I.5	Antibiotics for necrotising fasciitis
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: There is limited data on the epidemiology of this condition, particularly in the LMIC setting, where it likely is under diagnosed. Although rare it has a high mortality.
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.	This application focusses on medicines that are already listed on the EML and the EMLc – clindamycin, ceftriaxone, metronidazole and vancomycin. The application proposes to add the indication of necrotising fasciitis for these already listed antibiotics. The higher doses required for this very serious deep tissue infection have driven the recommendation to add new IV formulations for ceftriaxone (2gm powder for injection) clindamycin (600 mg and 900 mg) and Vancomycin 500 mg and 1 gm).
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: There is a very limited evidence base for this condition. There have been no new studies since the review of skin and soft tissue infections by McMaster for the 2017 EML. The 2014 IDSA Guidelines recommend piperacillin-tazobactam and vancomycin, cefotaxime and metronidazole or clindamycin, or meropenem for empiric use.
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 application notes the very limited evidence base and extrapolation of efficacy from other skin and soft tissue infections. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Very little.

Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☒ Not applicable Comments: The medicines have been listed for many years on the EML and their toxicity profile is well established.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: See above
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The antibiotics listed in the application are those used for this indication generally and given in international guidance. This severe infection requires broad spectrum antibiotic treatment, but no direct comparative efficacy studies have ever been conducted.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	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:

Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The medicines are all widely produced generic drugs.
Any additional comments	none
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.	The recommendation is to add the new indication of necrotising fasciitis to the EML for these antibiotics. The application currently limits the use of ceftriaxone in combination with metronidazole only when S. pyogenes infection has been ruled out. Group A strep infection causing NF can follow chicken pox in children and other infections. However surface swab skin cultures are often negative and the organism may be isolated only from tissue obtained at surgery. Particularly in the LMIC setting, timely surgery may not be feasible and urgent use of empiric antibiotics is critical to optimise outcomes. The committee could consider removing this restriction.
References (if required)	