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For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Cycloserine Capsules IP 250mg CYCLOTec



COMPOSITION

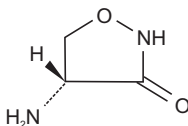
CYCLOTec

Each capsule contains:
Cycloserine IP 250mg

DESCRIPTION

CYCLOTec (Cycloserine Capsules, IP), 3-isoxazolidinone, 4-amino-, (R)- is a broad- spectrum antibiotic that is produced by a strain of *Streptomyces orchidaceus* and has also been synthesized. Cycloserine is a white to off-white powder that is soluble in water and stable in alkaline solution. It is rapidly destroyed at a neutral or acid pH.

Cycloserine has a pH between 5.5 and 6.5 in a solution containing 100 mg/mL. The molecular weight of cycloserine is 102.09, and it has an empirical formula of $C_5H_8N_2O_2$. The structural formula of cycloserine is as follows:



CLINICAL PHARMACOLOGY

After oral administration, cycloserine is readily absorbed from the gastrointestinal tract, with peak blood levels occurring in 4 to 8 hours. Blood levels of 25 to 30 $\mu\text{g/mL}$ can generally be maintained with the usual dosage of 250 mg twice a day, although the relationship of plasma levels to dosage is not always consistent. Concentrations in the cerebrospinal fluid, pleural fluid, fetal blood, and mother's milk approach those found in the serum. Detectable amounts are found in ascitic fluid, bile, sputum, amniotic fluid, and lung and lymph tissues. Approximately 65% of a single dose of cycloserine can be recovered in the urine within 72 hours after oral administration. The remaining 35% is apparently metabolized to unknown substances. The maximum excretion rate occurs 2 to 6 hours after administration, with 50% of the drug eliminated in 12 hours.

MICROBIOLOGY

Cycloserine inhibits cell-wall synthesis in susceptible strains of gram-positive and gram-negative bacteria and in *Mycobacterium tuberculosis*.

MECHANISM OF ACTION

Cycloserine, a broad-spectrum antibiotic, may be bactericidal or bacteriostatic, depending on its concentration at the site of infection and the susceptibility of the organism.

Cycloserine is an analog of the amino acid D-alanine. It interferes with an early step in bacterial cell wall synthesis in the cytoplasm by competitive inhibition of 2 enzymes, L-alanine racemase, which forms D-alanine from L-alanine, and D-alanine- D-alanine synthetase, which incorporates D-alanine into the pentapeptide necessary for peptidoglycan formation and bacterial cell wall synthesis.

INDICATION & USAGE

[Mycobacterial infections, atypical (treatment)]—Cycloserine is used in the treatment of atypical mycobacterial infections, such as *Mycobacterium avium* complex.

—Not all species or strains of a particular organism may be susceptible to cycloserine.

Cyclolec is indicated in the treatment of active pulmonary and extrapulmonary tuberculosis (including renal disease) when the causative organisms are susceptible to this drug and when treatment with the primary medications (streptomycin, isoniazid, rifampin, and ethambutol) has proved inadequate.

Like all antituberculosis drugs, Cyclolec should be administered in conjunction with other effective chemotherapy and not as the sole therapeutic agent.

Cyclolec may be effective in the treatment of acute urinary tract infections caused by susceptible strains of gram-positive and gram-negative bacteria, especially *Enterobacter* spp. and *Escherichia coli*. It is generally no more and is usually less effective than other antimicrobial agents in the treatment of urinary tract infections caused by bacteria other than mycobacteria. Use of Cyclolec in these infections should be considered only when more conventional therapy has failed and when the organism has been demonstrated to be susceptible to the drug.

CONTRAINDICATIONS-

Administration is contraindicated in patients with any of the following:

- Hypersensitivity to cycloserine
- Epilepsy
- Depression, severe anxiety, or psychosis
- Severe renal insufficiency
- Excessive concurrent use of alcohol

SIDE EFFECTS /ADVERSE EFFECTS

Drowsiness may occur. If it continues or becomes severe, inform your doctor. Notify your doctor if you experience: dizziness, headache, tremor, slurred speech, tingling of the hands or feet, mental confusion, irritability, anxiety, skin rash.

