Summary of Product characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Cycloserine Capsules USP 250 mg

2. QUALITATIVE ANDQUANTITATIVECOMPOSITION

Each capsule contains Cycloserine

USP 250 mg List of excipients:

Talc

for a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White to creamish pink powder filled in hard shell gelatin capsules with light orange opaque cap and white opaque body, axially imprinted with “MYLAN” over “CS250” in black ink on both cap and body.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cycloserine capsules 250 mg is indicated in combination with other antituberculosis agents for the treatment of all forms of tuberculosis caused by *Mycobacterium tuberculosis.*

Cycloserine capsules 250 mg is only indicated as a second line antimycobacterial drug when resistance to or toxicity from primary drugs has developed.

4.2 Posology and method of administration

Oral use

Cycloserine capsules 250 mg must always been given in combination with other antituberculosis agents.

Adults:
The usual dose is 500 mg to 1 g daily divided into two daily doses. A daily dosage of 1 g should not be exceeded.

Children:
Experience in children is limited. No paediatric dose has been established. A dose of 10mg/kg/day, divided into two daily doses, has been suggested. If available, therapeutic drug monitoring may be useful. Peak concentrations between 15-40 µg/ml have been recommended as appropriate.

Renalimpairment:
Data on cycloserine dosing in renal impairment are very limited. If use in this patient population is deemed necessary, it has been suggested that 250 mg be given every 24 hours if creatinine clearance is lower than 10 ml/min. Also in patients with creatinine clearance of 10-50 ml/min, an increased dosing interval should be considered. Patients with clinically significant renal dysfunction should be carefully clinically monitored for signs of toxicity, and doses should be adjustedaccordingly.

Hepaticimpairment:
Data on cycloserine use in hepatic impairment are scarce. Patients should be carefully monitored for signs of toxicity.

Cycloserine can be taken with or without food.

Duration of therapy
Therapy should be continued long enough to prevent relapse.
The duration of anti-tuberculous therapy depends on the regimen chosen, the patient's clinical and radiographical responses, smear and culture results, and susceptibility studies of *Mycobacterium tuberculosis* isolates from the patient or the suspected source case.

If therapy is interrupted, the treatment schedule should be extended to a later completion date depending, e.g. on the length of the interruption, the time during therapy (early or late) or the patient's status.

4.3 **Contraindications**

Hypersensitivity to the active substance or to any of the excipients. Epilepsy.
Psychiatric disease (e.g. depression, severe anxiety, psychosis). Concurrent use of alcohol (see 4.5).

4.4 Special warnings and precautions for use

Before initiation of treatment, bacterial susceptibility to the drug should be established.

Cycloserine capsules 250 mg should be discontinued or the dosage reduced if the patient develops symptoms of CNS toxicity, such as convulsions, psychosis, somnolence, depression, confusion, hyperreflexia, headache, tremor, vertigo, paresis, or dysarthria.

The drug should be discontinued if a hypersensitivity reaction (e.g. rash, hepatitis) occurs.

Neuropsychiatric status should be assessed at least at monthly intervals and more frequently if neuropsychiatric symptoms develop. The most dangerous risk of cycloserine is that of suicide, so mood should be carefully watched and any undue depression or personality change observed should be immediately reported.

Since CNS toxicity is more common with higher doses, patients receiving more than 500 mg daily should be particularly closely observed.

Cycloserine should be used very cautiously in patients with renal failure (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent administration of cycloserine with ethionamide, isoniazid or alcohol potentiates the neurotoxicity of cycloserine.

4.6 Pregnancy and lactation

Animal data do not indicate any teratogenicity. Data in human pregnancy are limited. Cycloserine should be given to pregnant women only if clearly needed and when there are no suitablealternatives.

Cycloserine passes into the breast milk. No adverse effects have been observed in breast-fed infants whose mothers were receiving cycloserine.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Nevertheless, the clinical status of the patient and the adverse reaction profile of Aspen- Cycloserine should be borne in mind when considering the patient's ability to drive or operate machinery. Negative effects of cycloserine on the ability to drive and use machines may be synergistic with the effects of alcohol (see section 4.3).

4.8 Undesirable effects

The most frequent and most important adverse reactions of cycloserine are psychiatric and central nervous system (CNS) disorders as detailed below. CNS adverse reactions appear to be dose-related, and occur within the first 2 weeks of therapy in about 15 to 30% of patients. CNS symptoms generally disappear when the drug is discontinued.

The adverse events considered at least possibly related to the treatment are listed below by body system, organ class and absolute frequency. They are not based on adequately sized randomized controlled trials, but on published literature data generated mostly during postapproval use. Therefore, often no frequency data can be given.

