

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Myambutol Tablets 400mg
Ethambutol Tablets 400mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Ethambutol Tablet contains 400mg of Ethambutol Hydrochloride (EP).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Grey coated tablets

4 CLINICAL PARTICULARS

4.1. Therapeutic Indications

The primary treatment and re-treatment of tuberculosis and for prophylaxis in cases of inactive tuberculosis or large-tuberculin-positive reaction. Ethambutol should only be used in conjunction with other anti-tuberculous drugs to which the patients organisms are susceptible.

4.2. Posology and Method of Administration

Route of administration: Oral

Posology

The dosage of Ethambutol must be adjusted according to the body weight of the patient.

Adults

For primary treatment and prophylaxis: Ethambutol should be administered in a single daily oral dose of 15mg/kg, concomitant drugs being maintained at their recommended dosage levels.

For re-treatment: For the first 60 days of treatment, Ethambutol should be administered in a single daily oral dose of 25mg/kg. Thereafter the dosage

should be reduced to 15mg/kg, concomitant drugs being maintained at their recommended dosage levels.

Children

For primary treatment and re-treatment: For the first 60 days of treatment, a single daily oral dose of 25mg/kg. Thereafter the dosage should be reduced to 15mg/kg, concomitant drugs being maintained at their recommended dosage levels.

For prophylaxis: A single daily oral dose of 15mg/kg, concomitant drugs being used at their recommended dosage levels.

Elderly

As for adults: However, patients with decreased renal function may need to have the dosage adjusted as determined by blood levels of Ethambutol.

In order to obtain maximum effect due to high serum levels, drug administration should be once daily.

Renal Impairment

Renal function should be checked before treatment with antituberculous drugs and appropriate dosage adjustments made. Ethambutol should preferably be avoided in patients with renal impairment

If used, where creatinine clearance is less than 30mL/minute, use 15–25 mg/kg (max. 2.5 g) 3 times a week and plasma ethambutol concentration should be monitored.

4.3 Contraindications

Ethambutol is contra-indicated in patients who are known to be hypersensitive to the drug. It is also contra-indicated in patients with known optic neuritis and poor vision unless clinical judgement determines that it may be used.

4.4 Special warnings and precautions for use

Renal function:

Toxic effects are more common if renal function is impaired.

Ocular toxicity:

Ethambutol may produce a unique type of visual impairment which is generally reversible and which appears to be due to optic neuritis and to be related to dose and duration of treatment.

Less than 1% of patients undergoing treatment with the higher dose regimen of 25mg/kg/day for two months, and 15mg/kg/day thereafter, have exhibited decrease in visual acuity. It is recommended that patients undergo a full ophthalmic examination before starting treatment. This should include visual acuity, colour vision, perimetry and ophthalmoscopy. Any change may be unilateral or bilateral and hence both eyes should be tested individually.

Routine ophthalmological examination for adults is not thereafter necessary, but patients should be informed the importance of reporting any change in vision. Routine ophthalmological examinations may be considered desirable when treating young children.

Any negative effects on vision are generally reversible when administration of the drug is discontinued promptly and recovery of visual acuity has usually occurred over a period of weeks to months after the drug was discontinued. Patients have then received Ethambutol at lower dosages without toxicity.

In rare cases, recovery may be delayed for up to one year or more or the effects may be irreversible.

Hepatic impairment:

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

Skin and subcutaneous tissue disorders:

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported post-marketing in association with ethambutol treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, ethambutol should be withdrawn immediately and an alternative treatment considered (as appropriate).

If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of ethambutol, treatment with ethambutol must not be restarted in this patient at any time.

In children, the presentation of a rash can be mistaken for the underlying infection or an alternative infectious process, and physicians should consider the possibility of a reaction to ethambutol in children that develop symptoms of rash and fever during therapy with ethambutol.

Other Warnings:

Consideration should be given to current clinical guidance on the appropriate use of antituberculous drugs.

This medicinal product contains sorbitol and sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Aluminium hydroxide may impair the absorption of ethambutol. Therefore antacids containing this ingredient should be avoided during treatment with ethambutol.

4.6 Fertility pregnancy and lactation

Pregnancy

There are no or limited data from the use of ethambutol in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.

Ethambutol is not recommended during pregnancy and in women of childbearing potential unless the potential benefit to the mother is considered to outweigh any possible risks.

Breast-feeding

Ethambutol/metabolites have been identified in breastfed newborns/infants of treated women. There is insufficient information on the effects of ethambutol in newborns/infants.

Breast-feeding is not recommended during Ethambutol treatment unless the benefit of breast-feeding to the child is considered to outweigh any possible risks.

