BE-TABS ISONIAZID 100 (TABLETS)

SCHEDULING STATUS:
S3

PROPRIETARY NAME
(and dosage form):

BE-TABS ISONIAZID 100 (TABLETS)

COMPOSITION
Each tablet contains:
Isoniazid 100 mg
Sugar Free

PHARMACOLOGICAL CLASSIFICATION
A.20.2.3 Tuberculostatics.

PHARMACOLOGICAL ACTION
Be-tabs Isoniazid 100 is bacteriostatic and in high concentrations, bactericidal against Mycobacterium tuberculosis. Its exact mechanism of action is not known, but it may relate to inhibition of mycolic acid synthesis and disruption of the cell wall in susceptible organisms. Isoniazid is readily absorbed when administered orally. Aluminium-containing antacids may interfere with absorption. Peak plasma concentrations of 3 to 5 micrograms/mL develop 1 to 2 hours after oral ingestion of usual doses. Isoniazid diffuses readily into all body fluids and cells. The drug is detectable in significant quantities in pleural and ascitic fluids, concentrations in the cerebrospinal fluid (CSF) are similar to those in the plasma. Isoniazid penetrates well into caseous material. The concentration of the agent is initially higher in the plasma and muscle than in the infected tissue, but the latter retains the drug for a long time in quantities well above those required for bacteriostasis. From 75% to 95% of a dose of isoniazid is excreted in the urine within 24 hours, mostly as metabolites. The main excretory products in human beings are the result of enzymatic acetylation (acetylisoniazid) and enzymatic hydrolysis (isonicotinic acid). Small quantities of an isonicotinic acid conjugate (probably isonicotinyl glycine), one or more isonicotinyl hydrazones, and traces of N-methylisoniazid also are detectable in the urine. Human populations show genetic heterogeneity with regard to the rate of acetylation of isoniazid. The distribution of slow and rapid inactivators of the drug is bimodal owing to differences in the activity of acetyltransferase. The rate of acetylation significantly alters the concentrations of the drug that are achieved in plasma and its half-life in the circulation. The half-life of the drug may be prolonged in the presence of hepatic insufficiency.

INDICATIONS
Isoniazid is indicated in the treatment of pulmonary tuberculosis, (possibly with other agents) in extrapulmonary lesions, including meningitis. Isoniazid is used for all forms of tuberculosis in which organisms are susceptible. Isoniazid is also used in high risk subjects for the prophylaxis of tuberculosis. It has been used successfully in the treatment of lupus vulgaris.

CONTRA-INDICATIONS
Isoniazid is contra-indicated in persons hypersensitive to it, and should not be given to patients with drug-induced liver disease, convulsive disorders, chronic alcoholism or impaired liver or kidney function.
INTERACTIONS:
Cross resistance between isoniazid, PAS or streptomycin does not occur. There may be increased toxicity when isoniazid is used with disulfiram. The risk of hepatotoxicity may be increased in patients receiving isoniazid in combination with rifampicin or other potentially hepatotoxic drugs. Isoniazid can inhibit the hepatic metabolism of a number of drugs, in some cases leading to increased toxicity. These include the antiepileptics carbamazepine, ethosuximide, and phenytoin, the benzodiazepines diazepam and triazolam, chlorzoxazone, and theophylline. The metabolism of enflurane may be increased in patients receiving isoniazid, resulting in potentially nephrotoxic levels of fluoride. Isoniazid has been associated with increased toxicity of cycloserine and warfarin.

DOSAGE AND DIRECTIONS FOR USE
National Treatment Policy and Protocols of Tuberculosis must be adhered to. Isoniazid should be taken on an empty stomach.
The usual dose in the treatment of tuberculosis is 4 mg - 5 mg per kg body mass daily, in single or divided doses to a maximum of 300 mg daily. Doses of up to 10 mg per kg body mass daily may be given during the first or second week of treatment of tuberculosis meningitis. In tuberculosis prophylaxis, daily doses of about 300 mg have been given for a year or longer.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS
Isoniazid is generally well tolerated at currently recommended doses. However, patients who are slow acetylators of isoniazid appear to have a higher incidence of some adverse effects. Also patients whose nutrition is poor are at risk of peripheral neuritis which is one of the commonest adverse effects of isoniazid. Other neurological adverse effects include psychotic reactions and convulsions. The neurotoxic effects of isoniazid affect both the peripheral and central nervous systems. Optic neuritis (followed by atrophy) may occur. Other manifestations of neurotoxicity include muscle twitching, dizziness, ataxia, paraesthesia, stupor and toxic encephalopathy. The prophylactic administration of 10 mg to 50 mg pyridoxine hydrochloride daily, to counteract peripheral neuritis, is recommended. A dose of 100 to 200 mg daily has been suggested for treatment if peripheral neuritis develops. Hypersensitivity is uncommon, but includes fever, skin eruptions (including erythema multiforme), vasculitis, hepatitis and blood dyscrasias. Severe liver damage may occur. Transient increases in liver enzymes occur in 10 to 20% of patients during the first few months and usually return to normal despite continued treatment. Elevated liver enzymes associated with clinical signs of hepatitis such as nausea and vomiting, or fatigue may indicate hepatic damage; in these circumstances, isoniazid should be stopped pending evaluation and if damage is confirmed should only be reintroduced cautiously once hepatic function has recovered. The incidence of liver damage is highest in patients over 35 years of age. The influence of acetylator status is uncertain. Fatalities have occurred following liver necrosis. Haematological effects reported following use of isoniazid include various anaemias, agranulocytosis, thrombocytopenia, and eosinophilia. Patients may experience gastro-intestinal discomfort, including nausea and vomiting. Other adverse effects include dry mouth, epigastric distress, urinary retention, methaemoglobinemia, tinnitus, pellagra, hyperglycaemia, lupus-like syndrome and gynaecomastia. Mycobacteria rapidly becomes resistant to isoniazid alone, and it should be given in conjunction with other tuberculostatics, except in prophylaxis.

Special precautions:
Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic, or pregnant, should receive pyridoxine usually in a dose of 10 mg daily. If symptoms of hepatitis such as malaise, fatigue, anorexia, and nausea develop isoniazid should be discontinued pending evaluation. Liver function should be checked before treatment with isoniazid and special care should be taken in alcoholic patients or those with pre-existing liver disease. Regular monitoring of liver function is recommended in patients with pre-existing liver disease, and isoniazid treatment should be suspended if serum aminotransferase concentrations are elevated to 5 times the normal upper limit or the bilirubin concentration rises. Careful monitoring should be considered for black and Hispanic women, in whom there may be an increased risk of fatal hepatitis. Periodic eye examinations during isoniazid treatment have also been suggested.

KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF IT'S TREATMENT
These include slurred speech, metabolic acidosis, hyperglycaemia, hallucinations, respiratory and CNS depression, convulsions and coma. Treatment involves emesis and lavage, usually following intubation, correction of acidosis with sodium bicarbonate and the intravenous administration of anti-convulsants and pyridoxine. Diazepam may be given intravenously to assist seizure control. Forced diuresis,
haemodialysis or peritoneal dialysis may be used.

**IDENTIFICATION**
White, scored tablet, 8.7 mm in diameter.

**PRESENTATION**
In bottles containing 100, 500 and 1000 tablets.
Buckets containing 5000 tablets.
Patient ready packs of different sizes.

**STORAGE INSTRUCTIONS**
Store in a cool dry place, below 25°C. Protect from light.
KEEP OUT OF REACH OF CHILDREN.

**REGISTRATION NUMBER**
E/20.2.3/108 (SA)
B 9315000 (Botswana)

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION**
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