A.18	Hypochlorous acid – disinfection, antisepsis, wound care
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Partially – the application focusses on two areas, topical surface decontamination and wound care/antisepsis. The focus on topical surface disinfectant is primarily Covid related, although considerable in vitro data is provided on other microbes, including bacteria and fungi. The focus on wound care is diabetic foot ulcer and venous leg ulceration.
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	There are a range of antiseptic/disinfectants on the EML. These include chlorhexidine, ethanol, peroxide povidone-iodine and chlorine based disinfectants (eg sodium hypochlorite – bleach). There are many other antiseptics on the market commercially, which are not on the EML (eg Octenidine etc). Many antiseptics have been approved by the EPA as disinfectants for Covid. There is limited evidence for the clinical efficacy of any specific products with very few direct comparative studies.
Have all important studies and all relevant evidence been included in the application?	☐ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included:
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☐ Yes ☒ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). The applications summarises a number of small trials with varying comparators focussing on wound infections and venous ulcers. There have been two small trials of HOCl in diabetic foot ulcers, with no RCT in venous ulcer. None of the studies are adequately powered to provide an assessment of hypochlorous acid compared to other topical antiseptics. There are two relevant Cochrane's.

	Antibiotic and antiseptics for venous leg ulcers (2014) and antiseptics for burns (2017). There was no clear evidence of benefit for antiseptics in general for both these clinical indications or for specific antiseptics compared to other agents. A placebo controlled trial of HOCl compared to prescribed exercise for venous leg ulcers (Factorial4VLU) is underway in Australia/NZ. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: There is very limited evidence of clinical safety from adequately powered RCTs. This is true for most other antiseptics as noted by the FDA and multiple formulations of HOCl have been approved by the FDA.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: There are no specific common adverse effects noted for HClO, compared to other antiseptics and it appears to have a good general safety record.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	HoCl is one of many antiseptics where there has been renewed interest related to Covid disinfectant. This is a long established antiseptic with broad antimicrobial activity. There is limited evidence of clinical benefit, either directly compared to placebo or compared to other antiseptics. Care must be taken in its production to ensure the optimal pH and it has a limited shelf life. The clinical benefit is uncertain compared to other antiseptics on the EML.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The level of evidence for its use in chronic ulcers and wounds is low.
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☐ No ☒ Not applicable Comments:

Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☐ No ☐ Not applicable Comments: It is on the WHO list of approved biocides for Covid.
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Other antiseptic agents such as bleach, paraquat and peroxide have significant safety concerns. HOCL has excellent in vitro activity against a wide range of pathogens including MDR bacteria widely implicated in nosocomial transmission in hospitals. Close attention in manufacturing is required but the costs are reducing and are given as a wholesale cost of around 2 US dollars/litre.
Any additional comments	A previous application was made in 2017 to the EML.
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	HOCl appears to be a safe and effective antiseptic with a broad activity against a wide pathogen spectrum. It appears to have a good safety profile and recent advances in manufacturing have improved standardisation of the product. The product has a relatively short shelf life and significant cost. There is though very limited high quality evidence of direct clinical benefit, mainly from small studies. On the current evidence it is difficult to recommend the addition of HOCl to the EML. Currently, higher quality randomised clinical trials are underway and if these show clear evidence of clinical utility, then a further application should be encouraged.
References (if required)	