Treatment Action Group

Secretary of the Expert Committee on the Selection and Use of Essential Medicines
Department of Essential Medicines and Health Products
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27, Switzerland

20 May 2021

Re. Statement of support for the addition of delamanid 25 mg dispersible tablet to the World Health Organization Model List of Essential Medicines for Children

Dear Expert Committee:

Treatment Action Group (TAG) submits this letter **in support** of adding a 25 mg dispersible tablet formulation of delamanid to the World Health Organization (WHO) Model List of Essential Medicines for Children (EMLc) for the treatment of tuberculosis (TB). TAG is an independent, activist, and community-based research and policy think tank committed to racial, gender, and LGBTQ+ equity; social justice; and liberation, fighting to end the HIV, TB, and hepatitis C virus (HCV) epidemics, including in children. TAG has been a leading voice in advocacy to support the earlier inclusion of children in TB research and development and efforts to expand access to child-friendly formulations of TB medicines.

Delamanid is currently recommended by the World Health Organization (WHO) as a Group C drug, for inclusion in treatment regimens for drug-resistant TB when a regimen composed of 4-5 effective drugs from Groups A and B cannot otherwise be constructed.[1] Delamanid is especially critical to building regimens effective against pre-extensively and extensively drug-resistant forms of TB (pre-XDR- and XDR-TB) and is also being implemented by many countries under operational research conditions as part of short, all-oral regimens for rifampicin- and multidrug-resistant TB (RR-/MDR-TB).

We note that the delamanid 25 mg dispersible tablet is one of very few pediatric TB formulations assessed in controlled trials in children with drug-resistant TB. Based on pediatric pharmacokinetic and safety studies conducted by Otsuka (NCT01856634/ NCT01859923), the WHO has recommended delamanid for the treatment of adolescents and children down to six years old with drug-resistant TB since 2016, with the WHO's recommendation further extended to include children down to three years old in 2018.[2] The WHO is currently undertaking a review to inform whether delamanid will be recommended for the treatment of children younger than

[1] World Health Organization. WHO consolidated guidelines on tuberculosis. Module 4: Treatment; Drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2020. https://www.who.int/publications/i/item/9789240007048.
[2] WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2019. https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf.

three years old.[3] In September 2020, the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion for the use of delamanid to treat pulmonary multidrug-resistant TB in adolescents and children weighing at least 30 kg.[4] Otsuka has reported expecting a positive EMA CHMP opinion for children weighing less than 30 kg in the coming months, and approval of its dispersible delamanid formulation in 2021.[5]

Concerns have been raised about the bioavailability and palatability of the existing 50 mg tablet when split, crushed, or dissolved as is often required for administration to children. In the absence of access to a child-friendly formulation (i.e., the 25 mg dispersible tablet), clinicians in the field treating children will continue manipulating the 50 mg formulation, including to avoid the use of injectable TB medications, which are painful and can cause permanent disability such as hearing loss with potential lasting implications on child development.

More than 30,000 incident cases of drug-resistant TB in children are estimated globally each year, however the number of children 0-14 years old reported to WHO as enrolled in treatment for drug-resistant TB was just 5,568 in 2019.[6] Access to child-friendly formulations of second line TB medicines, including delamanid, will be critical to closing this gap and ending unnecessary morbidity and mortality among children affected by drug-resistant TB.

Thank you for the opportunity to share our views on the importance of adding the delamanid 25 mg dispersible tablet to the WHO EMLc. If you need additional information on our support of this application, please contact Lindsay McKenna, Lindsay.McKenna@treatmentactiongroup.org.

Respectfully submitted,

Lindsay McKenna, MPH
TB Project Co-Director
Treatment Action Group

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[3] World Health Organization [Newsflash]. Development of updated WHO guidelines on the management of tuberculosis in children and adolescents. Geneva; World Health Organization; May 2021. https://www.who.int/news/item/07-05-2021-development-of-updated-who-guidelines-on-the-management-of-tuberculosis-in-children-and-adolescents.

[4] European Medicines Agency. Deltyba: Opinion [Internet]. 2020 September 17 (2020 September 26). https://www.ema.europa.eu/en/medicines/ human/summaries-opinion/deltyba.

[5] McKenna L. Tuberculosis Treatment Pipeline Report 2020. New York: Treatment Action Group; 2020. https://www.treatmentactiongroup.org/wp-content/uploads/2020/11/pipeline_tb_treatment_2020_final.pdf.

[6] Global tuberculosis report 2020. Geneva: World Health Organization; 2020. https://www.who.int/publications/i/item/9789240013131.