F.11	Rifampicin IV infusion - tuberculosis
Does the application adequately address the issue of the public health need for the medicine?	☐ ☐No ☐ Comments: The need for IV therapy is not in doubt and IV rifampicin is recommended in WHO guidelines in specific circumstances (e.g. TB meningitis) . The application does not provide an estimate of the numbers of patients who might need IV therapy globally. There is reference to the high early mortality on treatment, but the case that this is due to route of administration is not made.
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.	Rifampicin is a key drug in the treatment of TB and is listed on the EML in its oral preparation only. The proposal is to add IV therapy as an alternative option for treatment. The indication for IV therapy as proposed in the application (P1) include (i) Severe disease (ii) acute of chronic GI disease (iii) severe co-morbidities (iv) patient unwilling or unable to take treatment
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). Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? The report does not provide evidence of head-to-head comparison in the use of IV therapy against more traditional oral therapy or its use in key populations. Its use would be considered standard of care in those unable to swallow (particularly is reduced level of consciousness) and/or absorb medication

Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: The information provided is largely related to rifampicin as a whole, with very little relevant data on the route of administration. However, there is no reason to believe that toxicity is a greater issue with IV formulation compared to oral
Are there any adverse effects of concern, or that may require special monitoring?	☒No ☐ Not applicable Comments: As noted in the application, there is very limited safety data. Aside from the complications of IV therapy, there are not likely to be specific toxicities associated with IV therapy. It might be expected that toxicities are higher if drug levels are higher. However, safety considerations are not a major concern in this application.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	There are some circumstances (where oral therapy is impossible or gastrointestinal absorption is compromised) that IV therapy will be of clear benefit to the patient. However, for the overwhelming number of patients who are able to take medicine, there is no case for benefit of rifampicin. IV formulations may carry a small increased risk from the need for cannulation and related infection.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	There are very few studies that have addressed this question and those presented are of low quality.
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: The additional use of IV cannulation as outlined in the application.
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: No

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 X ☐ No ☐ Not applicable Comments:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Data is not presented on costs of medication
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.	In section 11 of the application, it is stated that IV rifampicin is a rare presence on most of the world markets. This would benefit from a reference to assess the scale and nature of the problem. The assertion that any lack of access is due to the fact that it is not listed on the EML/EMLc is not supported by evidence. Similarly, a concern expressed previously in relation to listing has been the potential to create financial incentives for practitioners to prescribe TB therapy when it is not required. However, more data would also be helpful in understanding the extent to which this is a problem and whether IV therapy, when provided, is covered by national programmes. I do not support the inclusion of IV therapy at this time
References (if required)	