F.6	Dolutegravir – paediatric formulation HIV
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Over 38 million people are living with HIV worldwide in 2020. In SSA approximately 13% of infected cases are in children with many of the infections occurring during the perinatal period. ARTs have demonstrated good efficacy for viral suppression thereby reducing morbidity, mortality, and new cases. Drug formulation plays a key role in adherence to treatment. A major problem of drug discontinuation is risk of resistance strains of HIV.
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 proposes the inclusion of an integrase inhibitor - dolutegravir (DTG)10mg scored dispersible tablets for treatment of HIV-1 infection among paediatric patients (at least 4 weeks of age and weighing at least 3kg) living with HIV/AIDS on the core list of the Model List of Essential Medicines for Children (EMLc). DTG 50mg film coated tablets are currently included in the WHO Model List of Essential Medicines (EML) and the EMLc for treatment of HIV in adults and pediatric patients weighing at least 25kg. This application proposes to add the newly approved dispersible tablet formulation (also called tablets for oral suspension) to span the pediatric ages and weight bands requiring a lower dose or more child-friendly formulation. Presently children receive doses broken down from 50mg tablets which pose risks of under/over dosing, medication contamination, and intolerable formats of medication, all which could lead to further complication. Literature from adult studies suggests that Dolutegravir (DTG), as a representative of the integrase inhibitor class of antiretroviral drugs (ARVs), has demonstrated superior effectiveness in multiple patient populations, a favorable safety profile, a high barrier to emergence of resistance, and an acceptable level of drug-drug interactions, making it an excellent candidate for use in a public health approach to HIV treatment. However results from paediatric studies are not yet available. This newly tentatively approved scored dispersible tablet formulation provides accurate dosing for infants and children as an easy-to-administer formulation that can either be dispersed in a small amount of water or taken directly by mouth.
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: Studies in our population of interests are still ongoing. Good quality evidence used in this application are from adult population.

Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes, partially ☐ 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). 1. Efficacy: most available evidence is from adult studies. Paediatric studies are still ongoing but preliminary results were used to project effectiveness comparatively with adults efficacy studies. Among these 75 paediatric patients who received either DTG film-coated tablets or DTG dispersible tablets according to the approved dosing recommendations for their weight band, 42 received DTG for at least 48 weeks. At Week 48, 69% of participants achieved HIV RNA <50 copies/mL and 79% achieved HIV RNA <400 copies/mL. The median CD4 count (percent) increase from baseline to Week 48 was 141 cells/mm3 (7%). 2. Tolerability and safety: Overall, the safety profile in P1093 participants was comparable to that observed in adults and both formulations were well tolerated by pediatric patients. The effectiveness observed in the trial was comparable to that of treatment-experienced adult subjects. 3. Cost: cheaper than other agents in the EML including LPV/r. there are also ongoing pricing arrangements to keep costs low. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Yes, ongoing studies are inclusive of geographical, gender, and income diversities.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes, partially ☐ No ☐ Not applicable
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable: Using DTG dispersible tablets for HIV in children will greatly improve compliance. It is of low cost. Although paediatric studies are still ongoing, the drug is already being used as 50mg which pose health issues for children. A dispersible option at 10mg will be useful especially for communities where maintaining hygiene and access to water is a problem.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Moderate

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:
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: several guidelines already mention the use of the agent in their recommendations:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The application proposes an agent – DTG - that will be used in the treatment of paediatric HIV and will facilitate compliance with treatment, reduce contamination of medicines, and reduce cost. Evidence of efficacy and safety in children is still in process of generation but preliminary findings are in accord with adult results.
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.	I recommend the inclusion DTG in the EML but we must weigh in risks of inclusion before available data from clinical trials for children.
References (if required)	