(1) Does the application adequately address the issue of the public health need for the medicine?
   Yes ☐  No ☐

   Please provide brief details:
   In the application for the inclusion of Imipenem/Cilastatin, Meropenem and Amoxicillin/Clavulanic acid in the WHO Model List of Essential Medicines, as reserve second-line drugs for the treatment of multidrug-resistant tuberculosis (complementary lists of anti-tuberculosis drugs for use in adults and children), it is not clear what the burden of disease of MDR TB that would be suitable for antibiotic treatment as above.

(2) Have all important studies/evidence of which you are aware been included in the application?
   Yes ☑  No ☐

   Please provide brief comments on any relevant studies that have not been included:
   Only a few clinical case reports of efficacy have been provided in the application.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
   Yes ☐  No ☑

   (a) Briefly summarise the reported benefits (e.g. clinical versus surrogate) and comment, where possible, on the actual magnitude of benefit associated with use of the medicine:

      The application gives in vitro data on efficacy, with no substantial clinical trial data on their additive efficacy in MDR-TB

   (b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details:

      No

(4) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?
   Yes ☐  No ☑
Please provide brief details:

Imipenem, Meropenem and Amoxicillin Clavulanate are well established off patent antibiotics with good safety profiles (although IMP has a seizure risk).

(5) Please comment on the overall benefit to risk ratio of the medicine (e.g., favourable, uncertain etc).

Uncertain

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?

Yes ☐ No ☐

Please provide brief details:

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes ☐ No ☐

Please provide brief details:

Would require new indication to be approved by the relevant regulatory authorities. TB is not on the current EMA licence as an indication.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

Yes ☐ No ☐

Please provide brief details:

New indication

(9) Please comment briefly on issues regarding cost and affordability of this medicine.

Generic off patent medicines. Meropenem/Imipenem require multiple times a day systemic treatment in hospital.

(10) Any additional comments?

The principle concern is an increased use of Carbapenem antibiotics in the empiric treatment of MDR-TB.

(11) Please frame the decisions and recommendations that the Expert Committee could make.

Further evidence of clinical efficacy, perhaps from registry based data, would be helpful.

(12) References (if required)