2019 Expert Committee on Selection and Use of Essential Medicines

Peer Review Report

[Ethambutol Injection - Formulation]

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

Please provide brief details: Provides option of parenteral first line treatment for TB (including MDR-TB) for patients with CNS disease and/or who cannot easily take oral formulations of drugs (e.g., ICU, post-operative settings where patient must be NPO, patients with altered level of consciousness)

(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:


(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: Benefit of ethambutol and place in TB treatment is well established. Additional benefit of proposed intravenous formulation expected to accrue in those specialized settings (see above) where a parenteral formulation of the drug is the most desired/necessary treatment choice.

(b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details: Yes, for ethambutol per se (not the IV formulation alone)
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: Well described concerns about ocular toxicity would extend to the IV formulation. Of note is potential difficulty in assessing this particular toxicity in young children.

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

Benefit would be that already known for Ethambutol with addition that IV formulation would enable continuation of treatment for patients who medically cannot take or tolerate the oral formulation. Potential benefit in patients with CNS infection associated with higher achievable concentrations at site of infection with IV formulation (i.e., no bioavailability issues with IV formulation).

ADDITIONAL CONSIDERATIONS:

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

Yes ☒ No ☐

Please provide brief details: Should be reserved for use by physicians experienced in treating complicated TB infection.

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: Current approval only in Germany, Switzerland, Ukraine, Uzbekistan, Tajikistan, Kazakhstan. Formulation has received favourable evaluation by EMA.

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

Yes ☒ No ☐

Please provide brief details: Use described in WHO 2016 guidelines for TB treatment
(9) Please comment briefly on issues regarding cost and affordability of this medicine.

With limited manufacturing and distribution of the drug, there are apparently no comparative cost and cost-effectiveness data for parenteral ethambutol.

(10) Any additional comments? Additional data needed from pediatric use/study to document age appropriate dosing and tolerability of parenteral formulation.

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

Although this formulation fills a potentially important therapeutic niche for a select group of patients with TB, would not consider addition as a complimentary, individual medicine in the EML or EMLc for restricted use in patients with CNS infection who cannot be safely administered the oral formulation of the drug. The paucity of available data on the formulation preclude its recommendation at this time. WHO prequalification or Expert Review Panel opinion should be sought before expanding recommendations for use beyond those denoted above.

(12) **References (if required)**