

FINAL PACKAGE INSERT 25 NOVEMBER 2016

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

ETHIONAMIDE MACLEODS 250 mg TABLETS (film-coated tablets)

COMPOSITION

Each film-coated tablet contains:

Ethionamide 250 mg

Sugar free

It also contains the following inactive ingredients: Maize starch, gelatin (Type B), sodium starch glycolate (Type A), colloidal anhydrous silica, acacia, purified talc, magnesium stearate, povidone (PVP K-30), hypromellose (5 cps), titanium dioxide (CI no. 77891), colour quinoline yellow supra (CI no. 47005), diethyl phthalate.

PHARMACOLOGICAL CLASSIFICATION

A 20.2.3 Tuberculostatic.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Ethionamide is tuberculostatic. It may be bacteriostatic or bactericidal depending on the concentration at the site of infection and the susceptibility of the organism. The mechanism of action is not known, but it appears to inhibit protein synthesis. Resistance develops rapidly when it is used in the absence of another effective medicine.

Pharmacokinetic properties

Ethionamide is well absorbed from the gastrointestinal tract and absorption is unaffected by food. It is widely distributed to most tissues and fluids, reaching concentrations in CSF equal to those in plasma. It has an elimination half-life of 3 hours. Ethionamide is extensively

metabolised in the liver to active and inactive metabolites which, together with 1 % unchanged medicine, are eliminated via the kidney.

INDICATIONS

ETHIONAMIDE MACLEODS 250 mg TABLETS is indicated as second line treatment of tuberculosis caused by sensitive strains of *Mycobacterium tuberculosis*, in combination with other effective antimycobacterial medicines, where bacterial resistance or a contraindication to a primary medicine exists.

CONTRA-INDICATIONS

Hypersensitivity to ethionamide or any of the ingredients of **ETHIONAMIDE MACLEODS 250 mg TABLETS**.

Patients sensitive to isoniazid, pyrazinamide or niacin may also be sensitive to **ETHIONAMIDE MACLEODS 250 mg TABLETS**.

Severe hepatic impairment/disease.

Pregnancy.

Safety in lactation has not been established.

WARNINGS AND SPECIAL PRECAUTIONS

Use with care in patients with depression or other psychiatric illness, liver impairment, chronic alcoholism, epilepsy, hypothyroidism and diabetes.

Avoid in porphyria.

ETHIONAMIDE MACLEODS 250 mg TABLETS should not be administered to patients with impaired hepatic function. Liver function tests should be carried out before and monthly during treatment with **ETHIONAMIDE MACLEODS 250 mg TABLETS**. **ETHIONAMIDE MACLEODS 250 mg TABLETS** should be discontinued if there is a five-fold increase in hepatic enzyme levels even in the absence of symptoms.

Concurrent administration of pyridoxine or nicotinamide has been suggested to prevent or relieve neurotoxic effects.

Caution is advised in administering **ETHIONAMIDE MACLEODS 250 mg TABLETS** in patients with depression or other psychiatric illness. Difficulty may be experienced in the management of diabetes mellitus. Periodic monitoring of blood glucose, thyroid function and visual function is recommended.

Many patients, due to gastrointestinal side-effects, cannot tolerate therapeutic doses of **ETHIONAMIDE MACLEODS 250 mg TABLETS** and have to stop treatment. Tolerance may be improved by reducing the dose, changing the time of administration, or by the concurrent administration of an antiemetic medicine.

Effects on ability to drive and use machines

ETHIONAMIDE MACLEODS 250 mg TABLETS may cause dizziness and/or drowsiness. Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving or operating machinery.

INTERACTIONS

Cross resistance may occur with thioacetazone. Additive neurological effects may occur with isoniazid. There is an increased risk of CNS toxicity when used concurrently with cicloserin and terizidone. Convulsions have been reported when **ETHIONAMIDE MACLEODS 250 mg TABLETS** is administered with cicloserin and special care should be taken when the treatment regimen includes both of these medicines. Excessive alcohol ingestion should be avoided as a psychotic reaction can occur.

The incidence of hepatotoxicity is increased when **ETHIONAMIDE MACLEODS 250 mg TABLETS** is given with rifampicin.

PREGNANCY AND LACTATION

Safety and efficacy has not been established during pregnancy and lactation.

DOSAGE AND DIRECTIONS FOR USE

In order to minimise gastrointestinal side-effects, **ETHIONAMIDE MACLEODS 250 mg**

TABLETS may be taken at bedtime or in divided doses with meals.

The concomitant use of pyridoxine is recommended to prevent neurotoxic side-effects.

Tablets should not be divided.

Adults:

15 – 20 mg/kg/day. Maximum of 1 g per day.

Children:

Over 10 years: As for adults.

Under 10 years: 10 mg/kg/day increasing gradually to 15 – 20 mg/kg/day. Maximum dose of 750 mg/day.

SIDE-EFFECTS

Blood and lymphatic system disorders:

Less frequent: Thrombocytopenia and purpura.

Immune system disorders:

Less frequent: Hypersensitivity reactions.

Endocrine disorders:

Less frequent: Endocrine disturbances.

Metabolism and nutrition disorders:

Less frequent: Difficulty in the management of diabetes mellitus, hypoglycaemia, hypothyroidism or goiter.

Psychiatric disorders:

Less frequent: Depression, anxiety, psychosis, restlessness.

Nervous system disorders:

Less frequent: Dizziness, drowsiness, headache, seizures, peripheral neuropathy responsive to pyridoxine and a pellagra-like encephalopathy responsive to niacin.

Eye disorders:

Less frequent: Optic neuritis, diplopia, blurred vision.

Vascular disorders:

Less frequent: Postural hypotension.

Gastrointestinal disorders:

Frequent: Diarrhoea, vomiting, nausea, abdominal pain, excessive salivation, metallic taste, stomatitis, anorexia and weight loss.

Hepato-biliary disorders:

Frequent: Hepatitis with or without jaundice, transient increase in serum bilirubin, AST and ALT.

Skin and subcutaneous tissue disorders:

Less frequent: Alopecia, photosensitivity, dermatitis (including photodermatitis), acne.

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Arthralgia.

Reproductive system and breast disorders:

Less frequent: Gynaecomastia, amenorrhoea, impotence.

General disorders and administrative site conditions:

Less frequent: Asthenia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

An acute overdose may lead to an accentuation of the symptoms listed under "Side effects".

Treatment should be symptomatic and supportive.

IDENTIFICATION

Yellow circular biconvex film-coated tablets with plain surface on both sides.

PRESENTATION

A soft tempered silver aluminium strip containing 14 tablets. Strips are packed in a pre-printed outer carton. Pack sizes: 14's, 28's, 56's and 84's.

Silver aluminium sachet (PET/Al/LLDPE), kept in a white plastic container (HDPE), which is sealed at the mouth with an aluminium tagger and is closed with a white HDPE screw-on lid.

Pack size: 250 tablets.

STORAGE INSTRUCTIONS

Store at or below 30 °C.

Protect from moisture and light. Keep strip in carton until required or keep aluminium sachet in HDPE container until required for use. The HDPE container must be kept well closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

49/20.2.3/0894

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

MACLEODS PHARMACEUTICALS SA (PTY) LTD

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25 November 2016