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**F.5 Delamanid (25 mg dispersible tablet)**

MSF strongly supports the WHO Global TB Program proposal to include the delamanid 25 mg dispersible tablet in the WHO Model List of Essential Medicines for Children (EMLc) and to change the age restriction from ≥ 6 years to ≥ 3 years.

In 2015, MSF has supported the inclusion of delamanid 50 mg tablet in the WHO Model List of Essential Medicines (EML) and in 2017, its inclusion in the EMLc, in the complementary list of anti-tuberculosis medicines, as a reserve second-line drug for the treatment of multidrug-resistant tuberculosis (MDR-TB), for use in children aged 6 years and more.

In 2019, following the 2018 update of the WHO treatment guideline for multidrug- and rifampicin-resistant tuberculosis recommending that the minimum age for delamanid administration be lowered to 3 years, MSF has supported the WHO Global TB Program proposal to lower the minimum age of administration of delamanid in children, from 6 to 3 years.

According to the 2020 WHO Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment, and the 2020 WHO operational handbook on tuberculosis, delamanid is recommended in all-oral longer regimens for MDR-TB in adults and children older than 3 years. These fully oral regimens allow to avoid injectable anti-tuberculosis medicines regimens, as aminoglycosides and capreomycin, presenting risks of nephrotoxicity and ototoxicity.

In 2019, MSF has already drawn the attention of the 22nd Expert Committee to the fact that the 50 mg film-coated tablet, the only available formulation is not an optimal paediatric dosage form for children below 20 kg: its administration requires to split and crush the tablet, for which no bioavailability data were published, at that time. According to the WHO Consolidated Guidelines on Drug-Resistant Tuberculosis Treatment, a crossover bioequivalence study has established that the 50 mg film-coated tablet and the 25 mg dispersible tablet are not bioequivalent. Not only splitting and crushing the film-coated tablet modifies the bioavailability, but also this non-recommended practice makes the medicine unpalatable.

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

- Delamanid 25 mg dispersible tablet, a child-friendly formulation has been developed and is available for compassionate use only, since April 2019.
- Although the manufacturer has committed to make this 25 mg dispersible formulation available to the Stop TB Partnership's Global Drug Facility and pending its expected approval by the EMA in late 2021, this child-friendly formulation is not yet ~~a~~available. Once again, MSF would like to emphasize that access to child-friendly formulations is essential to increase ease and safety of administration as well as adherence to treatment.

- The inclusion of this formulation in the EML will serve as a basis for National Essential Medicines lists and therefore will facilitate importations, alert manufacturers about the need for local registrations and will increase interest for pediatrics formulations. This inclusion will help to use this medicine more widely, in order to improve outcomes and reduce mortality for the patients developing MDR-TB.

- Previously all products in the WHO Model List of Essential Medicines for Children were also on the WHO Model List of Essential Medicines: if this logic is maintained, delamanid 25 mg dispersible tablet should also be included on the WHO Model List of Essential Medicines.

MSF has been using delamanid in its programs since January 2015 and recently imported delamanid 25 mg under compassionate use in India.

In light of these elements, MSF urges the 23rd Expert Committee on the Selection and Use of Essential Medicines to include the delamanid 25 mg dispersible tablet in the both the EML and EMLc and to lower the minimum age of administration of delamanid in children, from 6 to 3 years.

For Médecins Sans Frontières

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