Frequencies are defined as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000), very rare (≤1/10,000), 'not known'.

Nervous system disorders
Very common: headache, tremor, dysarthria, vertigo.
Not known: major and minor chronic seizures, convulsions, coma.

Psychiatric disorders
Very common: depression, confusion, anxiety, nervousness, drowsiness, dizziness, lethargy.

Cardiac disorders
Rare: Cardiac arrhythmias and sudden development of congestive heart failure in patients receiving 1 g or more per day.

General disorders
Rare: Hypersensitivity reactions, including rash, photosensitivity or hepatitis.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org' or National Regulatory Authority.

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4.9 Overdose

Acute toxicity can occur when more than 1 g is ingested by an adult. Chronic toxicity is dose related and tends to occur if more than 500 mg are administered daily. Toxicity commonly affects the central nervous system. Effects may include headache, vertigo, confusion, drowsiness, hyperirritability, paraesthesia, slurred speech and psychosis. Following ingestion of larger doses, paresis, convulsions and coma often occur.

Symptomatic and supportive therapy is recommended. Activated charcoal may be more effective in reducing absorption than emesis or gastric lavage. Cycloserine is removed by hemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials ATC Code for cycloserine: J04AB01

Properties
Cycloserine is a broad-spectrum antibiotic that is bacteriostatic to Mycobacterium tuberculosis at the clinically recommended doses.

Mechanism of action
Cycloserine is an analog of the amino acid D-alanine. It interferes with peptidoglycan formation and bacterial cell wall synthesis.

5.2 Pharmacokinetic properties

Absorption: Cycloserine is rapidly and almost completely absorbed

after oral administration. Following single dose administration of Cycloserine capsules 250 mg in healthy volunteers, the mean cycloserine C_{max} value was 14.3351± 4.41643 and 14.4391± 5.49907 µg/ml and the
corresponding values for AUC0-inf was 255.8586± 71.70097 and 242.3469± 65.37191 and
AUC0-t was 235.3578± 58.46183 and 223.6089± 55.14777 µg/h/ml for reference and test formulations accordingly. The median (range) cycloserine tmax value was 0.67 (0.33-3.00) and
0.50 (0.33-3.00) hours for reference and test formulations accordingly. With repeated doses of cycloserine, there is some accumulation of the drug during the first 3 days of therapy.

Distribution: Cycloserine is widely distributed into body tissues and fluids including lungs, ascitic fluid, pleural fluid and synovial fluid, in concentrations approximately equal to plasma concentrations of the drug. Cycloserine is bound to plasma proteins to a low extent (020%).

Elimination: The plasma half-life of cycloserine has been estimated to range between 4 and 30 hours with a mean of 10 hours. In patients with normal renal function, 60 - 70% of an oral dose of cycloserine is excreted unchanged in urine by glomerular filtration. 30-40% of the dose is metabolized in the liver. The metabolites are excreted in the urine. Small amounts of the drug are excreted in faeces.

5.3 Preclinical safety data

Conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction have not raised any special safety concerns for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Talc
Empty hard gelatin capsule shell, ' Size 1', Cap- Light Orange opaque, Body- White opaque, imprinted with "MYLAN" over "CS250" in black ink on both cap and body.

Composition of Empty Hard gelatin capsules "Size 1" for Cycloserine capsules 250 mg

Gelation, Iron oxide red, Iron oxide yellow, Titanium dioxide, Imprinting ink TEK SW-9008 (Black)

Composition of Imprinting ink TEK SW-9008 (Black)

Shellac, Propylene glycol, Black Iron oxide, Potassium hydroxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Do not store above 25°C, store in tight container.

Protect from moisture. Discard the product 30 days

after initial opening.

6.5 Nature and contents of

container 1x 10's Count

cold form blister pack:

- Cold form laminate 0.130MM
- Base Foil plain 0.020MM with 7GSM

10 x 10's Count cold form blister pack:

- Cold form laminate 0.130MM
- Base Foil plain 0.020MM with 7GSM

100's Count HDPE Bottle pack with desiccant:

- Round wide mouth white HDPE bottle 120CC.
- 38MMWhite opaque polypropylene screw cap with aluminium induction sealing liner.
- Silica gel canister

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Manufactured by:
Mylan Laboratories
Limited, Plot No. H-
12 & H-13 MIDC,
Waluj Industrial
Area, Aurangabad.
– 431136,
Maharashtra State,
India.

8. WHOREFERENCE NUMBER(PREQUALIFICATIONPROGRAMME)

CTD12073/17664

9. DATE OF FIRST PREQUALIFICATION/ RENEWAL OF PREQUALIFICATION

08-12-2025

10. DATE OF REVISION OF THE TEXT

08-12-2025