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CLEAN PROPOSED PROFESSIONAL INFORMATION FEBRUARY 2025

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

ETHIONAMIDE MACLEODS 250 mg TABLETS (film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains Ethionamide 250 mg.

Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Therapeutic 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.

4.2 Posology and method of administration

Posology

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.

Method of administration

Oral use

4.3 Contraindications

- Hypersensitivity to ethionamide or any of the ingredients listed in Section 6.1
- 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.

4.4 Special warnings and precautions for use

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.

4.5 Interactions with other medicines and other forms of interaction

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

ETHIONAMIDE MACLEODS 250 mg TABLETS is contraindicated during pregnancy.

Breastfeeding

ETHIONAMIDE MACLEODS 250 mg TABLETS is contraindicated during breastfeeding.

Fertility

No information is available.

4.7 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.

4.8 Undesirable effects

Tabulated list of adverse reactions

MedDRA System organ class	**Frequency**	**Adverse reactions**
Blood and lymphatic system	Less frequent	Thrombocytopaenia 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 goitre.
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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to Macleods Pharmaceuticals SA (Pty) Ltd. at safety@macleodspharma.com.

4.9 Overdose

An acute overdosage may lead to an accentuation of the symptoms listed under ‘’Side effects’’. Treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.2.3 Tuberculostatic.

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.

5.2 Pharmacokinetic properties

Absorption

Ethionamide is well absorbed from the gastrointestinal tract and absorption is unaffected by food.

Distribution

It is widely distributed to most tissues and fluids, reaching concentrations in CSF equal to those in plasma.

Biotransformation

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

Elimination

It has an elimination half-life of 3 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25°C.

Protect from moisture and light. Keep strip in carton until required or keep aluminium sachet in HDPE container until required for use.

6.5 Nature and contents of container

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.

7. HOLDER OF CERTIFICATE OF REGISTRATION

MACLEODS PHARMACEUTICALS SA (PTY) LTD

GROUND FLOOR, BLOCK 1,

BASSONIA ESTATE OFFICE PARK (EAST),

1 CUSSONIA DRIVE,

BASSONIA ROCK EXT 12

ALBERTON

GAUTENG

Contact details: safety@macleodspharma.com

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8. REGISTRATION NUMBER:

49/20.2.3/0894

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 25 November 2016

10. DATE OF REVISION OF THE TEXT

08 August 2025