Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ethambutol Hydrochloride 100mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
100 mg of ethambutol hydrochloride.
For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Yellow, circular biconvex film-coated tablets, plain on both sides.

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-tuberculosis drugs to which the patient's 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 or to any of the excipients. 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.

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

This medicine contains less than 1 mmol sodium (23 mg) per 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 adequate data from the use of ethambutol in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). 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 disorders
Rare: Thrombocytopaenia

Very rare:, leucopenia, neutropenia,.

Immune system disorders
Very rare: Hypersensitivity, anaphylactoid reactions, (see also Skin & subcutaneous tissue disorders).

Metabolic & nutrition disorders
Uncommon: Hyperuricaemia.
Very rare: Gout.

Nervous system disorders
Rare: Peripheral neuropathy, numbness, paraesthesia of the extremities,
Very rare: Dizziness, headache, disorientation.

Psychiatric disorders
Very rare: mental confusion, hallucination.

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

Respiratory, thoracic and mediastinal disorders
Very rare: Pneumonitis, pulmonary infiltrates, with or without eosinophilia.

Gastrointestinal disorders
Gastrointestinal disturbances 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.

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 national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Symptoms
The overdosage symptoms include nausea, abdominal pain, fever, mental confusion, visual hallucinations, and optic neuropathy (retrobulbar neuritis).

Treatment
There is no specific antidote, but gastric lavage should be employed if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterial
ATC Code for Ethambutol hydrochloride: J04AK02

Mechanism of action:
Ethambutol is bacteriostatic.

Mechanism of resistance
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.

Spectrum of antibacterial activity:
Ethambutol is effective against *Mycobacterium tuberculosi* and *M. bovi* 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.

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

Core Tablet:
Cellulose Microcrystalline, Maize Starch, Magnesium Stearate, Povidone, Silica Colloidal anhydrous, Sodium Starch glycolate.

Film Coating:
Opadry II(Yellow) 45F32810
Hypromellose 15cP, Iron oxide Yellow (E172), Polydextrose, Polyethylene glycol 4000 , Titanium Dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25^{o}C. Any unused product or waste material should be disposed of in accordance with local requirements.

6.5 Nature and contents of container

Al /PVC blister. Pack sizes of 10, 14, 20, 28, 30, 56, 60, 84, 90 and 112 tablets are available

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Aspire Pharma (Malta) Limited, Trident Park, Notabile Gardens, No. 2 , Level 3, Mdina Road, Central Business District, Birkirkara CBD2010, Malta

8 MARKETING AUTHORISATION NUMBER

PA23142/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st October 2010
Date of last renewal 30th June 2015

10 DATE OF REVISION OF THE TEXT

April 2024