WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information fromstringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[TB226 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains ethambutol hydrochloride 100 mg.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

[TB226 trade name] is a white, circular, shallow, biconvex, film-coated tablet, with a break-line on one side and plain on the other side.

[TB226 trade name] can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[TB226 trade name] is indicated in combination with other tuberculosis medicines for the treatment of tuberculosis due to *Mycobacterium tuberculosis* including in regimens for drug-resistant tuberculosis.

Treatment regimens should follow the most recent WHO treatment guidelines, supplemented by other authoritative guidelines.

This product is intended for use in children. Nonetheless, safety information is provided for adult health issues such as liver disease, pregnancy and breast-feeding, to allow full access to all relevant information.

4.2 Posology and method of administration

Posology

[TB226 trade name] is always given in combination with other tuberculosis medicines, according to the selected regimen. Official national or international guidelines, e.g. WHO guidelines, should be consulted for selecting the regimen and the duration of treatment.

Drug-susceptible tuberculosis

Children weighing less than 25 kg

The dose of ethambutol depends on the patient's weight and is around 15–25 mg/kg once daily.Recommended doses of [TB226 trade name] for treating children with drug-susceptible tuberculosis are shown below:

Patient's weight	Dose as 100-mg tablets	Dose in mg
4 kg to less than 8 kg	1 tablet once daily	100 mg once daily
8 kg to less than 12 kg	2 tablets once daily	200 mg once daily
12 kg to less than 16 kg	3 tablets once daily	300 mg once daily
16 kg to less than 25 kg	4 tablets once daily	400 mg once daily
25 kg or more	A formulation containing higher amount of ethambutol may be more suitable	

†Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

Adults and children weighing 25 kg or more

For these patients, formulations containing higher amounts of ethambutol are more suitable.

Drug-resistant tuberculosis

Children weighing less than 24 kg

The dose of ethambutol depends on the patient's weight and is around 15–25 mg/kg once daily.Recommended doses of [TB226 trade name]for treating children with drug-resistant tuberculosis are shown below:

Child's weight	Dose as 100-mg tablets	Dose in mg
3 kg to less than 5 kg	½ tablet once daily	50 mg once daily
5 kg to less than 7 kg	1 tablet once daily	100 mg once daily
7 kg to less than 10 kg	2 tablets once daily	200 mg once daily
10 kg to less than 16 kg	3 tablets once daily	300 mg once daily
16 kg to less than 24 kg	4 tablets once daily	400 mg once daily
24 kg or more	A formulation containing higher amount of ethambutol are more suitable	

Adults and children weighing 24 kg or more

For these patients, formulations containing higher amounts of ethambutol are more suitable.

Renal impairment

If the patient's creatinine clearance is less than 30 mL/minute, the dosing frequency of the relevant weight-based ethambutol dose should be reduced from once a dayto three times a week.Plasma ethambutol concentration should be monitored.

Missed doses and vomiting after a dose

It is important that the patient takes the medicine regularly as prescribed. Missing doses can increase the risk of resistance to [TB226 trade name] and reduce its effectiveness.

The patient should takea missed dose if it was due less than 12 hours ago. If more than 12 hours have passed since the dose was due, the patient should omit the missed dose and take the next scheduled dose at the usual time. The patient should not take a double dose.

If the patient vomits within 1 hour of taking [TB226 trade name], the patient should take an extra dose. If the patient vomits more than an hour after taking the dose, no extra dose is needed, and the next dose should be taken as usual when it is due.

Method of administration

[TB226 trade name] can be taken with food or between meals. It should be swallowed with water.

4.3 Contraindications

- Hypersensitivity to ethambutol or to any of the excipients of [TB226 trade name].
- Patients with optic neuritis or severe visual problems unless clinical judgement determines that ethambutol may be used.

4.4 Special warnings and precautions for use

Renal impairment

Toxic effects are more common if renal function is impaired. In particular, visual acuity should be monitored more closely in these patients. For dose adjustment in patients with creatinine clearance of less than 30 mL/minute, see section 4.2.

Visual impairment

Ethambutol can cause ocular toxicity and patients should be advised to report any eye problems such as vision changes, blurring, colour blindness, trouble seeing, or eye pain.

An ophthalmic examination is recommended before starting treatment and monthly during treatment. It should include testing for visual acuity, colour discrimination, and field of vision. Each eye must be tested separately and both eyes tested together.For patients with visual defects or renal insufficiency ophthalmic examination should be more frequent.

Patients who cannot report changes to their vision should be monitoredclosely for deterioration during treatment with ethambutol. In young children and those with communication difficulties, parents or other family members should be given advice about the need to report visual sideeffects.

