F.1	Abacavir + lamivudine + lopinavir/ritonavir fixed-dose combination - HIV
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: The case is made for the need for suitable treatment options for children with nearly 100,000 children under 15 estimated to die of HIV each year. Burden of infection is outlined on pp6-7 and the need for access to appropriate formulations is made. It is not explicit what the gap in existing options.
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.	The proposal is to include fixed dose granules of abacavir/3tc/lopinavir/ritonavir on the EMLc to allow appropriate dosing in children 3kg and above.
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: Detailed PK work is presented as an interim analysis of a study led by DNDi in (LOLIPOP). For 3TC and Lopinavir, bioequivalence was not demonstrated in certain groups. The documents state further data is expected to be available in Q1 2021.
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). Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Very limited data on efficacy is presented from the LOLIPOP study with 33 patients. The data that is presented is encouraging, with a suggestion that viral suppression is equivalent with the formulation, but numbers are very small. However, it does need to be recognised that such studies are difficult (even without COVID) and have been carried out in appropriate populations.

Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: There is some limited data presented from the LOLIPOP study. In general the formulation appears popular, but there are significant AEs (e.g. 52% vomiting). However, not clear how formulation compares to reference.
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.)	It is likely that the formulation will offer a useful treatment option for children. However, with the interim data presented there remains some uncertainty about the PK ,particularly in lower weight groups. Presentation of full study data would be helpful to understand this in more detail.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	There is one small study with interim results, full results are likely to be of high quality.
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: Granule formulation is developed to allow variable weight-based dosing for children. The steps in preparation are straightforward and described in the application. Although HLAB5701 testing may be used in some settings, the low prevalence of risk alleles is reflected in WHO guidance that testing is not necessary before use in children.
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: It is stated that an FDA application is underway – an update on this progress would be helpful.

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: Since 2013, the World Health Organization recommended the use of Lopinavir/ritonavir-based regimens in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs) as first-line therapy for all children infected with HIV younger than three years The 2018 WHO guidelines for treating and preventing HIV infection recommended a dolutegravir (DTG)-based regimen in com-bination with Abacavir(ABC) and Lamivudine(3TC) as the preferred first-line regimen for children for whom approved DTG dosing is available . In the absence of appropriate DTG formulations and dosing for infants and young children, ABC + 3TC in combination with LPV/r are considered as an acceptable alternative
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Data is presented on likely costs of granule formulations in comparison to existing combinations- it is noted that final prices are not available pre-marketing. It is stated that patents are not being enforced by abbvie, not clearly if this is binding or if there are voluntary licensing agreements in place
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.	Based on the evidence presented, two issues appear unclear. Firstly, what is the relative importance of this formulation in comparison to existing ABC/3TC/Dol combinations and secondly, the need for more detailed Pk and efficacy data in target age group. At this time, further information would be helpful before supporting inclusion of this formulation in EMLc
References (if required)	