sanofi-aventis south africa (pty) ltd

1.3.1.1 SOUTH AFRICAN PACKAGE INSERT

WINTHROP ISONIAZID 100 mg; 200 mg or 300 mg /

Tablets 100 mg; 200 mg or 300 mg isoniazid per tablet

PI and PIL: Regulation 9 & 10 Format compliance – immediate implementation

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Date submitted and implemented: 27.11.2015

PROPOSED PACKAGE INSERT (Clean):

SCHEDULING STATUS: S4

WINTHROP ISONIAZID 100 MG TABLETS

WINTHROP ISONIAZID 200 MG TABLETS

WINTHROP ISONIAZID 300 MG TABLETS

COMPOSITION:

Per tablet:

Isoniazid 100 mg, 200 mg, 300 mg

PHARMACOLOGICAL CLASSIFICATION:

A 20.2.3 Tuberculostatics

PHARMACOLOGICAL ACTION:

Isoniazid is rapidly active against actively dividing Mycobacterium tuberculosis, and bacteriostatic against semi-dormant organisms.

INDICATIONS:

Isoniazid is indicated alone for the prophylaxis of tuberculosis and in conjunction with other antituberculosis medicine for the treatment of tuberculosis.

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CONTRAINDICATIONS:

Hypersensitivity to isoniazid or other chemically related medication such as ethionamide, pyrazinamide and niacin.

Safety in pregnancy and lactation has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

The risk-benefit ratio should be considered when the following medical problems exist:

- alcoholism
- hepatic or renal function impairment
- convulsive disorders
- history of psychosis

Special precautions:

Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic or pregnant (see CONTRAINDICATIONS), should receive pyridoxine, usually at a dose of 10 mg daily, with doses of 100 – 200 mg daily for treatment if peripheral neuritis develops.

Use with caution in porphyria.

Hepatotoxicity: Transient elevation of liver enzymes occurs in 10% of patients. Overt hepatitis occurs in less than 1% but may be fatal. There is an increased risk of hepatitis in patients over 50 years, slow acetylators and those who consume alcohol on a daily basis.

Liver function tests should be performed every 3 months during treatment and isoniazid discontinued if liver enzymes are raised more than five times the normal upper limit. Patients who develop malaise, anorexia and nausea together with raised liver enzyme levels should discontinue isoniazid promptly pending investigation.

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INTERACTIONS:

Chronic use of isoniazid may decrease the plasma clearance and/or prolong the duration of action of alfentanil, coumarin anticoagulants, benzodiazepines, carbamazepine, phenytoin and theophylline. Concurrent use of paracetamol, alcohol, rifampicin and other hepatotoxic medication, may increase the potential for isoniazid-induced hepatotoxicity. Aluminium containing antacids may delay and decrease absorption and serum concentrations of isoniazid.
Ingestion of certain types of cheese e.g. Swiss or Cheshire, or fish e.g. tuna, may result in itching of the skin, rapid or pounding heart, chills or headache. Glucocorticoid corticosteroids may increase hepatic metabolism and/or excretion of isoniazid.

Concurrent use of cycloserine, disulfiram and other neurotoxic medicines may increase the potential for CNS toxicity. Isoniazid may increase the formation of potentially nephrotoxic inorganic fluoride metabolites when used concurrently with enflurane.
Interactions with ketoconazole and miconazole have been reported.
False positive reactions with copper sulphate urine glucose tests may occur.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established. See “WARNINGS AND SPECIAL PRECAUTIONS”

DOSAGE AND DIRECTIONS FOR USE:

Adults:

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Usual dose : 100 mg three times daily with meals

Recommended dose :3 to 5 mg per kg body mass every 24 hours in two or more doses

Children : 10 to 20 mg per kg body mass daily

If aluminium containing antacids are taken, they must be taken at least one hour after isoniazid.

SIDE EFFECTS:

Gastrointestinal effects (nausea, vomiting, pellagra) and hypersensitivity reactions (skin eruptions, fever, lymphadenopathy, vasculitis associated with positive antinuclear antibodies) may occur. Skin rashes including a pellagra-like dermatitis in malnourished patients may occur, that responds to niacin. Haematological effects have been reported (sideroblastic, haemolytic and infrequently aplastic anaemias, agranulocytosis, thrombocytopenia and eosinophilia). Neurological effects include psychotic reactions and convulsions. Other adverse effects: hyperglycaemia, metabolic acidosis, lupus-like syndrome, rheumatoid syndrome, urinary retention and gynaecomastia. Optic neuritis has been reported.
Peripheral neuropathy has also been associated with isoniazid administration. Pyridoxine supplementation prevents the development of peripheral neuritis, as well as most other nervous system dysfunctions.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of isoniazid overdose includes slurred speech, metabolic acidosis, hyperglycaemia, hallucinations, respiratory and CNS depression, convulsions and coma.
Treatment consists of gastric lavage, symptomatic and supportive therapy.

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IDENTIFICATION:

100 mg: White, biconvex, scored tablet

200 mg: Light pink, biconvex tablet

300 mg: Light yellow, flat, scored tablet with bevelled edges

PRESENTATION:

100 mg tablets: 28', 84', 100', 500', 1000' and 5000'

200 mg and 300 mg tablets: 28', 84', 100', 1000' and 5000'

STORAGE INSTRUCTIONS:

Store below 25 °C in well closed containers, protected from light.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER :

300 mg: C/20.2.3/194

REFERENCE NUMBER:

100 mg: A17 (Act 101/1965)

200 mg: A809 (Act 101/1965)

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

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