F.2	Amoxicillin + clavulanic acid – new strength formulation
Does the application adequately address the issue of the public health need for the medicine?	☐ Yes ☐ No ☒ Not applicable Comments: There is no doubt that the association of amoxicillin and clavulanic acid represent a public health need but the question is raised with this new dosage form. How to evaluate the issue of public health need, when other dosage form exist for such association, so the issue of the public health need is already met. The pertinence of introducing the 875 mg comparing with other dosage is not well established, not well argued by the need of this kind of dose in the therapeutic protocols
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 main reason for the addition of the 875mg +125mg formulation is to allow the use of a higher dose of amoxicillin while maintaining the activity of clavulanic acid for the treatment of community-acquired pneumonia and intra-abdominal infections that are likely to be caused by beta-lactamase-producing bacterial isolates, recommended for the empiric treatment of more severe infections or those caused by resistant organisms. This application, focus also on reducing pill burden. Empiric treatment with amoxicillin + clavulanic acid is recommended in the EML for treatment of several bacterial 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: Literature is lacking in this specific issue There is no comparative clinical studies comparing the efficacy of this new dosage % the classical one 875-125 % 1000 mg-125 mg, no trial has directly compared the efficacy of using different doses of oral amoxicillin + clavulanic acid for intra-abdominal infections In the best of our knowledge, no antibiotics guidelines were included in favour of this new dosage form and the need to the 875 mg.

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). No comparative studies between this dosage form and classical dosage were included, No cost-effectiveness DATA were described. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Yes at the same level than other dosage form classical one We need data in cost effectiveness and benchmark of price of this dosage comparatively with other dosage.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Amoxicillin is largely used even at very high dosage, no safety concern with this new dosage For clavulanic acid, the dosage is the same that used in other classical formulation.
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.)	Uncertain. This association is largely used in medicine Introducing a novel dosage form must introduce more benefit which is not well developed. Why we need 875 mg is there some guidelines in favour of the 875 mg ?
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Moderate because the literature and scientific data are lacking about the real benefit of this dosage.

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 association is largely registered in different country, For the new ratio we need more data, even from real world data were such dosage is commercialised. May be we need a bench mark
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.	To introduce this new dosage we need more advantages, on efficacy, security or economic aspect. No sufficient data demonstrating that 125 mg clavulanic is more safe that 250 mg, in case of a use of a double pill. No sufficient data, even using modern PK-PD principles Price for example 10 dollars is very high when we find that other dosage 500/125 costs less.
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.	We maybe need a benchmark in which country this dosage form is available. What is the issue when it was introduced? More efficacy and security evidence and world real DATA is needed. Antibiotics guidelines were not included justifying this new dosage, as it is known antibiotics largely depend on the resistance situation in a given setting and country. Lack of sufficient efficacy security data and even modern PK-PD principles and studies are not mentioned. No studies describing compliance to treatment: 2 pills of 500 mg comparing one pills of 875. It's not only about the new dosage, risk of misusage.

	The risk is that new dosage form will be more expensive than classical one should be considered. Why not 1g:125 ?
References (if required)	