M E M O R A N D U M

From:	Director, HHS	**To:**	Director, HPS	**Date:** 15 December 2020
Our ref:	HHS/TAC	**Attention:**	Secretary of the WHO Expert Committee on Selection and Use of Essential Medicines	
Your ref:		**Through:**		
Originator:	MV/MP/DLAA	**Subject:**	EXCLUSION OF ARV FORMULATIONS FROM WHO MODEL LIST OF ESSENTIAL MEDICINES AND WHO MODEL LIST OF ESSENTIAL MEDICINES FOR CHILDREN (2021 REVISION)	

In order to update the list of antiretrovirals (ARVs) recommended for treatment of HIV-infected adults and children on the 21st edition of WHO Model List of Essential Medicines and 7th edition of WHO Model List of Essential Medicines for Children (1), the Global HIV, Hepatitis and STIs Programmes (HHS) suggests below several deletions for the next revision. These recommendations were made to align the Model Lists with the 2019 WHO ARV guidelines (2) and the recently revised Optimal Formulary and Limited Use List for Paediatric ARVs (Dec 2020 to be launched in Q1 2021) from the group of partners convened by WHO via the Global Accelerator for Pediatric Formulations (GAP-f) platform (link). The following deletions are recommended for both WHO medicines lists.

Recommended deletions for both WHO medicines lists can be found in the attached Annex 1.

Thank you for you kind attention on this matter.

Dr Meg Doherty

ENCL: As stated.

Antiretroviral drug	Rationale for deletion from 21st EML and/or 7th EMLc
6.4.2.1 Nucleoside/Nucleotide reverse transcriptase inhibitors	
Lamivudine (3TC) Tablet: 150 mg.	Proposed for deletion from the EMLc only. This pediatric formulation of 3TC has been excluded from the paediatric optimal formulary and limited use list in the 2020 revision since a 3NRTI regimen for TB-cotreatment is not needed anymore in the context of the introduction of dolutegravir. 3TC 150 mg remains included in the EML as a component of preferred fixed-dose combination formulations.
Abacavir (ABC) Tablet (dispersible, scored): 60 mg (as sulfate).	Proposed for deletion from the EMLc. This pediatric formulation of ABC has been excluded from the paediatric optimal formulary and limited use list in the 2020 revision since a 3NRTI regimen for TB-cotreatment is not needed anymore in the context of the introduction of dolutegravir.
6.4.2.2 Non-nucleoside reverse transcriptase inhibitors	
Efavirenz (EFV or EFZ) Tablet: 200 mg (scored)	Proposed for deletion from the EML and EMLc. This pediatric formulation of EFV has been excluded from the optimal formulary and limited use list in the 2020 revision because a EFV-containing regimen is not among the preferred or alternatives regimens for children included in WHO guidelines. Active phase out is being supported by major procurement agencies as a EFV-containing regimen is now considered suboptimal in light of the high level of NNRTI resistance documented in many countries around the world. EFV 600 mg tablets remain included on the EML. EFV also remains included on the EML as a component of preferred fixed-dose combination formulations.

6.4.2.3 Protease inhibitors	
Ritonavir (RTV) Oral liquid: 400 mg/5 mL	Proposed for deletion from the EML and EMLc. This pediatric formulation of RTV was excluded from the pediatric optimal formulary and limited use list in the 2018 revision but was retained on the Model Lists in 2019 until availability of alternative RTV formulations was established. It was flagged by the 2019 Expert Committee for deletion in 2021 without further discussion (1). Furthermore, this formulation has become un-necessary for LPVr super-boosting as dolutegravir availability will provide a more suitable option for TB co-treatment. RTV 25 mg and 100 mg heat-stable tablets remain included on the EML and EMLc.
Ritonavir (RTV) Oral powder: 100 mg in sachet	Proposed for deletion from the EMLc. This pediatric formulation of RTV has been excluded from the pediatric optimal formulary and limited use list in the 2020 revision as this formulation doesn't provide dose flexibility and has become un-necessary for LPVr super-boosting as dolutegravir availability will provide a more suitable alternative for TB co-treatment.
Atazanavir Solid oral dosage form: 100 mg; (as sulfate).	Proposed for deletion from the EML and EMLc. This pediatric formulation of ATV has been excluded from the pediatric optimal formulary and limited use list in the 2020 revision as this formulation requires separate administration of RTV and is less preferable than existing available alternatives (ie dolutegravir 10mg and 50 mg as well as solid formulations of LPVr). For this reason use in countries is very limited.

Atazanavir Solid oral dosage form: 300 mg; (as sulfate).	Proposed for deletion from the EML This formulation of ATV should be deleted because this formulation requires separate administration of RTV and is less preferable compared to its FDC ATVr which is listed in the EML already.
Lopinavir + ritonavir (LPV/r) Oral liquid: 400 mg + 100 mg/5 mL	This formulation of LPV/r has been excluded from the pediatric optimal formulary and limited use list in the 2020 revision because replaced by LPVr solid oral dose forms (pellets and granules) which were included in the EML and EMLc in 2019.
6.4.2.4 Integrase inhibitors	
Raltegravir (RAL) Chewable tablet: 100 mg Tablet: 400 mg	RAL 100 mg chewable tablet is proposed for deletion from the EML and EMLc RAL 400 mg tablet is proposed for deletion from the EMLc only. The 100 mg chewable tablet formulation of RAL was replaced by the 25 mg chewable tablet in the 2018optimal formulary and limited use for children but was retained on the Model Lists in 2019 until availability of the 25 mg formulation was established. It was flagged by the 2019 Expert Committee for deletion in 2021 without further discussion (1). Due to the very limited use of RAL following dolutegravir availability, deletion of the RAL 400 mg tablet from the EMLc is also recommended. The 25 mg chewable tablet and the 100 mg granules should be maintained.
FIXED-DOSE COMBINATIONS	
Lamivudine + nevirapine + zidovudine Tablet: 200 mg + 300 mg + 150 mg.	Proposed for deletion from the EML. This fixed dose formulation containing NVP should be deleted because is not among the preferred or alternatives regimens included in WHO guidelines. Active phase out is being supported by major procurement agencies as this regimen is now considered suboptimal in light of the high level of NNRTI resistance

	documented in many countries around the world.
Lamivudine + nevirapine + zidovudine Tablet: 30 mg + 50 mg + 60 mg.	Proposed for deletion from the EMLc. This fixed dose pediatric formulation containing NVP has been excluded from the pediatric optimal formulary and limited use list for children in the 2020 revision because this regimen is not among the preferred or alternatives regimens included in WHO guidelines. Active phase out is being supported by major procurement agencies as this regimen is now considered suboptimal in light of the high level of NNRTI resistance documented in many countries around the world.

We also support the separate application for the addition of the dolutegravir 10 mg scored dispersible tablets to the EMLc, as they allow access to DTG for the paediatric population and are a critical formulation to implement current WHO guidelines and deliver the preferred ART regimens recommended for children above 3 kg and 4 weeks of age.

Reference List

1. WHO. The selection and use of essential medicines. Report of the WHO Expert Committee, 2019 (including the 21st WHO Model List of Essential Medicines and the 7th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization. (WHO Technical Report Series, No. 1021); 2019.
2. Update of recommendations on first- and second-line antiretroviral regimens. Geneva, Switzerland: World Health Organization; 2019 (WHO/CDS/HIV/19.15).
Licence: CC BY-NC-SA 3.0 IGO. Available from https://apps.who.int/iris/handle/10665/325892. .