Pharmaniaga Isoniazid Tablet 100mg

DESCRIPTION
Yellow, round, flat bevelled edge tablet with KK marking on one side and breakline on the other.

COMPOSITON
Each tablet contains 100 mg of isoniazid.

PHARMACODYNAMIC
Isoniazid has no significant antibacterial action against any micro-organisms except the mycobacteria; against mycobacterium tuberculosis it is bacteriostatic in extremely low concentrations.

Isoniazid is used mainly in the treatment of pulmonary tuberculosis but it appears to be effective also in the treatment of extrapulmonary lesions, including meningitis and genito-urinary disease.

PHARMACOKINETICS
Absorption: Readily and completely absorbed after oral administration.

Distribution: Readily diffuses into all tissues and fluids including the cerebrospinal fluid. Isoniazid is retained in the skin and in infected tissue; it crosses the placenta and is secreted in the milk of lactating mothers.

Protein binding: Isoniazid does not appear to be bound in the blood.

Half-life: Plasma elimination half-life, in rapid acetylators about 1.2 hours and in slow acetylators about 3.5 hours.

Metabolic reactions: Acetylation, hydrolysis and glycine conjugation, hydrazone formation, and n-methylation; acetylation is polymorphic and two groups of acetylators have been identified, rapid and slow acetylators. The rate of hydrolysis is more rapid in the rapid acetylators than in the slow ones. The metabolites formed include acetyl isoniazid, isonicotinic acid, isonicotinuric acid, isonicotinoyl-hydrazones of pyruvic and glutaric acids, and n-methylisoniazid.

Excretion: Over 90% of a dose is excreted in the urine in 24 hours, most being excreted in the first 12 hours, 4-32% is unchanged, but no more than 10% of a dose is excreted in the faeces.

INDICATIONS
Isoniazid is used primarily in conjunction with other anti-tuberculosis drugs in the treatment of all forms of tuberculosis. Isoniazid is also used in the treatment of tuberculosis meningitis and non-tuberculosis mycobacterium infections.

CONTRAINDICATIONS
Patients who are known to be hypersensitive to isoniazid or drug-induced liver disease.

ADVERSE REACTIONS
Blood and lymphatic system disorders
Frequency not known: Agranulocytosis, Aplastic anaemia, Haemolytic anaemia

Ear and labyrinth disorders
Frequency not known: Deafness, Tinnitus, Vertigo. These have been reported in patients with end stage renal impairment. Vertigo may be troublesome with doses of 10mg per kg body weight

Gastrointestinal disorders
Frequency not known: Constipation, Dry mouth Nausea, Pancreatitis acute, Vomiting and other gastrointestinal effects

General disorders and administration site conditions
Frequency not known: Pyrexia

Hepatobiliary disorders
Frequency uncommon: Hepatitis
Frequency not known: Acute hepatic failure, Liver injury, Jaundice

The risk of these undesirable effects increases with age, especially over the age of 35; it may be serious and sometimes fatal with the development of necrosis.

Investigations
Frequency not known: Hepatic enzyme increased

Metabolism and nutrition disorders
Frequency not known: Acidosis, Hypoglycaemia, Nicotinic acid deficiency. Nicotinic acid deficiency may be related to an isoniazid-induced pyridoxine deficiency which affects the conversion of tryptophan to nicotinic acid.

Musculoskeletal and connective tissue disorders
Frequency not known: Systemic lupus erythematosus, lupus-like syndrome

Nervous system disorders
Frequency not known: Neuropathy peripheral, Optic neuritis, Seizure. Hyperreflexia may be troublesome with doses of 10mg per kg body weight

Psychiatric disorders
Frequency not known: Elevated mood, Psychotic disorder.

Although isoniazid usually has a mood elevating effect, mental disturbances, ranging from minor personality changes to major mental derangement have been reported; these are usually reversed on withdrawal of the drug

Renal and urinary disorders
Frequency not known: Dysuria

Reproductive system and breast disorders
Frequency not known: Gynaecomastia

Respiratory, thoracic and mediastinal disorders
Frequency not known: Interstitial lung disease

Skin and subcutaneous tissue disorders
Frequency rare: Toxic epidermal necrolysis, eosinophilia systemic symptoms, Frequency not known: Erythema multiforme, Stevens-Johnson syndrome,

Vascular disorders
Frequency not known: Vasculitis

Miscellaneous
Withdrawal symptoms, which may occur on the cessation of the treatment, include headache, insomnia, excessive dreaming, irritability and nervousness

WARNINGS AND PRECAUTIONS
All patients should have baseline liver function tests performed and repeated at regular intervals during treatment. If serum AST rises to more than three times normal, or there is any increase in bilirubin, treatment should be withdrawn. Special precautions are required in patients with impaired liver function. Any deterioration in liver function in these patients is an indication for stopping treatment.

