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F.9 - Isoniazid for IV infusion (300 mg, 500 mg, 900 mg)

MSF notices the proposal from INCURE to include isoniazid IV for infusion in the core list of both 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 isoniazid 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 WHO 2016 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 isoniazid in patients who should normally be able to take oral isoniazid.

- 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 IV formulation of isoniazid lead to improved mortality or morbidity for patients with severe forms of TB.

- 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 isoniazid. Before this drug is made more widely available, a protocol with indications, dosage 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 isoniazid for many years, IV formulations are only registered in a limited number of countries such as USA, UK, Russian Federation, Ukraine, Kazakhstan, and Uzbekistan.

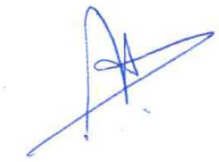
- No cost-effectiveness data for injectable isoniazid have been presented in the application, stating that there is no shown evidence in pharmaco-economical convenience of injectable isoniazid.

- Due to the very restricted indications of injectable isoniazid, there is no need of several dosage forms: if a formulation has to be chosen for its inclusion in the EMLs, the 300 mg formulation will suffice.

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

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

For Médecins Sans Frontières



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