International Office
Rue de Lausanne 78
CP 116
1211 Geneva 21
Switzerland

Phone: +41 (0)22 8498400
Fax: +41 (0) 22 849 84 04

www.msf.org

F.7 - Ethambutol for IV infusion (1000 mg, 2000 mg)

MSF notices the proposal from INCURE to include ethambutol IV for infusion in the core list of the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc), as an anti-tuberculosis medicine.

Currently, oral formulations of ethambutol are included in the EML and EMLc, as single medicines or in fixed-dose combinations with other anti-tuberculosis medicines.

MSF would like to draw the attention of the Expert Committee to the following points:

- According to the 2017 WHO "Guidelines for treatment of drug-susceptible tuberculosis and patient care", oral treatment regimens (ideally fixed dose combinations) are recommended for the treatment of drug-susceptible tuberculosis. According to the 2016 WHO document "Target regimen profiles for TB treatment, Candidates: rifampicin-susceptible, rifampicin-resistant and pan-TB treatment regimens", intravenous formulations should be reserved for severe forms of disease, such as central nervous tuberculosis or sepsis tuberculosis.
  MSF would like to emphasize the risk of overuse or misuse of injectable ethambutol in patients who should normally be able to take oral ethambutol.

- For critically ill patients, patients unable to swallow (patients with advanced HIV disease, patients in ICU), IV formulations may be convenient. However, there is currently no evidence that intravenous formulations of ethambutol lead to improved mortality or morbidity for patients with severe forms of TB. It is likely that IV rifampicin at high doses and IV formulation of isoniazid would have a greater impact on morbidity and mortality than an IV formulation of ethambutol. Therefore the risk versus benefit balance, even for patients with severe forms of TB, is not clear.

- Intravenous therapy for tuberculosis is for very limited indications and the co-administration of other anti-tuberculosis drugs in intravenous formulations is necessary: there is currently no intravenous formulation of pyrazinamide available.

- Currently due to lack of WHO recommendations, there are no clinical protocols available to guide clinicians in appropriate use and dosing of injectable ethambutol. Before this drug is made more widely available, a protocol with indications, dosage, precautions and administration should be developed.

- Compared to the oral route of administration, the IV route of administration is complicated and associated with specific risks: daily slow IV injection (1 to 3 hours), the need of implanted port (surgically placed) or peripherally implanted central catheter, the well-known risks of inflammation, infection at the insertion site and thrombosis.

- Despite the availability of the oral forms of ethambutol for many years, IV formulations are only registered in a limited number of countries such as France (1000 mg), Ukraine, Uzbekistan, Tajikistan, Kazakhstan, Moldova (1000 and 2000 mg).

- No cost-effectiveness data for injectable ethambutol have been presented in the application, stating that there is no shown evidence in pharmaco-economical convenience of injectable ethambutol.

- Due to the very restricted indications of injectable ethambutol and the very limited size of the market, there is no need of several dosage forms: if a formulation has to be chosen for its inclusion in the EMLs, the 1000 mg formulation will suffice.

- Injectable formulations of ethambutol should always be approved by a stringent regulatory authority (SRA), or WHO-prequalified medicines. At the present time, no call for submission to WHO prequalification has been issued for injectable forms of ethambutol.

MSF urges the Expert Committee to consider all these elements when making a decision on the inclusion of injectable ethambutol in the WHO Model List of Essential Medicines and the WHO Model List of Essential Medicines for Children.

For Médecins Sans Frontières

Myriam Henkens, MD, MPH
International Medical Coordinator