Isoniazid should not be given to patients who have experience severe adverse reactions including drug-induced liver disease. Care should be taken in giving isoniazid to patients suffering from convulsive disorders, diabetes mellitus, chronic alcoholism, or impaired liver or kidney function or to patients taking other potentially hepatoxic agents. If symptoms of hepatitis such as malaise, fatigue, anorexia, and nausea develop isoniazid should be discontinued immediately.

Isoniazid should be used with caution in patients with a history of psychosis.

Advanced age, female gender, slow acetylators, malnutrition, HIV infection, pre-existing liver disease, and extra-pulmonary tuberculosis were identified as risk factors for isoniazid-induced hepatotoxicity.

Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic, pregnant, or infected with HIV, should be given pyridoxine.

PREGNANCY AND LACTATION
Pregnancy: Isoniazid crosses the placenta. Therefore, isoniazid should only be used in pregnant women or in women of child-bearing potential if the potential benefit justifies the potential risk to the foetus. It is considered that untreated tuberculosis represents a far greater hazard to a pregnant woman and her foetus than does treatment of the disease. Pyridoxine supplementation is recommended.

Lactation: Isoniazid passes into breast milk. When administered to nursing mother, breast-fed infants should be monitored for possible signs of isoniazid toxicity. Administration of pyridoxine to the breast-feeding mother and infant may be considered.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
No specific statement, but unlikely to effect the ability to drive or use machinery.

INTERACTION WITH OTHER MEDICAMENTS
When isoniazid is given to patients who inactivate it slowly or to patients receiving paraminosalicyclic acid concurrently, tissue concentrations may be enhanced, and adverse effects are more likely to appear. There may be an increased risk of liver damage in patients receiving rifampicin and isoniazid but liver enzymes are raised only transiently.

Isoniazid can inhibit the hepatic metabolism of a number of drugs, in some cases leading to increased toxicity. These include the antiepileptics carbamazepine, primidone, and phenytoin, the benzodiazepines diazepam and triazolam, chlorzoxazone, and disulfiram.

Isoniazid is an inhibitor of monoamine oxidase (MAO) and diamine oxidase (DAO), therefore can reduce tyramine and histamine metabolism, causing symptoms such as headache, sweating, palpitations, flushing, and hypotension. Patients should be advised against ingesting foods rich in tyramine and/or histamine during treatment with isoniazid, such as cured meat, some cheeses (e.g. matured cheeses), wine, beer and some fish (e.g. tuna, mackerel, salmon).

Isoniazid has been reported to cause substantial elevations of serum concentrations of carbamazepine and symptoms of carbamazepine toxicity at isoniazid doses of 200mg daily or more. The concurrent used is not recommended unless the effects can be closely monitored and suitable downward dosage adjustments made (a reduction between one-half or one-third was reported effective).

Concomitant benzodiazepine (diazepam) and isoniazid therapy has been reported to result in an increased risk of benzodiazepine toxicity (sedation, respiratory depression).

Isoniazid may reduce the therapeutic effects of levodopa.

Concomitant administration of isoniazid with itraconazole may result in significant decreases in itraconazole serum concentrations and therapeutic failure. Co-administration is not recommended.

Isoniazid may decrease ketoconazole serum levels. Concurrent use should be well monitored and dosage increases made if necessary.

Because the clearance of isoniazid was found doubled when zalcitabine was given in patients, concurrent use of isoniazid and zalcitabine should be monitored to ensure isoniazid effectiveness.

There may be an increased risk of distal sensory neuropathy When isoniazid is used in patients taking stavudine (d4T).

There may be a potential interaction between isoniazid and foods containing histamine or tyramine.

DOSAGE AND ADMINISTRATION
Usual adult and adolescent dose:
Tuberculosis Prophylaxis: Oral, 300mg once a day.
Treatment: In combination with other anti-tubercular – Oral 300mg of isoniazid once a day for the entire treatment period; or 15mg/kg body weight (up to 900mg) twice a week for the remainder of the therapy after the initial two months of 300mg once a day.

Usual pediatric dose:
Tuberculosis Prophylaxis: Oral,
10mg/kg body weight, up to 300mg once a day.
Treatment: In combination with other antituberculars - Oral, 10 to 20mg/kg body weight, Of isoniazid, up to 300mg once a day.

OVERDOSAGE
The most commonly reported adverse events associated with isoniazid overdose are nausea, vomiting and central nervous system toxicity such as vertigo, seizures and coma.

Treatment of overdosage of gastric lavage following intubation and the control of convulsions by anti-convulsants given intravenously as well as the intravenous injection of large doses of pyridoxine. Any acidosis is corrected with sodium bicarbonate. Forced diuresis may be tried and haemodialysis or peritoneal dialysis has been used.

ROUTE OF ADMINISTRATION
Oral

STORAGE CONDITIONS
Store below 30°.
Protect from light.

SHELF LIFE
Product should not be used beyond the expiry date imprinted on the product packaging.

PRESENTATION
In blisters of 100 tablets.

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PRODUCT REGISTRATION HOLDER / MANUFACTURER:
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