C.2	Proposal to upgrade cefalexin to first choice for skin and soft tissue infections
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Bacterial skin infections occur worldwide and can affect all age groups; erysipelas is more frequent in children and elderly patients. Cellulitis, the most common skin infection, accounted for 0.04% (4 in 10.000) of the overall burden of all diseases combined in 2013. In 2017, the Global Burden of Disease study reported 43 million new cases of cellulitis worldwide.
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.	Staphylococcal (non-MRSA) and streptococcal infections are the leading causes of mild to moderate community-acquired skin and soft tissue infections worldwide. Cefalexin offers good coverage for staphylococcal (non-MRSA) and streptococcal infections with a spectrum of activity and tolerability that is comparable with the other two first choice options currently recommended in the EML/EMLc for the empiric treatment of skin and soft tissue infections (cloxacillin and amoxicillin-clavulanic acid). These three antibiotic options represent equally adequate alternatives for the treatment of mild community-acquired skin and soft tissue infections.
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 review of benefits for the empiric use of cefalexin for skin and soft tissue infections consists of the evidence that was presented for the 2017 EML update. No major changes or additional evidence discouraging its use for this indication have occurred since. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Yes.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: The same considerations made in the above section also apply to the review of harms and toxicity of cefalexin.

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The overall benefit to risk ratio of cefalexin as the first choice for treatment of mild to moderate skin and soft tissue infections is favourable.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	High.
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: Cefalexin has regulatory approval globally and is available as generic and is listed in multiple pharmacopoeia.
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: Cefalexin was recommended in the 2017 EML/EMLc for the empiric treatment of skin and soft tissue infections.
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Cefalexin has regulatory approval globally and is available as generic.
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.	1. Cefalexin offers good coverage for staphylococcal (non-MRSA) and streptococcal infections with a spectrum of activity and tolerability that is comparable with the other two first choice options currently recommended in the EML/EMLc for the empiric treatment of skin and soft tissue infections (cloxacillin and amoxicillin-clavulanic acid). 2. Cefalexin was recommended in the 2017 EML/EMLc for the empiric treatment of skin and soft tissue infections. 3. Cefalexin has regulatory approval globally and is available as generic and is listed in multiple national pharmacopoeia. I highly recommend upgrading cefalexin to first choice for mild-moderate skin and soft tissue infections on the WHO Model List of Essential Medicines and WHO Model List of Essential Medicines for Children.
References (if required)	