A.16 Hypochlorous acid – EML and EMLc

Reviewer summary

☒ Supportive of the proposal **(adding to the 15.1 Antiseptics)**

☒ Not supportive of the proposal **(adding to 15.2 Disinfectants)**

Justification (based on considerations of the dimensions described below):

- **Public health relevance**

  The importance and necessity of environmental disinfection measures are well recognized for infection control, especially in healthcare settings. Wound infection is a common condition encountered in life and in clinical practice. Using topical antiseptics to treat mild superficial skin infections is advisable to avoid the use of antibiotics. For moderate and severe wound infections, topical antiseptics are used as adjunct therapy with antimicrobial agents.

- **Evidence of comparative efficacy and safety**
  1. The **safety** of Hypochlorous acid (HOCl) for human use has been **evaluated thoroughly over the past century**. In the last 15 years, more advanced HOCl solutions, most manufactured through electrochemistry, have emerged as safe and viable wound-cleansing agents and infection treatment adjunct therapies. **HOCL solutions bring both safety and high-level potency to bear.** HOCl exposure caused no harm and was deemed safe for skin and eyes (2019 review), and can be used as a choice of dental disinfectant (2020 review)
  2. **HOCl is the most effective form of all chlorine-based antimicrobial compounds that has the highest in vitro bactericidal activity against a broad range of microorganisms,** compared to conventional disinfectants.
  3. **HOCl is well-documented to have no toxicity** to mammalian cells, and, within minutes after use, HOCl degrades to dilute salt water that can be mopped up when spilled and disposed of anywhere.
  4. There is more clinical evidence about its safety and effectiveness. **Regarding the resolution of infection and improvement in wound healing by adjunct HOCl use**, **strong evidence was found for use in diabetic foot wounds**; **moderate evidence for use in septic surgical wounds**; **low evidence for venous leg ulcers, wounds of mixed etiology, or chronic wounds**; and no evidence for burn wounds. **HOCl exhibits superior safety and efficacy to povidone-iodine for wound care and reducing the frequency of dialysis-associated infections**. Based on the existing evidence, expert panel recommended HOCl should be used in addition to tissue management, infection, moisture imbalance, edge of the wound (the TIME algorithm) and aggressive debridement.
  5. In addition to the antiseptic contributions that HOCl can bring to wound management, there is abundant evidence that exogenous HOCl applied topically faciliate faster healing and faster restoration of normal tissue architecture with minimal scarring.
- **Cost and cost-effectiveness considerations**
  1. Current HOCl product pricing at scale can probably be achieved at less than one Euro per wholesale liter, with minor regional variations, based on water, salt and energy costs.
  2. No studies evaluate the cost and cost-effectiveness of HOCL relative to its comparators.
- **Any other issues that may be relevant in determining the status of a medicine as 'essential' (e.g., recommendations in WHO guidelines, feasibility of use, diagnostic requirements, availability, access).**
  1. **FDA approved HOCL** for disinfection of food-contact surfaces, high-level disinfection, sterilization, and wound care applications. **European Medicines Agency (EMA) approved** HOCl in some formulations as a Class III medical device for wound management**.** HOCl is easy to perform, comfortable, and safe in the treatment of infected acute traumatic wounds.
  2. **Consensus and guidance statements** about **HOCl for infection control and topical medical use have been issued in recent years** by several governmental agencies responsible for healthcare product regulatory oversight, and by medical professional specialty organizations focused on advantageous technical innovations that better serve their physician's needs.
  3. Medical product regulatory authorities in the EU, UK, Canada, Japan, Mexico, Australia, New Zealand and US, amongst others, all require registration of HOCl products for approval and clearance for sale as disinfectants.

	4. **There are now multiple local manufacturing systems around the world creating a plentiful, affordable, high-quality HOCl supply**. **Recommendation:** The summarized evidence for efficacy and safety of HOCL for disinfection and antisepsis is convincing. Considering chlorine-based compounds (liquid, powder and solid) are already listed in the 15.2 Disinfectants in the 2023 EML and EMLc, a separate listing for the proposed formulation of HOCL solution is not necessary to ensure various formulations for selection and use as alternatives and wide accessibility in various settings. **For wound care, adding HOCL to the 15.1 Antiseptics in the EML and EMLc can be considered based on its powerful microbicidal and antibiofilm properties, and superiority of efficacy, safety and performance over the povidone iodine (which has been listed in the 15.1 Antiseptics in the EML and EMLc).** The advantages of HOCL in powerful microbicidal and antibiofilm properties, good clinical efficacy, and desirable safety profile and high-level potency to bear offer a better alternative choice for physicians and patients. So far, HOCL is not wildly accessible across the countries and no cost-effectiveness data are not available. From the viewpoint of clinical therapy, HOCL is preferred for wound care if it is available. The study is needed to evaluate the cost-effectiveness of HOCL and other Antiseptics.
Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives? (**https://list.essentialmeds.org/**)	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)	☒ Yes ☐ No ☐ Not applicable
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms?	☒ Yes ☐ No ☐ Not applicable
Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable
Are there any issues regarding price, cost-effectiveness and budget implications in different settings?	☒ Yes ☐ No ☐ Not applicable
Is the medicine available and accessible across countries? (e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes)	☐ Yes ☒ No ☐ Not applicable
Does the medicine have wide regulatory approval?	☐ Yes, for the proposed indication ☐ Yes, but only for other indications (off-label for proposed indication) ☒ No ☐ Not applicable