Ethambutol should be stopped immediately if vision is impaired.

Hepatic impairment

Liver function tests should be performed in patients who develop symptoms suggestive of hepatitis or who become generally unwell during treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Aluminium hydroxide reduces the absorption of ethambutol. Therefore, if therapy for excess stomach acid is required, acid-suppressing drugs or antacids that do not contain aluminium hydroxide should be used during ethambutol therapy.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy

[TB226 trade name] can be used during pregnancy as part of a combination regimen to treat tuberculosis.

Ethambutol does not pose any additional risks to the patient or fetus. Tuberculosis can be particularly dangerous in pregnancy and should be managed with effective treatment. Close monitoring during pregnancy will allow any concerns to be managed promptly.

Breastfeeding

Ethambutol passes into breast milk. However, adverse effects in children breast-fed by women taking ethambutol have not been reported and it may be used during breastfeeding.

Fertility

There are no data on ethambutol's effects on fertility.

4.7 Effects on ability to drive and use machines

Patients should not drive or operate machinery if affected by visual disturbances or side effects such as numbness, paraesthesia, dizziness and disorientation.

4.8 Undesirable effects

The most important adverse reactions of ethambutol is retrobulbar neuritis with reduced visual acuity.

Adverse events considered at least possibly related to ethambutol are listed below. Frequencies are defined as very common (up to 1 in 10), common (between 1 in 100 and 1 in 10), uncommon (between 1 in 1000 and 1 in 100), rare (between 1 in 10 000 and 1 in 1000), very rare (less than 1 in 10 000), and 'not known'.

Nervous system disorders

Rare	peripheral neuritis, peripheral neuropathy, paraesthesia (especially in the extremities), numbness
Very rare	disorientation, dizziness, headache

Eye disorders

Uncommon	optic neuritis (decreased visual acuity, loss of vision, scotoma, colour blindness, visual disturbance, visual field defect, eye pain)

Psychiatric disorders

Very rare	mental confusion and hallucination

Gastrointestinal disorders

Not known	nausea, vomiting, anorexia, flatulence, abdominal pain, diarrhoea, metallic taste, anorexia

Hepatobiliary disorders

Very rare	hepatic failure
Not known	hepatitis, jaundice, increase in liver enzymes

Renal and urinary disorders

Very rare	nephrotoxicity including interstitial nephritis

Blood and lymphatic systems disorders

Rare	thrombocytopenia,
Very rare	leucopenia, neutropenia

Respiratory, thoracic and mediastinal disorders

Very rare	pneumonitis, pulmonary infiltrates, with or without eosinophilia

Metabolism and nutrition disorders

Uncommon	hyperuricaemia
Very rare	gout

Immune system disorders

Very rare	hypersensitivity, anaphylactoid reactions (see also ‘Skin and subcutaneous tissue disorders’)

Skin and subcutaneous tissue disorders

Rare	rash, pruritus, urticaria
Very rare	photosensitive lichenoid eruptions, bullous dermatitis, Stevens-Johnson syndrome, epidermal necrolysis

Musculoskeletal and connective tissue disorders

Very rare	joint pains

General disorders

Very rare	Malaise, pyrexia

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine’s benefits and risks.

4.9 Overdose

Symptoms

Gastrointestinal disturbances, vomiting, fever, headache, anorexia, dizziness, hallucinations and visual disturbances

Treatment

There is no specific antidote and treatment is supportive. Gastric lavage may be of value if started within a few minutes of ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterial (other drugs for treatment of tuberculosis).

ATC code: J04AK02

Mechanism of action

Ethambutol at the recommended doses is bacteriostatic. It has very little sterilising activity. Its mechanism of action is not known, but it is thought to inhibit cell wall synthesis by preventing the incorporation of mycolic acids; this stops cell multiplication and can lead to cell death. Ethambutol is only active against bacteria undergoing cell division.

Ethambutol is active against virtually all strains of *Mycobacterium tuberculosis* and *M. bovis* and is also active against other mycobacteria such as *M. kansasii*. When used alone for treatment of tuberculosis, tubercle bacilli from these patients developed resistance to ethambutol. The development of resistance is unpredictable and may occur in a step-like manner. No cross-resistance between ethambutol and other antituberculosis agents has been reported. Ethambutol delays or prevents the emergence of mycobacterial resistance when it is used with other antituberculosis drugs.

5.2 Pharmacokinetic properties

Absorption of [TB226 trade name]

No pharmacokinetic data are available for [TB226 trade name]. A bioequivalence study was conducted with [TB134 trade name] which contains 400 mg ethambutol hydrochloride and is essentially the same as [TB226 trade name] in qualitative terms and with respect to the ratio of active and other ingredients.

