F.5	Delamanid 25 mg dispersible tablet
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	This application is not proposing to add a new medicine to the WHO EMLc, but to include a different strength of an existing one. Delamanid has featured as an antituberculosis medicine on the complementary list of the WHO EML and EMLc since 2015 and 2017, respectively, as a 50 mg tablet formulation, which is available on the market. All-oral longer regimens, which can include delamanid are recommended by WHO for children with multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB) aged 3 years and above (1, 2). The availability of a child-friendly formulation of delamanid (25 mg dispersible tablet) could enable appropriate dosing of children aged 11 years old and younger, improving the likelihood of adherence to treatment in a particularly vulnerable population. The new formulation is better in paediatric disease and for patients who have coma or difficulties to swallow solid pills
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☒ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included: For this new strength, dispersible tablet, specially for children, studies of palatability are lacking specially for children were the compliance of TBC treatment is very important.
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). Available data on Delamanid efficacy and safety are still limited. However, according to WHO guidelines, the overall benefits of the inclusion of delamanid in MDR-TB regimen appear to outweigh the observed harms Relative bioavailability of bedaquiline dispersible tablets are lacking Pharmacokinetic and bioequivalence studies are lacking. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☐ No ☒ Not applicable Comments:

Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: Delamanid may require special monitoring of cardiac adverse events. Because it is shown to cause prolongation of the QT interval, patients with a QTcF>500ms should not receive the drug. Patients receiving Delamanid should be monitored for symptoms of cardiac toxicity and by electrocardiogram (ECG).
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Due to the potential for serious adverse events, this drug will not be recommended for all MDR-TB patients. MDR-TB patients in whom Delamanid may have a particular role include those with: - Higher risk for poor outcomes (e.g. drug intolerance or contraindication, extensive or advanced disease). - Additional resistance to fluoroquinolones or injectable drugs. - XDR-TB
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Evidence of treatment outcomes is low because the limited data.
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments: EGC is available in all hospital and TB care centres and can be used routinely for cardiac monitoring.
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The product is currently available from the manufacturer (Otsuka) via Compassionate Use (4). Market availability of this product is foreseen in late 2021.

Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	Favorable for this new strength, specially to avoid concerns about the feasibility of administering the correct dose to children aged 3–5 years. It is proven that, there were concerns that bioavailability may be altered if the 50 mg tablet was split, crushed or dissolved. Delamanid 50 mg tablet is also susceptible to oxidation. Moreover, recognising that some clinicians are splitting the 50 mg tablets to treat children, which is not a recommended practice, and considering that when the 50 mg tablet (unscored) is broken, the contents are bitter and unpalatable, and the impact of crushing could appreciably alter (most likely reduce) the bioavailability of delamanid.
References (if required)	