

**Products: EH 400/150-B and EH 400/150**

**ETHAMBUTOL HYDROCHLORIDE in combination with ISONIAZID**

**Uses:**

An optional component of several anti-TB chemotherapeutic regimens currently recommended by WHO.

**Contraindications and Precautions:**

Preparation not suitable for use in children

See also individual monographs for Ethambutol Hydrochloride and Isoniazid below

**Dose:**

Use for continuation phase of 8-month regimen in place of thioacetazone with isoniazid *by mouth*, **ADULT** ethambutol hydrochloride 25 mg/kg and isoniazid 5 mg/kg daily

**ETHAMBUTOL**

**General information**

A synthetic congener of 1,2-ethanediamine that is active against *M. tuberculosis*, *M. bovis* and some non-specific mycobacteria. It is used in combination with other anti-TB drugs to prevent or delay the emergence of resistant strains.

It is readily absorbed from the gastrointestinal tract. Plasma concentrations peak in 2-four hours and decay with a half-life of three to four hours. Ethambutol is excreted in the urine both unchanged and as inactive hepatic metabolites.

About 20% is excreted in the faeces as unchanged drug.

**Clinical information**

**Uses**

An optional component of several anti-TB chemotherapeutic regimens currently recommended by WHO.

**Dosage and administration**

By mouth:

Adults: 15 mg/kg daily

30 mg/kg three times weekly, or

45 mg/kg (40-50 mg/kg) twice a week

Children: 15 mg/kg daily

Dosage must always be carefully calculated on a weight basis to avoid toxicity, and should be reduced in patients with impaired renal function.

## **Contraindications**

- Known hypersensitivity
- Pre-existing optic neuritis from any cause
- Inability to report symptomatic visual disturbances—children under 5 years)
- Severe renal impairment

## **Precautions**

- Visual disturbances—ocular examination recommended before and during treatment (see note below)
- Reduce dose in renal impairment and monitor plasma concentration
- Use in the elderly

Note: Patients should report visual disturbances immediately and discontinue treatment; children who are incapable of reporting symptomatic visual changes accurately should be given alternative therapy, as should, if possible, any patient who cannot understand warnings about visual adverse effects

Whenever possible, renal function should be assessed before treatment.

## **Use in pregnancy**

The six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used. If a fourth drug is needed during the initial phase, ethambutol should be preferred to streptomycin.

## **Adverse effects**

Dose-dependent optic neuritis can readily result in impairment of visual acuity and colour vision. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly.

Signs of peripheral neuritis occasionally develop in the legs.

## **Overdosage**

Emesis and gastric lavage may be of value if undertaken within a few hours of ingestion. Subsequently, dialysis may be of value. There is no specific antidote and treatment is supportive.

## **Storage**

Tablets should be stored in well-closed containers.

# **ISONIAZID**

## **General information**

Isoniazid, the hydrazide of isonicotinic acid is highly bactericidal against replicating tubercle bacilli.

It is rapidly absorbed and diffuses readily into all fluids and tissues. The plasma half-life, which is genetically determined, varies from less than one hour in fast acetylators to more than three hours in slow acetylators. It is largely excreted in the urine within 24 hours, mostly as inactive metabolites.

## Clinical information

### Uses

Tuberculosis treatment, in combination with other drugs

Tuberculosis prophylaxis and occasionally to prevent:

- transmission to close contacts at high risk of disease
- progression of infection to primary complex in recently infected, asymptomatic individuals
- recrudescence of infection in immunodeficient individuals.

### Dosage and administration

*By mouth*, ADULT and CHILD

- 5 mg/kg (4–6 mg/kg) daily (maximum, 300 mg daily)
- *or* 10 mg/kg 3 times weekly
- *or* 15 mg/kg twice weekly

Tuberculosis, treatment in critically ill patients unable to take oral therapy (combination therapy), *use intramuscular injection*, **ADULT** 200–300 mg as single daily dose; **CHILD** 10–20 mg/kg daily

Tuberculosis, prophylaxis, *by mouth*

- **ADULT** 300 mg daily for at least 6 months
- **CHILD** 5 mg/kg daily for at least 6 months

Note: Isoniazid should be taken on an empty stomach; if taken with food to reduce gastrointestinal irritation, oral absorption and bioavailability may be impaired

### Contraindications

- Known hypersensitivity
- Drug induced hepatic disease

### Precautions

- Hepatic impairment (monitor hepatic function)
- Malnutrition
- Chronic alcohol dependence
- Chronic renal failure
- Diabetes mellitus
- HIV infection—prophylactic pyridoxine 10 mg daily required because risk of peripheral neuritis
- Epilepsy (isoniazid may provoke attacks)
- Slow acetylator status (increased risk of adverse effects)
- History of psychosis
- Pregnancy
- Breast-feeding
- Porphyria

Note: Patients at risk of peripheral neuropathy as a result of malnutrition, chronic alcohol dependence or diabetes should additionally receive pyridoxine, 10 mg daily.

Note: For liver disorders, patients or their care-givers should be told how to recognise signs of liver disorder, and advised to discontinue treatment and seek immediate medical attention if symptoms such as nausea, vomiting, malaise or jaundice develop

### **Adverse effects**

Isoniazid is generally well tolerated at recommended doses. Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment.

The risk of peripheral neuropathy is excluded if vulnerable patients receive daily supplements of pyridoxine. Other less common forms of neurological disturbance, including optic neuritis, toxic psychosis and generalized convulsions, can develop in susceptible individuals, particularly in the later stages of treatment and occasionally necessitate the withdrawal of isoniazid.

Hepatitis is an uncommon but potentially serious reaction that can usually be averted by prompt withdrawal of treatment. More often, however, a sharp rise in serum concentrations of hepatic transaminases at the outset of treatment is not of clinical significance, and usually resolves spontaneously during continuation of treatment.

### **Drug interactions**

Isoniazid tends to raise plasma concentrations of phenytoin and carbamazepine by inhibiting their metabolism in the liver. The absorption of isoniazid is impaired by aluminium hydroxide.

### **Overdosage**

Nausea, vomiting, dizziness, blurred vision and slurring of speech occur within 30 minutes to three hours of overdosage. Massive poisoning results in coma preceded by respiratory depression and stupor. Severe intractable seizures may occur. Emesis and gastric lavage can be of value if instituted within a few hours of ingestion. Subsequently, haemodialysis may be of value.

Administration of high doses of pyridoxine is necessary to prevent peripheral neuritis.

### **Storage**

Tablets should be kept in well-closed containers, protected from light. Solution of injection should be stored in ampoules protected from light.