Ethambutol

Section: 6. Anti-infective medicines > 6.2. Antibacterials > 6.2.5. Antituberculosis medicines

EMLc | ATC codes: J04AK02

Indication	Tuberculosis ICD11 code: 1B1Z
INN	Ethambutol
Medicine type	Chemical agent
List type	Core
Additional notes	WHO recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations, including modified dosage forms, non-refrigerated products and paediatric dosage forms of assured pharmaceutical quality.
Formulations	**Oral > Solid > dispersible tablet:** 100 mg (EMLc) **Oral > Solid > tablet:** 100 mg (hydrochloride) ; 400 mg (hydrochloride)
EML status history	First added in 1977 (TRS 615) Changed in 1979 (TRS 641) Changed in 1989 (TRS 796) Changed in 2007 (TRS 950) Changed in 2019 (TRS 1021) Changed in 2021 (TRS 1035) Changed in 2023 (TRS 1049)
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	Ethambutol
DrugBank	Ethambutol

Expert Committee recommendation

The Expert Committee accepted the rationale and justifications presented by the Global Tuberculosis Programme and recommended the deletion of the following formulations of antituberculosis medicines from the EML and/or EMLc as requested in the application: • amikacin injection 100 mg/2 mL (as sulfate) in 2 mL vial • linezolid powder for oral liquid 100 mg/5 mL • p-aminosalicylic acid granules 4 g in sachet. The Committee recommended the inclusion of a new formulation of p-aminosalicylate sodium (powder for oral solution: 5.52 g in sachet (equivalent to 4 g p aminosalicylic acid)) on the complementary list of the EML and EMLc to replace the deleted formulation of p-aminosalicylic acid, which has been discontinued by the only manufacturer. The Expert Committee recalled the recommendation of the 2021 Committee on the deletion of the following formulations of antituberculosis medicine formulations and recommended their removal from the EML and EMLc. The Committee noted that deletion of these formulations is supported by the Global Tuberculosis Programme, and that no application had been received to support their ongoing inclusion on the Model Lists: • ethambutol: oral liquid 25 mg/mL (EMLc) • ethionamide: tablet 125 mg (EML and EMLc) • isoniazid: oral liquid 50 mg/5 mL (EMLc) • pyrazinamide: oral liquid 30 mg/mL

(EMLc).

Background

At its meeting in 2021, the Expert Committee considered an application for deletion of various antituberculosis medicine formulations from the EML and EMLc, including ethambutol, ethionamide and pyrazinamide oral liquid, and ethionamide 125 mg tablets. The Committee recognized that dispersible tablet formulations are preferred child-friendly formulations and provide flexible dosing options. However, because of concerns about limited uptake and availability of dispersible tablets formulations of ethambutol, ethionamide, isoniazid and pyrazinamide in some countries, the Committee did not recommend the deletion of oral liquid formulations of ethambutol, isoniazid and pyrazinamide, nor the 125 mg tablet formulation of ethionamide at that time. To allow countries time to transition to the adoption of the preferred, listed dispersible-tablet formulations, the Committee advised that these formulations would be deleted from the Model Lists in 2023 without further consideration, unless an application was received to support their ongoing inclusion (1). No application to support ongoing inclusion has been received.

Benefits

The rationale presented in the applications for the requested deletions is summarized below. Amikacin injection 100 mg/2 mL Amikacin is recommended by WHO for the treatment of multidrug-resistant tuberculosis in people aged 18 years and older where susceptibility has been demonstrated. There is no current recommendation for its use in children and adolescents younger than 18 years due to an unfavourable benefit–risk balance and poor tolerability. In rare situations, amikacin may be used as salvage therapy, for which the dosage for children older than 2 years is 15–20 mg/kg a day, which can be achieved using the alternative listed strength of amikacin injection (250 mg/mL). This alternative strength is also more appropriate for dosing adults with multidrug-resistant tuberculosis, where higher doses are used (750–1000 mg a day). Linezolid powder for oral liquid 100 mg/5 mL This formulation is reported to be the subject of supply and availability issues, and to be more expensive than the alternative listed formulation of linezolid 150 mg dispersible tablets. The powder for oral liquid requires reconstitution before administration and contains a number of excipients associated with safety concerns. Linezolid 150 mg dispersible tablets have been included on the EMLc since 2019 and are included in the list of finished pharmaceutical products prequalified by WHO. p-aminosalicylic acid granules 4 g The application reports that p-aminosalicylic acid granules 4 g have been discontinued by the sole manufacturer because of high production costs and decreasing demand. An alternative product containing the equivalent of 4 g p-aminosalicylic acid as 5.52 g p-aminosalicylate sodium is available and is proposed in the application to replace the 4 g p-aminosalicylic acid formulation being proposed for deletion. Ethambutol oral liquid 25 mg/mL; ethionamide tablet 125 mg; isoniazid oral liquid 50 mg/5 mL; pyrazinamide oral liquid 30 mg/mL Refer to the Background section, above.

WHO guidelines

The proposed changes are aligned with recommendations in current WHO guidelines for the treatment of drug-susceptible and drug-resistant tuberculosis.

1. The selection and use of essential medicines. Report of the WHO Expert Committee, 2021 (including the 22nd WHO Model List of Essential Medicines and the 6th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization; 2021 (WHO Technical Report Series, No. 1035; https://apps.who.int/iris/handle/10665/351172, accessed 6 October 2023).

