F.2	Amoxicillin + clavulanate – new strength formulation
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
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 proposal is to add the 875 mg amoxicillin + 125 mg clavulanate to the EML for the indications of community acquired pneumonia (CAP) and Intra- abdominal infections (IAI) in adults. The 500+125, 250+62.5 and 125+31.25 mg oral preparations are already listed on the EML/c.
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 higher dose of amoxicillin in the proposed formulation is recommended for more severely unwell patients taking oral medication providing a higher concentration of amoxicillin while maintaining the addition of clavulanate. The addition of this new formulation will allow a reduction in pill burden with the goal of enhancing adherence. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? This application focusses on adults in both the HIC and LMIC setting.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Co-amoxicillin has been on the EML for decades and its safety profile is well established.

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: Co-amoxicillin is recognised to cause diarrhoea, but there is limited direct comparative data on the relative frequency of this with different formulations. The higher ratio of amoxicillin and lower relative doses of clavulanate are in general associated with less diarrhoea.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The higher dose provides improved amoxicillin drug levels when given 3 times daily compared to the existing 500 mg tablet. This increases the likelihood of adequate coverage of more resistant pathogens, particularly the pneumococcus.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The evidence for the benefit is not randomised controlled trial level, but based on pharmacokinetic/pharmacodynamic models.
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: This formulation is widely available from multiple generic manufacturers.
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: The new forthcoming EML Antibiotic Handbook recommends the 875+125 mg formulation.
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The cost is generally slightly higher but comparable to the 500 mg+125 mg formulation.

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 to add the new strength formulation to the EML. The preparation has significant PK advantages, providing the option for a reduced pill burden.
References (if required)	