





		EMLc	ATC codes: J01MA12
Indication	Multi-drug resistant Mycobacterium tuberculosis	ICD11 code: ML32.00	
INN	Levofloxacin		
Medicine type	Chemical agent		
Antibiotic groups	 WATCH		
List type	Complementary (EML) (EMLc)		
Additional notes	Medicines for the treatment of multidrug-resistant tuberculosis (MDR-TB) should be used in specialized centres adhering to WHO standards for TB control.		
Formulations	Oral > Solid > dispersible tablet: 100 mg (EMLc) Oral > Solid > tablet: 250 mg ; 500 mg ; 750 mg (EML)		
EML status history	First added in 1999 (TRS 895) Changed in 2003 (TRS 920) Changed in 2011 (TRS 965) Changed in 2013 (TRS 985) Changed in 2017 (TRS 1006) Changed in 2019 (TRS 1021)		
Sex	All		
Age	Also recommended for children		
Therapeutic alternatives	The recommendation is for this specific medicine		
Patent information	Patents have expired in most jurisdictions Read more about patents . 		
Wikipedia	Levofloxacin 		
DrugBank	Levofloxacin 		

Expert Committee recommendation

The Expert Committee recommended the addition of the proposed dispersible tablet formulations of ethambutol and isoniazid to the core list of the EMLc, and of cycloserine, ethionamide, levofloxacin, linezolid and moxifloxacin to the complementary list of the EMLc for the treatment of children with drug-sensitive and drug-resistant TB. The Committee considered that the availability of quality-assured, age-appropriate formulations will help improve access to effective treatment for children with TB.

Background

The application requested the addition of various new formulations of currently listed medicines for tuberculosis (TB) for use in children, including levofloxacin dispersible tablet 100 mg. All of the medicines for which additional formulations are requested for listing are currently included on the Model Lists in various formulations and strengths. In 2007, the World Health Assembly called for WHO to promote the development of child-friendly medicines with a particular focus on treatment for HIV, tuberculosis, malaria and chronic disease (1). In 2017, the Expert Committee recommended the addition to the EMLc of two fixed-dose combination, child-friendly dispersible tablet formulations of isoniazid + rifampicin +/- pyrazinamide for use in children with drug-sensitive tuberculosis infection. The Committee considered that the availability of these age-appropriate formulations would offer benefits including appropriate dosing, ease of administration and reduced pill burden (2).

Public health relevance

It is estimated that of the 10 million people who developed TB in 2017, 1 million of them were children. Children aged < 15 years accounted for 7.1% of the 6.4 million new or relapsed cases of TB notified to national TB programmes and reported to WHO. Children aged < 15 years accounted for 15% and 10% of total TB deaths among HIV-negative and HIV-positive people, respectively – higher than their share of estimated cases, suggesting poorer access to diagnosis and treatment (3).

Benefits

Evidence for the clinical effectiveness of the medicines was evaluated at the time of their individual listings. Paediatric-friendly formulations The proposed new formulations are mostly dispersible formulations, meaning they can be mixed in liquid, making it easier to get the correct doses and for children to swallow. They are flavoured to overcome the bitterness associated with breaking, crushing and otherwise manipulating adult formulations. The proposed formulations are at lower strengths, aligned with the dosing needs of children according to the 2019 update of the WHO consolidated guidelines on drug-resistant tuberculosis treatment (4). With the exception of linezolid 150 mg dispersible tablet (which is still in development), the proposed formulations are all quality-assured, either through the WHO Prequalification for Medicines Programme, or by the Global Fund Expert Review Panel.

Harms

Evidence for the safety of the medicines was evaluated at the time of their individual listings.

Cost / cost effectiveness

No information was provided in the application.

WHO guidelines

These medicines are all recommended the most recent WHO guidelines for treatment of drug-sensitive tuberculosis (2017) (5), treatment of latent TB infection (2018) (6), treatment of isoniazid mono-resistant TB (2018) (7) and treatment of drug-resistant TB (2019) (4).

Availability

The proposed new formulations are in the Stop TB Partnership's Global Drug Facility product catalogue and are reportedly being procured by programmes.

Other considerations

Comments on the application were received from the WHO Global TB Programme. The technical unit advised that it supported the application, which was developed in consultation with the Global TB Programme, and was fully in line with the latest WHO recommendations on the management of multidrug-resistant TB (MDR-TB), rifampicin-resistant TB (RR-TB) and isoniazid-resistant TB. The technical unit stated that the addition of child-friendly formulations of second-line antituberculosis medicines will greatly benefit children with drug-resistant tuberculosis.

1. Resolution WHA60.20. Better medicines for children. In: Sixtieth World Health Assembly, Geneva, 14–23 May 2007. Resolutions and decisions. Geneva: World Health Organization; 2007. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHASSA_WHA60-Rec1/E/reso-60-en.pdf, accessed 30 October 2019.

2. The selection and use of essential medicines. Report of the WHO Expert Committee, 2017 (including the 20th WHO Model List of Essential Medicines and the 6th WHO Model List of Essential Medicines for Children) (WHO Technical Report Series, No. 1006). Geneva: World Health Organization; 2017. Available from <https://apps.who.int/iris/bitstream/handle/10665/259481/9789241210157-eng.pdf>, accessed 30 October 2019.

3. Global tuberculosis report 2018. Geneva: World Health Organization; 2018. Available from <https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf>, accessed 30 October 2019.

4. WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2019. Available from: <https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf>, accessed 30 October 2019.

5. Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017. Available from: <https://apps.who.int/iris/bitstream/handle/10665/255052/9789241550000-eng.pdf>, accessed 30 October 2019).
6. Latent tuberculosis infection: Updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018. Available from <https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/>, accessed 30 October 2019.
7. WHO treatment guidelines for isoniazid-resistant tuberculosis: Supplement to the WHO treatment guidelines for drug-resistant tuberculosis. Geneva: World Health Organization; 2018. Available from: <https://apps.who.int/iris/bitstream/handle/10665/260494/9789241550079-eng.pdf>, accessed 30 October 2019.