Most adverse reactions occurring during therapy with Cyclolec involve the nervous system or are manifestations of drug hypersensitivity. The following side effects have been observed in patients receiving Cyclolec:

Nervous system symptoms (which appear to be related to higher dosages of the drug, i.e., more than 500 mg daily)

Convulsions, Drowsiness and somnolence, Headache, Tremor, Dysarthria, Vertigo, Confusion and disorientation with loss of memory, Psychoses, possibly with suicidal tendencies, Character changes, Hyperirritability, Aggression, Paresis, Hyperreflexia, Paresthesia, Major and minor (localized) clonic seizures, Coma,

Cardiovascular

Sudden development of congestive heart failure in patients receiving 1 to 1.5 g of Cycloserine daily has been reported

Allergy (apparently not related to dosage)

Skin rash**Miscellaneous**

Elevated serum transaminase, especially in patients with preexisting liver disease

OVERDOSAGE**SIGNS AND SYMPTOMS**

Acute toxicity from cycloserine can occur if more than 1 g is ingested by an adult. Chronic toxicity from cycloserine is dose related and can occur if more than 500 mg is administered daily.

Patients with renal impairment will accumulate cycloserine and may develop toxicity if the dosing regimen is not modified. Patients with severe renal impairment should not receive the drug. The central nervous system is the most common organ system involved with toxicity. Toxic effects may include headache, vertigo, confusion, drowsiness, hyperirritability, paresthesias, dysarthria, and psychosis. Following larger ingestions, paresis, convulsions, and coma often occur. Ethyl alcohol may increase the risk of seizures in patients receiving cycloserine.

The oral median lethal dose in mice is 5290 mg/kg.

TREATMENT

Overdoses of cycloserine have been reported rarely. The following is provided to serve as a guide should such an overdose be encountered.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

In adults, many of the neurotoxic effects of cycloserine can be both treated and prevented with the administration of 200 to 300 mg of pyridoxine daily.

The use of hemodialysis has been shown to remove cycloserine from the bloodstream. This procedure should be reserved for patients with life-threatening toxicity that is unresponsive to less invasive therapy.

PRECAUTIONS & WARNING**GENERAL**

Avoid alcohol while taking cycloserine. Alcohol will increase your risk of having a seizure during treatment with this medication. Also, alcohol will increase dizziness and drowsiness.

Use caution when driving, operating machinery, or performing other hazardous activities. Cycloserine may cause dizziness or drowsiness. If you experience dizziness or drowsiness, avoid these activities.

PREGNANCY CONDITION**FERTILITY**

A study in 2 generations of rats showed no impairment of fertility relative to controls for the first mating, but somewhat lower fertility for the second mating.

FDA PREGNANCY CATEGORY C.

Cycloserine is in the FDA pregnancy category C. This means that it is not known whether cycloserine will harm an unborn baby. Do not take this medication without first talking to your doctor if you are pregnant

NURSING MOTHER

Cycloserine passes into breast milk, and it is not known whether cycloserine will harm a nursing baby. Do not take this medication without first talking to your doctor if you are breast-feeding a baby.

PEDIATRIC

Safety & effectiveness in pediatric patients have not been established.

GERIATRICS

No information is available on the relationship of age to the effects of cycloserine in geriatric patients. However, elderly patients are more likely to have an age-related decrease in renal function, which may require an adjustment of dosage in patients receiving cycloserine

DOSAGE AND ADMINISTRATION

Take this by mouth as directed usually every 12 hours for the first two weeks. This medication works best when the amount of medicine in your body is kept at a constant level. Do this by taking the medication at evenly spaced intervals throughout the day and night. Continue using this for the full time prescribed. It may be necessary to continue therapy for tuberculosis for several months to one year or more. Stopping the medication too early may result in ineffective treatment.

Cyclotec is effective orally and is currently administered only by this route. The usual dosage is 500 mg to 1 g daily in divided doses monitored by blood levels. The initial adult dosage most frequently given is 250 mg twice daily at 12-hour intervals for the first 2 weeks. A daily dosage of 1 g should not be exceeded.

STORAGE

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store protected from moisture. Keep out of the reach of children.

PRESENTATION

CYCLOTEC: 5 Strips of 10 Capsules each in a carton.

Mfd in India by :

UNITED BIOTECH (P) LIMITED

Bagbania, Baddi-Nalagarh Road,

Distt. Solan (HP) - 174 101

