CLEAN PROPOSED PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

TERIZIDONE MACLEODS 250 mg CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains terizidone 250 mg.

Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Blue colour cap and blue colour body size “0” hard gelatine capsule containing white to off white granules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Multidrug-resistant tuberculosis (MDR-TB).

Treatment of MDR-TB in combination with other appropriate antimycobacterial medicines where sensitivity to **TERIZIDONE MACLEODS 250 mg CAPSULES** has been established.

4.2 Posology and method of administration

Posology

Adults

One capsule every six to eight hours.

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Method of administration

Oral use

4.3 Contraindications

- Hypersensitivity to terizidone, cicloserin or any of the excipients listed in section 6.1.
- Severe renal insufficiency.
- Epilepsy.
- Depression.
- Psychosis.
- Severe anxiety.
- Chronic alcoholism.
- Porphyria.

4.4 Special warnings and precautions for use

Warning:

Neurological reactions are dose related and may be reduced by keeping the plasma concentrations below 30 µg/ml.

TERIZIDONE MACLEODS 250 mg CAPSULES should not be used as monotherapy in TB.

TERIZIDONE MACLEODS 250 mg CAPSULES should be stopped if skin reactions or symptoms of neuro-toxicity develop (see Nervous system side effects). Large doses or the intake of alcohol increases the risk of seizures.

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

Haematological, renal and hepatic functions should be monitored. Patients with mild to moderate renal impairment need lower doses.

4.5 Interactions with other medicines and other forms of interaction

Patients receiving **TERIZIDONE MACLEODS 250 mg CAPSULES** and taking alcohol are at an increased risk of convulsions.

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Neurotoxic effects may be potentiated by use of **TERIZIDONE MACLEODS 250 mg CAPSULES** with ethionamide, and concurrent use of **TERIZIDONE MACLEODS 250 mg CAPSULES** and isoniazid may result in increased CNS toxicity such as dizziness and drowsiness.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in preganancy has not been established.

TERIZIDONE MACLEODS 250 mg CAPSULES passes to the foetus, amniotic fluid, therefore should be avoided in pregnant women.

Breastfeeding

Safety in lactation has not been established.

TERIZIDONE MACLEODS 250 mg CAPSULES should be avoided in breastfeeding women.

4.7 Effects on ability to drive and use machines

TERIZIDONE MACLEODS 250 mg CAPSULES may cause anxiety, disorientation, confusion, dizziness and 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 disorders	Less frequent	Megaloblastic anaemia, sideroblastic anaemia
Immune system disorders	Less frequent	Hypersensitivity reactions
Metabolism and nutrition disorders	Less frequent	Folate and Vitamin B12 deficiency

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Psychiatric disorders	Frequent	Depression, anxiety, confusion, disorientation, psychosis with suicidal tendencies, aggression, irritability, paranoia, mania.
Nervous system disorders	Less frequent	Dizziness, vertigo, headache, drowsiness, speech difficulties, tremor, paresis, hyperreflexia, dysarthria, paraesthesia, coma, convulsions.
Gastrointestinal disorders	Less frequent	Gastrointestinal irritation
Hepatobiliary disorders	Less frequent	Increase in serum aminotransferases (especially in patients with liver disease).
Skin and subcutaneous disorders	Less frequent	Skin reactions, photosensitivity.

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 "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms of overdose

Overdosage may lead to an accentuation of the side-effects listed above such as anxiety, confusion, somnolence, disorientation, depression, psychosis with suicidal tendencies, aggression, irritability and paranoia, vertigo, headache, drowsiness, speech difficulties, tremor, paresis, hyperreflexia, dysarthria, paraesthesia, coma, convulsions and heart failure, in which case a doctor should be consulted immediately.

Treatment of overdose

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Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.2.3 Tuberculostatics

Terizidone is a derivative of cicloserin. Cicloserin, a structural analogue of d-alanine, acts by inhibiting cell wall synthesis by inhibiting the enzyme, alanine racemase which converts L-alanine to d-alanine and d-alanine: d-alanine ligase, thereby stopping reactions in which d-alanine is incorporated into bacterial cell wall synthesis. Terizidone is a broad spectrum antibiotic with activity against mycobacteria such as *Mycobacterium tuberculosis*, including strains that are resistant to other tuberculostatics.

5.2 Pharmacokinetic properties

Terizidone is well absorbed, ensuring high blood and urinary concentrations following ingestion of the medicine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

microcrystalline cellulose,

disodium edetate,

hypromellose,

stearic acid,

hard gelatine capsule containing gelatine,

sodium methyl paraben,

sodium propyl paraben,

sodium lauryl sulphate,

titanium dioxide (CI No. 77891),

brilliant blue (CI No. 42090) and

carmoisine (CI No. 14720).

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6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C in a dry place.

Keep the blister in the carton until required for use.

Keep the container closed.

6.5 Nature and contents of container

Alu-Alu strip pack:

Silver-coloured, printed aluminium foil laminated with 150 gauge polyethylene (soft tempered) and silver-coloured, plain aluminium foil laminated with 150 gauge polyethylene (soft tempered) packed in a pre-printed unit carton. Pack size: 100's (10 x 10).

HDPE container pack:

150 ml round, white, heavy weight HDPE with 38 mm neck finish closed with 38 mm white continuous thread polypropylene closure with pulp and heat seal 123 white printed liner packed in a pre-printed carton. Pack size: 100 tablets.

7. HOLDER OF THE 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

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GAUTENG

8. REGISTRATION NUMBER:

50/20.2.3/0105

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29 September 2017

10. DATE OF REVISION OF THE TEXT

06/03/2023

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