4.7 Effects on Ability to Drive and Use Machines

Patients who suffer from visual impairment during treatment with ethambutol should not drive or operate machinery.

Numbness, paraesthesia, dizziness, disorientation are also among possible side effects that may affect a patient's ability to drive or operate machinery, if affected, patients should not drive or operate machinery.

4.8 Undesirable effects

In this section, frequencies of undesirable effects are defined as follows:
Frequency: very common (>1/10); common (>1/100, <1/10); uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000), very rare (<1/10,000).

Blood & lymphatic system disorders:

Rare: Thrombocytopenia

Very rare: Leucopenia, neutropenia

Immune system disorders:

Very rare: Hypersensitivity, anaphylactoid reactions, (see also Skin and subcutaneous tissue disorders)

Metabolic & nutrition disorders:

Uncommon: Hyperuricaemia

Very rare: Gout

Nervous system disorders:

Rare: Peripheral neuropathy, numbness, paraesthesia of the extremities

Very rare: headache, dizziness, disorientation

Psychiatric disorders:

Very rare: mental confusion, hallucinations

Eye disorders

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

Respiratory, thoracic & mediastinal disorders:

Very rare: Pneumonitis, pulmonary infiltrates, with or without eosinophilia

Gastrointestinal disorders:

Gastrointestinal disorders such as anorexia, nausea, vomiting, abdominal pain and diarrhoea have been noted in patients on multiple drug anti-tuberculosis therapy including ethambutol although not in test patients receiving ethambutol as sole therapy.

Hepatobiliary disorders:

Hepatic reactions with hepatitis, jaundice, abnormal liver function test values, and very rarely, hepatic failure, have been reported in patients treated with multiple drug therapy including ethambutol. Liver function tests should be performed in patients who develop symptoms suggestive of hepatitis or who become generally unwell during treatment.

Skin & subcutaneous tissue disorders:

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

Frequency not known: Drug reaction with eosinophilia and systemic symptoms (DRESS) (see section 4.4)

Musculoskeletal and connective tissue disorders:

Very rare: Joint pains

Renal & urinary disorders

Very rare: Interstitial nephritis

General disorders and administration site conditions:

Very rare: Malaise, pyrexia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' in the Google Play or Apple App Store.

4.9. Overdose

Symptoms: Gastrointestinal disturbances, vomiting, fever, headache, anorexia, dizziness, hallucinations and/or visual disturbances.

Treatment: No specific antidote, but gastric lavage should be employed if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ethambutol is bacteriostatic. It is effective against *Mycobacterium tuberculosis* and *M. bovis* with an MIC of 0.5 - 8 µg per ml. While it has activity against some atypical mycobacteria including *M. Kansarii*, activity against other micro-organisms has not yet been reported.

It is effective against tubercle bacilli resistant to other tuberculostatics. Cross-resistance has not yet been reported. Primary resistance to ethambutol is uncommon but resistant strains of *M. tuberculosis* are readily produced if ethambutol is used alone.

5.2 Pharmacokinetic properties

Ethambutol is readily absorbed after oral administration and this absorption is not significantly impaired by food. After a single dose of 25mg/kg body weight, within 4 hours peak plasma concentrations of up to 5µg/ml are obtained, by 24 hours the concentration decreases to less than 1µg/ml. Most of a dose is excreted unchanged in the urine and up to 20% in faeces, within 48 hours. From 8 - 15% of a dose appears in urine as inactive metabolites.

Ethambutol readily diffuses into red blood cells and into the cerebrospinal fluid when the meninges are inflamed. It has also been reported to cross the placenta.

5.3 Preclinical safety data

Nothing further of relevance to prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose; gelatin 125 bloom; sorbitol solution 70%; magnesium stearate; stearic acid.

Film Coating: Aquapolish D Grey*.

*Aquapolish D Grey contains hydroxypropylmethylcellulose, hydroxypropylcellulose, microcrystalline cellulose, stearic acid, talcum, titanium dioxide (E171), iron oxide yellow (E172), iron oxide red (E172), iron oxide black (E172).

6.2 Incompatibilities

None.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Ethambutol should be stored at room temperature (below 25°C) in the original pack.

6.5 Nature and contents of container

PP bottle with a PP child resistant closure. Pack sizes of 28 or 56 tablets.
Not all pack sizes may be marketed.

6.6 Special instructions for disposal

None

7. MARKETING AUTHORISATION HOLDER

Genus Pharmaceuticals Holdings Limited
T/A Genus Pharmaceuticals

Linthwaite,
Huddersfield,
HD7 5QH, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 17225/0005.

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

06/04/2009

10 DATE OF REVISION OF THE TEXT

22/07/2024