The absorption characteristics of [TB134 trade name] have been determined after administration of one ethambutol hydrochloride 400 mg tablet in healthy volunteers in the fasting state as follows:

Pharmacokinetic Parameter	**Arithmetic mean ± standard deviation**
Time to attain maximum concentration (T_{max})	3.3 ± 1.3 h
Maximum concentration (C_{max})	0.972 ± 0.327 µg/mL
Area under the curve ($AUC_{0-\infty}$), a measure of the extent of absorption	6.04 ±1.73 µg·h/mL

Pharmacokinetics of ethambutol

Absorption	
Oral bioavailability	70–80%
Food effect	None
Distribution	
Volume of distribution (mean)	20 L
Plasma protein binding *in vitro*	10–40%
Tissue distribution	Relatively low concentrations distributed to CSF

Metabolism	
	Hepatic
Elimination	
Elimination half life	3–4 h
Mean systemic clearance (Cl/F)	41 L/h
% of dose excreted in urine	60–80%
% of dose excreted in faeces	20%

Special populations

Half-life is increased up to 8 hours in cases of renal impairment.Ethambutol is not removed from the blood by haemodialysis.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans at recommended doses based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet: Tablet core:
Microcrystalline cellulose
Povidone
Stearic acid
Maize starch
Sodium starch glycolate
Colloidal anhydrous silica
Purified talc
Magnesium stearate

Film coat: Hypromellose

Ethylcellulose

Macrogol

Purified talc

Titanium dioxide

This medicine is essentially ‘sodium-free’. It contains less than 1 mmol sodium (23 mg) per tablet.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months (Blister packs)

60 months (HDPE bottle packs

6.4 Special precautions for storage

Do not store above 30ºC. Protect from light. Store in the original container.

Keep out of reach and sight of children.

6.5 Nature and contents of container

Bulk pack: 1000 tablets in a self-sealing polythene bag, inside a 650mL HDPE container sealed with an aluminium tagger.

Blister packs: dark amber coloured PVC/PVdC-Alu blisters. Pack sizes: 7 x 10, 10 x 10, and 24 x 28

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

Preparation and administration - extemporaneous formulation for children

[TB226 trade name] may be made into a mixture with water if the patient cannot swallow tablets. Each tablet should be made into a mixture with at least 10 mL water.

The mixture should be swirled or stirred to mix the tablets completely. The patient should drink all the mixture. The container should then be rinsed with more water and the patient should drink this also to ensure that the whole dose is taken.

7. SUPPLIER

Macleods Pharmaceuticals Limited

Atlanta Arcade, 3rd Floor, Church Road, near Leela Hotel,

Andheri-Kurla Road

Andheri (East)

400 059, Mumbai

India

Tel No.: + 91 22 66 76 28 00

Fax No.: 91 22 28 21 65 99

E-mail: sjadhav@macleodspharma.com and vijay@macleodspharma.com

8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

TB226

9. DATE OF PREQUALIFICATION

04 November 2013

10. DATE OF REVISION OF THE TEXT

November 2023
Section 6 was updated in August 2025.

References

Drug-susceptible tuberculosis

WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240048126, accessed 25 August 2023).

WHO operational handbook on tuberculosis Module 4: Treatment – drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240050761, accessed 25 August 2023).

Drug-resistant tuberculosis

WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240063129, accessed 25 August 2023).

WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240065116, accessed 25 August 2023).

Web Annexes. In: WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/bitstream/handle/10665/365309/9789240065352-eng.pdf, accessed 25 August 2023).

Children and adolescents

WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240046832, accessed 25 August 2023).

Note

WHO guidelines and handbooks are available on WHO TB knowledge sharing platform (https://tbksp.org/en, accessed 25 August 2023)

Product information

Myambutol (ethambutol hydrochloride): label. U.S. Food and Drug Administration; January 2007 (https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/016320s063lbl.pdf, accessed 25 August 2023).

Ethambutol 100 mg Tablets (Kent Pharma UK Ltd): summary of product characteristics. London: Medicines and Healthcare products Regulatory Agency; 6 April 2021 (https://mhraproducts4853.blob.core.windows.net/docs/a842c1b4891938d074441414d7fa24e9230c5842, accessed 25 August 2023).

Ethambutol/Myambutol Tablets 400mg (Genus Pharmaceuticals Holdings Limited): summary of product characteristics. London: Medicines and Healthcare products Regulatory Agency; 31 January 2019 (https://mhraproducts4853.blob.core.windows.net/docs/5cf69bf9d9deaa32d8913ee75a2abd5006eca029, accessed 16 September 2023)

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines