

## **TB Procurement and Market-Shaping Action Team (TPMAT) Recommendations on Updates to the WHO Essential Medicines List and Essential Medicines List for Children 2021**

### **Introduction**

The World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc) are updated every two years. Applications to add, delete or modify a medicine are submitted during an open application period. The applications are posted on the WHO's website and interested parties can submit letters of support (or against) a change. The applications and letters are then reviewed by an Expert Committee to determine if the application is accepted.

TPMAT, led by GDF, did a complete analysis of the 22<sup>nd</sup> EML and the 8<sup>th</sup> EMLc at the end of 2020. Using the TB Medicines Dashboard and other resources, TPMAT partners identified missing medicines and formulations that needed to be added and medicines and formulations that were no longer recommended that needed to be removed. TPMAT partners coordinated developing applications for the identified medicines and formulations and letters of support these applications.

TPMAT partners also monitored the applications once they were made public in case any additional applications for TB medicines were submitted. TPMAT partners reviewed all additional applications to determine if they were in alignment with best practices and contributed to access goals for TB medicines. Letters of support or opposition were then submitted by TPMAT partners based on this assessment.

The first table below shows the TPMAT-led recommendations and applications for changes to the EML and EMLc. The second table shows the TPMAT response and recommendations to applications submitted by other partners.

## TPMAT-Led Recommendations to Update the EML and EMLc

Medicine and formulation	TPMAT Recommendation	TPMAT Partner that Submitted the Application	Recommendation Rationale	Accepted by WHO Expert Committee
Amikacin 100mg powder for injection	Remove from the EML	WHO Global TB Programme (WHO GTB)	Amikacin is recommended by WHO as a Group C medicine in longer regimens for DRTB. <sup>1</sup> This formulation has a low efficiency for dose delivery and requires reconstitution before administration. The Expert Committee recommended to replace with amikacin 100mg/2mL in 2mL vial	
	Remove from the EMLc			
Amikacin 500mg powder for injection	Remove from the EML	WHO GTB	Amikacin is recommended by WHO as a Group C medicine in longer regimens for DRTB. <sup>1</sup> This formulation requires reconstitution before administration. The Expert Committee recommended to replace with amikacin 250mg/mL in 2mL vial	
	Remove from the EMLc			
Amikacin 1000mg powder for injection	Remove from the EML	WHO GTB	Amikacin is recommended by WHO as a Group C medicine in longer regimens for DRTB. <sup>1</sup> There is no quality-assured supply of this formulation and it requires reconstitution before administration. The Expert Committee recommended to replace with amikacin 250mg/mL in 2mL vial	
	Remove from the EMLc			
Amoxicillin/clavulanic acid oral powder for suspension 125mg/31.25mg/5 mL	Remove from the EML	WHO GTB	Clavulanic acid formulations are recommended by WHO to be used in conjunction with a carbapenem (e.g., meropenem or imipenem-cilastatin) in the treatment of DRTB. <sup>1</sup> Other formulations of this product are available that enables appropriate dosing in children, uses smaller volumes for administration and can help consolidate the market around one formulation.	
	Remove from the EMLc			
Bedaquiline 20mg tablets	Add to the EML (restricted to children)	Supplier	Bedaquiline is recommended by WHO for use in the Shorter Regimen and as a Group A medicine in longer regimens for DRTB in children 6 years of age and above. <sup>1</sup> A child-friendly formulation is now quality-assured and could support bedaquiline use in children.	
	Add to the EMLc			

