I.6	Antibiotics for neonatal meningitis
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: The application provides a short summary of the epidemiology and public health importance of neonatal meningitis and the difficulty of differentiating clinically between neonatal sepsis and meningitis. It is very difficult clinically to tell if a sick baby that requires treatment for sepsis may also have meningitis and lumbar puncture is not always feasible or appropriate in a very ill baby.
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.	The application is for the addition of the indication of neonatal meningitis for gentamicin, which is already listed for neonatal sepsis.
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: The treatment of neonatal meningitis has been summarised in detail the EML 2017 application. There have been no major new studies since this application. There is a limited evidence base on the optimal choice of antibiotic to treat neonatal meningitis, especially in the LMIC setting.
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 efficacy data for the optimal antibiotic regimens to treat neonatal sepsis is very limited. A Cochrane review of antibiotic regimens for neonatal sepsis in May 2021 (last review 2005) only included 5 new small trials and concluded that the current evidence was insufficient to support any antibiotic regimen being superior to any other. As noted above there is considerably less data on neonatal meningitis than sepsis (and no Cochrane). 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: The 2017 EML summarised the safety of gentamicin in neonates, which has been on the EMLc since its launch. The renal and auditory toxicity is clearly recognised. The dosing used for neonatal meningitis is the same as for neonatal sepsis but the duration is longer – WHO guidelines suggest 3 weeks. The risk of significant audiology and renal toxicity is increased with longer durations of treatment.
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: See above – therapeutic drug monitoring is recommended where available, especially for longer treatment courses. Renal function and audiology outcomes are also recommended where available.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	There is significant toxicity recognised with gentamicin, but it has a well recognised role in the treatment of neonatal sepsis and meningitis that has been established over many decades globally.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The overall quality of the evidence is poor, but there has been no large global trials of the optimal antibiotic treatment of neonatal meningitis.
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: Therapeutic Drug Monitoring where available.
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: WHO Pocket Book 2013 recommends ampicillin and gentamicin as the first line treatment for neonatal meningitis, as does the WHO 2017 Recommendations on newborn health.

Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Gentamicin is a low cost antibiotic for this treatment and access is very wide.
Any additional comments	
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 for the EMLc listed antibiotic gentamicin to approve the addition of the indication of neonatal meningitis to the current indication of neonatal sepsis.
References (if required)	