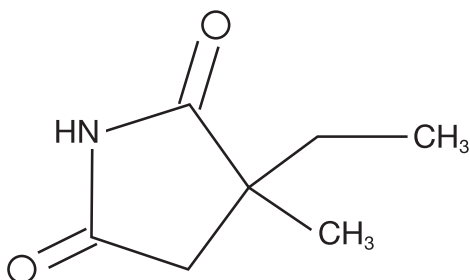


# Ethosuximide Capsules, USP

## DESCRIPTION

Ethosuximide is an anticonvulsant succinimide, chemically designated as alpha-ethyl-alpha-methyl-succinimide, with the following structural formula:



Each Ethosuximide capsule contains 250 mg ethosuximide, USP. Also contains: polyethylene glycol 400, NF. The capsule contains FD&C yellow No. 6; FD&C red No. 3; gelatin, NF; glycerin, USP; and sorbitol.

## CLINICAL PHARMACOLOGY

Ethosuximide suppresses the paroxysmal three cycle per second spike and wave activity associated with lapses of consciousness which is common in absence (petit mal) seizures. The frequency of epileptiform attacks is reduced, apparently by depression of the motor cortex and elevation of the threshold of the central nervous system to convulsive stimuli.

## INDICATIONS AND USAGE

Ethosuximide is indicated for the control of absence (petit mal) epilepsy.

## CONTRAINDICATION

Ethosuximide should not be used in patients with a history of hypersensitivity to succinimides.

## WARNINGS

Blood dyscrasias, including some with fatal outcome, have been reported to be associated with the use of ethosuximide; therefore, periodic blood counts should be performed. Should signs and/or symptoms of infection (eg, sore throat, fever) develop, blood counts should be considered at that point.

Ethosuximide is capable of producing morphological and functional changes in the animal liver. In humans, abnormal liver and renal function studies have been reported.

Ethosuximide should be administered with extreme caution to patients with known liver or renal disease. Periodic urinalysis and liver function studies are advised for all patients receiving the drug.

Cases of systemic lupus erythematosus have been reported with the use of ethosuximide. The physician should be alert to this possibility.

## Usage in Pregnancy:

Ethosuximide crosses the placenta.

Reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an

elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

Cases of birth defects have been reported with ethosuximide. The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodological problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, eg, genetic factors or the epileptic condition itself, may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants. It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

The prescribing physician will wish to weigh these considerations in treating or counseling epileptic women of childbearing potential.

Ethosuximide is excreted in human breast milk. Because the effects of ethosuximide on the nursing infant are unknown, caution should be exercised when ethosuximide is administered to a nursing mother. Ethosuximide should be used in nursing mothers only if the benefits clearly outweigh the risks.

## PRECAUTIONS

### General:

Ethosuximide, when used alone in mixed types of epilepsy, may increase the frequency of grand mal seizures in some patients.

As with other anticonvulsants, it is important to proceed slowly when increasing or decreasing dosage, as well as when adding or eliminating other medication. Abrupt withdrawal of anticonvulsant medication may precipitate absence (petit mal) status.

### Information for Patients:

Ethosuximide may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a motor vehicle or other such activity requiring alertness; therefore, the patient should be cautioned accordingly.

Patients taking ethosuximide should be advised of the importance of adhering strictly to the prescribed dosage regimen.

Patients should be instructed to promptly contact their physician if they develop signs and/or symptoms (eg, sore throat, fever), suggesting an infection.

#### **Drug Interactions:**

Since ethosuximide may interact with concurrently administered antiepileptic drugs, periodic serum level determinations of these drugs may be necessary (eg, ethosuximide may elevate phenytoin serum levels and valproic acid has been reported to both increase and decrease ethosuximide levels).

#### **Pregnancy:**

See WARNINGS.

#### **Pediatric Use:**

Safety and effectiveness in pediatric patients below the age of 3 years have not been established. (See DOSAGE AND ADMINISTRATION section.)

### **ADVERSE REACTIONS**

**Body as a Whole:** Allergic Reaction.

**Gastrointestinal System:** Gastrointestinal symptoms occur frequently and include anorexia, vague gastric upset, nausea and vomiting, cramps, epigastric and abdominal pain, weight loss, and diarrhea. There have been reports of gum hypertrophy and swelling of the tongue.

**Hemopoietic System:** Hemopoietic complications associated with the administration of ethosuximide have included leukopenia, agranulocytosis, pancytopenia, with or without bone marrow suppression, and eosinophilia.

**Nervous System:** Neurologic and sensory reactions reported during therapy with ethosuximide have included drowsiness, headache, dizziness, euphoria, hiccups, irritability, hyperactivity, lethargy, fatigue, and ataxia. Psychiatric or psychological aberrations associated with ethosuximide administration have included disturbances of sleep, night terrors, inability to concentrate, and aggressiveness. These effects may be noted particularly in patients who have previously exhibited psychological abnormalities. There have been rare reports of paranoid psychosis, increased libido, and increased state of depression with overt suicidal intentions.

**Integumentary System:** Dermatologic manifestations which have occurred with the administration of ethosuximide have included urticaria, Stevens-Johnson syndrome, systemic lupus erythematosus, pruritic erythematous rashes, and hirsutism.

**Special Senses:** Myopia.

**Genitourinary System:** Vaginal bleeding, microscopic hematuria.

### **OVERDOSAGE**

Acute overdoses may produce nausea, vomiting, and CNS depression including coma with respiratory depression. A relationship between ethosuximide toxicity and its plasma levels has not been established.

The therapeutic range of serum levels is 40 mcg/mL to 100 mcg/mL, although levels as high as 150 mcg/mL have been reported without signs of toxicity.

#### **Treatment:**

Treatment should include emesis (unless the patient is or could rapidly become obtunded, comatose, or convulsing) or gastric lavage, activated charcoal, cathartics and general supportive measures. Hemodialysis may be useful to treat ethosuximide overdose. Forced diuresis and exchange transfusions are ineffective.

### **DOSAGE AND ADMINISTRATION**

Ethosuximide is administered by the oral route. The *initial* dose for patients 3 to 6 years of age is one capsule (250 mg) per day; for patients 6 years of age and older, 2 capsules (500 mg) per day. The dose thereafter must be individualized according to the patient's response. Dosage should be increased by small increments. One useful method is to increase the daily dose by 250 mg every four to seven days until control is achieved with minimal side effects. Dosages exceeding 1.5 g daily, in divided doses, should be administered only under the strictest supervision of the physician. The *optimal* dose for most pediatric patients is 20 mg/kg/day. This dose has given average plasma levels within the accepted therapeutic range of 40 to 100 mcg/mL. Subsequent dose schedules can be based on effectiveness and plasma level determinations.

Ethosuximide may be administered in combination with other anticonvulsants when other forms of epilepsy coexist with absence (*petit mal*). The optimal dose for most pediatric patients is 20 mg/kg/day.

#### **HOW SUPPLIED**

Ethosuximide Capsules USP, 250 mg are supplied as: Transparent, orange oblong softgel capsules with VP 25 etched in the middle of the capsule.

NDC 61748-025-01 – Bottles of 100.

Store at 20°-25°C (68°-77°F); excursion permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Dispense in a tight container as defined in the USP.

#### **Rx only**

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