignments in connection with the technology or to other actors with interest in the technology)

The proposer is employed at Willingsford Ltd.