SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ethambutol 400 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ethambutol hydrochloride 400 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.

Grey, round biconvex, film coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For 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-tuberculosis drugs to which the patient's organisms are susceptible.

Consideration should be given to official guidance on the appropriate use of antimicrobial agents.

4.2 Posology and method of administration

Posolo

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Dosage should be determined according to the body weight of the patient. The usual daily dosage is 15-25mg/kg body weight given as a single dose.

Ethambutol should not be used as a sole anti-tuberculosis agent, but should be given with at least one other anti-tuberculosis drug to avoid development of resistant strains.

Adults

For primary treatment and prophylaxis: Ethambutol should be administered in a single daily dose of 15 mg/kg body weight; concomitant drugs should be maintained at their usual recommended dosage.

For re-treatment: For the first 60 days of treatment, ethambutol should be administered in a single daily dose of 25 mg/kg body weight. Thereafter the dosage should be reduced to 15 mg/kg body weight; concomitant drugs should be maintained at their usual recommended dosage levels.

Paediatric population

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

For prophylaxis: A single daily dose of 15 mg/kg body weight; concomitant drugs being maintained at their usual recommended dosage levels.

As children may be less likely or unable to report ocular toxicity, particular caution may be warranted (see Section 4.4).

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

Elderly

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

Method of administration: Oral use

4.3 Contraindications

Hypersensitivity to ethambutol or to any of the other ingredients listed in section 6.1.

Known optic neuritis and poor vision or retrobulbar neuritis, unless clinical judgement determines that the benefit outweighs the potential risk.

4.4 Special warnings and precautions for use

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. Each eye should be tested separately as ocular toxicity can be unilateral or bilateral.

Routine ophthalmological examination for adults is not thereafter necessary, but patients should be informed of the important of reporting any change in vision. Routine ophthalmological examination 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 doses without toxicity.

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

Renal function:

Toxic effects are more common if renal function 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.

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 medicine contains less than 1mmol sodium (23 mg) per 400 mg tablet, that is to say essentially 'sodium free'.

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 andin 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.

Dizziness, disorientation, numbness and paraesthesia 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:

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); not known (frequency cannot be estimated from the available data)

SOC	LLT	Occurrence
Blood and lymphatic system disorders:	thrombocytopenia	rare
	leukopenia, neutropenia eosinophilia	very rare
Immune system disorders	hypersensitivity, anaphylactoid reactions allergic reactions, anaphylaxis, allergic pneumonitis.	very rare
Metabolism and nutrition disorders	hyperuricaemia.	uncommon
	gout.	very rare
Psychiatric disorders	mental confusion, hallucination	very rare
Nervous system disorders	peripheral neuritis, peripheral neuropathy, paraesthesia of the extremities, numbness	rare
	burning pain, weakness (hands and feet), dizziness, headache, disorientation	very rare
	tremor	unknown
Eye disorders	retrobulbar neuritis*	Common
	optic neuritis, (decreased visual acuity, loss of vision, scotoma, colour blindness, visual disturbance, visual field defect, eye pain)	Uncommon
Respiratory, thoracic and mediastinal disorders	pneumonitis, pulmonary infiltrates, with or without eosinophilia	very rare
Gastrointestinal disorders:	nausea, vomiting, anorexia, abdominal pain & diarrhoea have been noted in patients on multiple drug anti- tuberculosis therapy including ethambutol although not in test patients receiving ethambutol as sole therapy.	not known

	Flatulence, metallic taste, loss of appetite, upset stomach	
[1]**Hepatobiliary disorders:**	Hepatic reactions with hepatitis, jaundice, transient increase in liver enzymes, 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.	not known
	hepatic failure	very rare
Musculoskeletal and connective tissue disorders	joint pains	very rare
Skin & subcutaneous Tissue disorders	Rash, pruritus, urticaria.	Rare
	photosensitive lichenoid eruptions, bullous dermatitis, Stevens Johnson syndrome, epidermal necrolysis.	very rare
	drug reaction with eosinophilia and systemic symptoms (DRESS)	Not known
Renal and urinary disorders:	nephrotoxicity including interstitial nephritis.	very rare
General disorders and administration site conditions:	malaise, pyrexia.	very rare

* This effect is thought to be dose related, and frequency is dependent on both dose and duration of treatment. It occurs most frequently with doses of 25 mg/kg body weight and after two months of therapy, however optic neuritis has also occurred after only a few days of therapy. The effect is often reversible upon discontinuation of therapy. To avoid permanent damage visual acuity should be checked regularly during treatment and therapy discontinued immediately when visual disturbances occur.

Visual disturbances may be unilateral or bilateral; therefore each eye should be tested separately (see section 4.4). Typical signs include: blurred vision, eye pain, impairment of colour vision (red-green colour blindness), constriction of visual field (central or peripheral scotoma), and any loss in vision. Recovery of visual acuity has usually occurred over a period of

weeks to months after the drug was discontinued, and patients have then received Ethambutol at lower dosage without toxicity.

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

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 Yellow Card Scheme at: www.mhra.go.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: There is no specific antidote, but gastric lavage should be employed if necessary.

5.1 Pharmacodynamic properties

ATC Code: J04AK02 - Other drugs for treatment of tuberculosis

Ethambutol is bacteriostatic. It is effective against *Mycobacterium tuberculosi* and M.bovis with an MIC of 0.5 – 8µg per ml. While it has activity against some atypical mycobacteria including *M.Kansasii*, 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

Absorption: Ethambutol is readily absorbed after oral administration and this absorption is not significantly impaired by food.

Distribution: After a single oral dose of 25 mg/kg bodyweight, within 4 hours peak plasma concentrations of up to 5µg/ml are obtained, by 24 hours the concentration decreases to less than 1µg/ml. 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.

Metabolism and Excretion: Most of a dose is excreted unchanged in the urine and up to 20% in the faeces, within 48 hours. From 8 – 15% of a dose appears in the urine as inactive metabolites.

5.3 Preclinical safety data

Ethambutol has been shown to be teratogenic in pregnant mice and rabbits when given in high doses. When pregnant mice or rabbits were treated with high doses of ethambutol hydrochloride, fetal mortality was slightly but not significantly (P>0.05) increased. Female rats treated with ethambutol hydrochloride displayed slight but insignificant (>0.05) decreases in fertility and litter size. In foetuses born of mice treated with high doses of ethambutol hydrochloride during pregnancy, a low incidence of cleft palate, exencephaly and abnormality of the vertebral column were observed. Minor abnormalities of the cervical vertebra were seen in the newborn of rats treated with high doses of ethambutol hydrochloride during pregnancy. Rabbits receiving high doses of ethambutol hydrochloride during pregnancy gave birth to two foetuses with monophthalmia, one with a shortened right forearm accompanied by bilateral wrist-joint contracture and one with hare lip and cleft palate.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium starch glycolate

Maize starch

Povidone

Colloidal anhydrous silica

Microcrystalline cellulose

Magnesium stearate

Opadry Grey OY-GM-27600 (polydextrose, hypromellose, titanium Dioxide (E171), macrogol, iron oxide black (E172), iron oxide yellow (E172).

6.2 Incompatibilities

None.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Al/PVC/PVDC blisters. Pack size of 56 tablets.
PP tablet containers. Pack size of 56 tablets.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Kent Pharma UK Limited, 2nd Floor, Connect 38, 1 Dover Place, Ashford, Kent, England, TN23 1FB.

8 MARKETING AUTHORISATION NUMBER(S)

PL 51463/0012

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/01/2025

10 DATE OF REVISION OF THE TEXT

04/08/2025