TPMAT recommendations to WHO  
Essential Medicines List 2021

Medicine and formulation	TPMAT Recommendation	TPMAT Partner that Submitted the Application	Recommendation Rationale	Accepted by WHO Expert Committee
Delamanid 25mg dispersible tablet	Add to the EML (restricted to children)	WHO GTB	Delamanid is recommended by WHO as a Group C medicine in longer regimens for DRTB in children 3 years of age and above. A child-friendly formulation was available under compassionate use and a commercially available formulation became available in 2021. A child-friendly formulation could support delamanid use in children.	
	Add to the EMLc			
Ethambutol 25mg/mL oral liquid	Remove from the EML	WHO GTB	Ethambutol is recommended by WHO for the treatment of DSTB and in the shorter regimen and as a Group C medicine in longer regimens for DRTB. <sup>1,2</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a liquid formulation. The Expert Committee did not remove this formulation in 2021 to allow more time for programmes to transition to the dispersible formulation but indicated it will be deleted in 2023 without further consideration. <sup>3</sup>	
	Remove from the EMLc			
Ethionamide 125mg tablet	Remove from the EML	WHO GTB	Ethionamide is recommended by WHO for use in the shorter regimen and as a Group C medicine in longer regimens for DRTB. <sup>1</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a non-dispersible formulation. The Expert Committee did not remove this formulation in 2021 to allow more time for programmes to transition to the dispersible formulation but indicated it will be deleted in 2023 without further consideration. <sup>3</sup>	
	Remove from the EMLc			
Isoniazid 50mg/5mL oral liquid	Remove from the EML	WHO GTB	Isoniazid is recommended by WHO for use in the treatment of DSTB, in the shorter regimen for DRTB and in TB Preventative Therapy. <sup>1,2,4</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a liquid formulation. The Expert Committee did not remove this formulation in 2021 to allow more time for programmes to transition to the dispersible formulation but indicated it will be deleted in 2023 without further consideration. <sup>3</sup>	
	Remove from the EMLc			

TPMAT recommendations to WHO  
Essential Medicines List 2021

Medicine and formulation	TPMAT Recommendation	TPMAT Partner that Submitted the Application	Recommendation Rationale	Accepted by WHO Expert Committee
Isoniazid 50mg tablet scored	Remove from the EML	WHO GTB	Isoniazid is recommended by WHO for use in the treatment of DSTB, in the shorter regimen for DRTB and in TB Preventative Therapy. <sup>1,2,4</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a non-dispersible formulation.	
	Remove from the EMLc			
Isoniazid/pyrazinamide/rifampicin 75mg/400mg/150mg tablet	Remove from the EML	WHO GTB	WHO recommends the use of fixed-dose combination products for the treatment of DSTB that include rifampicin, isoniazid, pyrazinamide and ethambutol in the intensive phase and rifampicin and isoniazid in the continuation phase. <sup>2</sup> This formulation does not include all WHO-recommended medicines and there is no quality-assured formulation available.	
Isoniazid/rifapentine 300mg/300mg tablet	Add to the EML	WHO GTB	Rifapentine and Isoniazid in a one-to-one ratio are recommended by WHO in the once-weekly-for-three-months TPT regimen (3HP). <sup>4</sup> This FDC may increase adherence and completion of the 3HP TPT regimen in adults and children who can swallow the tablet.	
	Add to the EMLc			
Linezolid 2mg/mL in 300mL bag injection for infusion	Remove from the EML	WHO GTB	Linezolid is recommended by WHO as a Group A medicine in the longer regimen for DRTB and as part of the BPaL regimen. <sup>1</sup> There are oral formulations of linezolid that are suitable for both adults and children and are preferable to injectable-based treatment and align with WHO's recommendations on the use of all-oral regimens.	
	Remove from the EMLc			
Linezolid 400mg tablet	Remove from the EML	WHO GTB	Linezolid is recommended by WHO as a Group A medicine in the longer regimen for DRTB and as part of the BPaL regimen. <sup>1</sup> There is no quality-assured formulation that is commercially available. There are other suitable oral formulations for both adults and children.	
	Remove from the EMLc			
Moxifloxacin 400mg tablet	Add to core list of EML	WHO GTB	Moxifloxacin has been assessed by WHO for use in a 4-month treatment regimen for DSTB. <sup>5</sup> The core list includes all medicines for the treatment of DSTB.	

