




		EMLc	ATC codes: J04AB01
Indication	Multi-drug resistant tuberculous Mycobacterium	ICD11 code: ML32.00	
INN	Cycloserine		
Medicine type	Chemical agent		
List type	Complementary Terizidone may be an alternative		
Formulations	Oral > Solid: 250 mg ; 125 mg (EMLc)		
EML status history	First added in 1999 (TRS 895) Changed in 2003 (TRS 920) Changed in 2007 (TRS 950) Changed in 2015 (TRS 994) Changed in 2019 (TRS 1021)		
Sex	All		
Age	Also recommended for children		
Therapeutic equivalence	The recommendation is for this specific medicine		
Patent information	Patents have expired in most jurisdictions Read more about patents . 		
Wikipedia	Cycloserine 		
DrugBank	Cycloserine 		

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 cycloserine 125 mg solid oral dose form.

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. Guidelines for the programmatic management of drug-resistant tuberculosis - 2011 update. Geneva: World Health Organization; 2
2. Ahuja SD, Ashkin D, Avendano M, Banerjee R, Bauer M, Bayona JN, et al. Multidrug resistant pulmonary tuberculosis treatment reg
3. Hwang TJ, Wares DF, Jafarov A, Jakubowiak W, Nunn P, Keshavjee S. Safety of cycloserine and terizidone for the treatment of drug

