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.11 - Rifampicin 600 mg for IV infusion

MSF notices the proposal from INCURE to include rifampicin 600 mg for IV infusion in both 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 rifampicin 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 rifampicin in patients who should normally be able to take oral rifampicin.
- Whilst there is data to support the use of high doses of rifampicin for patients with TB meningitis[1], recent evidence indicates that oral forms of rifampicin can be used to achieve higher doses and intravenous formulations may not be necessary to achieve the higher plasma doses of rifampicin [2]. WHO has not yet reviewed these data.
- 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 form 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 the injectable rifampicin. 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),

with the need of implanted port (surgically placed) or peripherally implanted central catheter, with the well-known risks of inflammation, infection at the insertion site and thrombosis.

- Despite the availability of the oral form of rifampicin for many years, IV formulations are only registered in a limited number of countries such as USA, Russian Federation, Ukraine, Belarus and China.

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

- Injectable formulations of rifampicin 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 rifampicin.

MSF urges WHO to review data on higher doses of rifampicin for TB meningitis and plasma levels produced by different doses of rifampicin given by oral and injectable administration.

MSF urges the Expert Committee to consider all these elements when making a decision on the inclusion of injectable rifampicin 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

References

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2. Wasserman S. Plasma pharmacokinetics of high dose oral versus intravenous rifampicin in patients with tuberculous meningitis: a randomized controlled trial. February 2021. Available from https://doi.org/10.1101/2021.02.11.21250624