TPMAT recommendations to WHO  
Essential Medicines List 2021

Medicine and formulation	TPMAT Recommendation	TPMAT Partner that Submitted the Application	Recommendation Rationale	Accepted by WHO Expert Committee
P-aminosalicylic acid 500mg tablet	Remove from the EML	WHO GTB	PAS is recommended by WHO as a Group C medicine in the longer regimen for DRTB. <sup>1</sup> There is no quality-assured formulation that is commercially available. There are other suitable oral formulations for both adults and children.	
	Remove from the EMLc			
Pyrazinamide 30mg/mL oral liquid	Remove from the EML	WHO GTB	Pyrazinamide is recommended by WHO for the treatment of DSTB and in the shorter regimen and as a Group C medicine in longer regimens for DRTB. <sup>1,2</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a liquid formulation. The Expert Committee did not remove this formulation in 2021 to allow more time for programmes to transition to the dispersible formulation but indicated it will be deleted in 2023 without further consideration. <sup>3</sup>	
	Remove from the EMLc			
Pyrazinamide 150mg tablet scored	Remove from the EML	WHO GTB	Pyrazinamide is recommended by WHO for the treatment of DSTB and in the shorter regimen and as a Group C medicine in longer regimens for DRTB. <sup>1,2</sup> There is a quality-assured, dispersible tablet formulation that is commercially available and preferable to a non-dispersible formulation.	
	Remove from the EMLc			
Pyrazinamide 500mg tablet	Add to the EML	GDF	Pyrazinamide is recommended by WHO for the treatment of DSTB and in the shorter regimen and as a Group C medicine in longer regimens for DRTB. <sup>1,2</sup> The 500mg formulation is commercially available in a quality-assured formulation that could help reduce the pill burden.	
	Add to the EMLc			
Rifapentine 150mg tablet	Remove indication restriction from the EML	WHO GTB	Rifapentine is recommended by WHO for the treatment of DSTB and in multiple regimens for TPT. <sup>4,5</sup> Rifapentine had been included in the EML and EMLc, but restricted for use in TPT regimens only.	
	Remove indication restriction from the EMLc			

TPMAT recommendations to WHO  
Essential Medicines List 2021

Medicine and formulation	TPMAT Recommendation	TPMAT Partner that Submitted the Application	Recommendation Rationale	Accepted by WHO Expert Committee
Rifapentine 300mg tablet	Add to the EML	WHO GTB	Rifapentine is recommended by WHO for the treatment of DSTB and in multiple regimens for TPT. <sup>4,5</sup> This formulation could be used across all different rifapentine-based regimens and to reduce pill burden.	
	Add to the EMLc			

Other Recommendations to the EML and EMLc

Medicine and formulation	Recommendation from Submitting Organization	Recommendation from TPMAT	TPMAT Recommendation Rationale	TPMAT Recommendation Accepted by WHO Expert Committee
Ethambutol 1000mg vial for injection	Add to EML and EMLc	Do NOT add to EML or EMLc	WHO does not generally recommend the use of injectable agents for the treatment of TB. A full, WHO- recommended regimen could not be developed with the available agents (neither DS nor DRTB). Quality-assured formulations are not available.	
Ethambutol 2000mg vial for injection	Add to EML and EMLc			
Isoniazid 300mg vial for injection	Add to EML and EMLc	Do NOT add to EML or EMLc	WHO does not generally recommend the use of injectable agents for the treatment of TB. A full, WHO- recommended regimen could not be developed with the available agents (neither DS nor DRTB). Quality-assured formulations are not available.	
Isoniazid 500mg vial for injection	Add to EML and EMLc			
Isoniazid 900mg vial for injection	Add to EML and EMLc			
Rifampicin 600mg vial for injection	Add to EML and EMLc	Do NOT add to EML or EMLc	WHO does not generally recommend the use of injectable agents for the treatment of TB. A full, WHO- recommended regimen could not be developed with the available agents (neither DS nor DRTB).	

## Final WHO EML and EMLc released in September 2021

The final 22<sup>nd</sup> EML and 8<sup>th</sup> EMLc are available here: <https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists>

---

<sup>1</sup> WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2020.

<sup>2</sup> Guidelines for the treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017.

<sup>3</sup> The selection and use of essential medicines: report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2021 (including the 22nd WHO Model List of Essential Medicines and the 8th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization; 2021.

<sup>4</sup> WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment. Geneva: World Health Organization; 2020.

<sup>5</sup> Treatment of drug-susceptible tuberculosis: rapid communication. Geneva: World Health Organization; 2021.