

Product: H 300-B and H 300

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.