World Health Organization

Updates to section *6.2.5 Antituberculosis medicines* of the 2021 WHO Model List of Essential Medicines (22nd list) and Model List of Essential Medicines for Children

MEDICINE	FORMULATION(S)	RECOMMENDED LISTING *(1)*	COMMENTS
ADDITIONS			
Moxifloxacin	Tablet: 400 mg	**Added** to the EML for the new indication of drug-susceptible (DS-) TB.	In line with the WHO recommendation for a 4-month treatment regimen comprising rifapentine, isoniazid, pyrazinamide and moxifloxacin as an alternative to the standard 6-month regimen with rifampicin, isoniazid, pyrazinamide and ethambutol, for adolescents and adults aged 12 years and above. *(2)*
Rifapentine	Tablet: 300 mg	This higher strength formulation of rifapentine was **added** to the EML and EMLc for TB preventive treatment (TPT) and to the EML for the new indication of DS-TB *(2)*	This higher strength formulation of rifapentine will help to reduce pill burden, thus improving treatment adherence to WHO-recommended regimens for treatment and prevention. A 4-month treatment regimen comprising rifapentine, isoniazid, pyrazinamide and moxifloxacin is recommended by WHO as an alternative to the standard 6-month regimen with rifampicin, isoniazid, pyrazinamide and ethambutol, for adolescents and adults aged 12 years and above.*(2)*

Isoniazid + Rifapentine	Tablet (scored): 300 mg + 300 mg (fixed-dose combination (FDC))	**Added** to the EML and EMLc for TPT	This formulation helps to reduce pill burden, thus improving treatment adherence to WHO-recommended TPT regimens.
Pyrazinamide	Tablet: 500 mg	**Added** to the EML and EMLc for use in treatment regimens for DS-TB	This formulation helps to reduce pill burden for patients thus improving treatment adherence to WHO-recommended treatment regimens. A 400 mg formulation of pyrazinamide is also already listed in the WHO EML and EMLc.
Bedaquiline	Tablet: 20 mg	This child-friendly formulation of bedaquiline was **added** to the EMLc for the treatment of multi-drug and rifampicin resistant (MDR/RR-) TB in children aged 5 years and above.	This formulation is functionally scored to divide the tablet in two equal halves when split. The whole or halved tablet can be dispersed in a small volume of water and mixed with a beverage or crushed and mixed with food. This formulation is well tolerated by children and is palatable. **It should be noted that a key update from a recently convened guideline development group (GDG) meeting on child and adolescent TB includes the use of bedaquiline in children aged below 6 years to treat MDR/RR-TB as part of all oral treatment regimens.***(3)* The evidence reviewed by the GDG was not available for review by the EML Expert Committee in 2021 and will be submitted for the 2023 update of the WHO EMLs.
Delamanid	Tablet (dispersible): 25 mg	This child-friendly formulation of delamanid was **added** to the EMLc for the treatment of multidrug- and rifampicin-resistant (MDR/RR-) TB in children aged 3 years and above.	This formulation is not functionally scored. It will be available from the Stop TB Partnership Global Drug Facility (GDF) by the end of 2021. **It should be noted that a key update from a recently convened guideline development group meeting on child and adolescent TB includes the use of delamanid in children aged below 3 years to treat MDR/RR-TB as part of longer regimens.***(3)* The evidence reviewed by the GDG was not available for review by the EML Expert

			Committee in 2021 and will be submitted for the 2023 update of the WHO EMLs.
Amikacin	Injection: 250 mg (as sulfate)/mL in 2 mL vial	This injection solution formulation of amikacin was **added** to the EML and EMLc	This formulation has advantages over powder for injection formulations as it does not require reconstitution for administration. Other formulations of Amikacin were removed from the list (see below)
DELETIONS			
Isoniazid	Tablet (scored): 50 mg	The Committee recommended **deletion** from the EML and EMLc of these formulations noting that they are not optimal formulations and strengths for tuberculosis treatment, in line with recommendations in current WHO treatment guidelines	No added value for dosing purposes and dispersible tablet formulations are now available
Pyrazinamide	Tablet (scored): 150 mg		
Isoniazid + Pyrazinamide + Rifampicin	Tablet: 75 mg + 400 mg + 150 mg (FDC)		No quality-assured supplier has been identified for this FDC and ethambutol-containing FDCs are already listed in the WHO EML, which allow for a lower pill burden for the treatment of DS-TB
Amikacin	Powder for injection: 100 mg		These formulations require reconstitution, and are therefore less ideal than a liquid formulation, especially in resource-limited settings. Also, no quality-assured formulation was identified for the 1 g powder for injection.
	Powder for injection 500 mg		
	Powder for injection 1 g (as sulfate) in vial		
Amoxicillin/Clavulanic Acid	Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 mL;		Using this formulation of Amoxicillin/clavulanic acid would result in higher volumes of liquid to be administered. Consolidating the TB market around a specific formulation of Amoxicillin/Clavulanic Acid for children, namely the oral liquid formulation of 250 mg amoxicillin +62.5 clavulanic acid/5 mL, which is already listed in the WHO EML and EMLc is important.
Linezolid	Injection for intravenous administration: 2 mg/mL in 300 mL bag		Oral formulations of linezolid are already listed in the WHO EMLs, including a 150 mg dispersible tablet, which allow implementation

			of regimens conforming to WHO recommendations to treat drug-resistant TB.
Linezolid	Tablet: 400 mg		No quality-assured market formulations were identified.
***p*-aminosalicylic acid**	Tablet: 500 mg		
OTHER CHANGES			
Ethambutol	Tablet: 100 mg; 400 mg (hydrochloride)	Specific formulation strengths replace strength ranges for ethambutol and isoniazid tablets, to facilitate rational selection and provide better clarity for countries in making national selection decisions	
Isoniazid	Tablet: 100 mg; 300 mg		

[1] World Health Organization. Executive summary: the selection and use of essential medicines 2021: report of the 23rd WHO Expert Committee on the selection and use of essential medicines (https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.01, accessed 12 October 2021)

[2] World Health Organization. Treatment of drug-susceptible tuberculosis: rapid communication. June 2021 (https://www.who.int/publications/i/item/9789240028678, accessed 18 October 2021)

[3] World Health Organization. Rapid communication on updated guidance on the management of tuberculosis in children and adolescents. August 2021 (https://www.who.int/publications/i/item/9789240033450, accessed 18 October 2021)