Ethosuximide Capsules, USP

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

HN
O
CH₃

Each ethosuximide capsule contains 250 mg ethosuximide, USP. Also contains: polyethylene glycol 400, NF. The capsule contains FD & C 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
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 (e.g., sore throat, fever) develop, blood counts should be considered at that point.

Effects on Liver and Kidneys
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.

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

Suicidal Behavior and Ideation
Antiepileptic drugs (AEDs), including ethosuximide, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for an indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Pooled analyses of 19 placebo-controlled clinical trials (monotherapy and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had twice the risk of suicidal ideation or behavior compared to patients randomized to placebo. In these trials, which had a median duration of treatment of 12 weeks, the incidence rate of suicidal ideation or behavior among 27,863 AED-treated patients was 0.43%, compared to 0.24% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal ideation or behavior for every 530 patients treated. There were four suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

The risk of suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

Patients and their caregivers should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Serious Dermatologic Reactions
Serious dermatologic reactions, including Stevens-Johnson syndrome (SJS), have been reported with ethosuximide treatment. SJS can be fatal. The onset of symptoms is usually within 28 days but can occur later. Ethosuximide should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS, use of this drug should not be resumed and alternative therapy should be considered.

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 suggest an increased 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, e.g., 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 hypotension and hypoxia to the newborn. 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.

Information for Patients
Inform patients of the availability of a Medication Guide, and instruct them to read the Medication Guide prior to taking ethosuximide. Instruct patients to take ethosuximide only as prescribed.

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 (e.g., sore throat, fever), suggesting an infection.

Patients, their caregivers, and families should be counseled that AEDs, including ethosuximide, may increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Prior to initiation of treatment with ethosuximide, the patient should be instructed that a rash may herald a serious medical event and that the patient should report any such occurrence to a physician immediately.

Patients should be encouraged to enroll in the North American Antiepileptic Drug (NAEAD) Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To enroll, patients can call the toll free number 1-888-233-2334 (see PRECAUTIONS: Pregnancy section).

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

Pregnancy
To provide information regarding the effects of in-utero exposure to ethosuximide, physicians are advised to recommend that pregnant patients taking ethosuximide enroll in the NAAED Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by patients themselves. Information on the registry can also be found at the website: http://www.aedpregnancyregistry.org/

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. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

Gastrointestinal System: Gastrointestinal symptoms occur frequently and include anorexia, vague abdominal distress, constipation, 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, and/or bone marrow suppression, and eosinophilia.

Nervous System: Neuropsychologic and sensory reactions reported during therapy with ethosuximide have included diplopia, headache, dizziness, euphoria, hallucinations, 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, acne, and purpura, pruritic erythematous rash, and hirsutism.

Special Sensory Systems: Myopia.

Genitourinary System: Vaginal bleeding, microscopic hematuria.

OVERDOSE
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
Distributed by:
Manufactured by: Swiss Caps AG, Kirchberg, Switzerland
Code# 2075
Dispense in a tight container as defined in the USP.

Transparent, orange oblong softgel capsules with VP 25 etched in the middle of the cap-

Ethosuximide Capsules USP, 250 mg are supplied as:

- Dosage and Administration
- Treatment
- Systemic Lupus Erythematosus.

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/day, in divided doses, should be administered only under the strict 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
Coded 2075
Revised Feb 2014

Manufactured by: Swiss Caps AG, Kirchberg, Switzerland

Distributed by: VersaPharm, Incorporated
1775 W. Oak Parkway, Marietta, GA 30062

MEDICATION GUIDE

ETHOSUXIMIDE (eth’o sux’ i mi d)

CAPSULES, USP

Read this Medication Guide before you start taking ethosuximide capsules and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about ethosuximide capsules, ask your healthcare provider or pharmacist.

What is the most important information I should know about ethosuximide capsules?

Do not stop taking ethosuximide capsules without first talking to your healthcare provider.

Stopping ethosuximide capsules suddenly can cause serious problems.

Ethosuximide capsules can cause serious side effects, including:

1. Rare but serious blood problems that may be life-threatening. Call your healthcare provider right away if you have:

- fever, swollen glands, or sore throat that come and go or do not go away
- frequent infections or an infection that does not go away
- easy bruising
- red or purple spots on your body
- bleeding gums or nose bleeds
- severe fatigue or weakness

2. Systemic Lupus Erythematosus. Call your healthcare provider right away if you have any of these symptoms:

- joint pain and swelling
- muscle pain
- fatigue
- low-grade fever

- pain in the chest that is worse with breathing
- unexplained skin rash

3. Like other antiepileptic drugs, ethosuximide capsules may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase inactivity and talking (mania)
- other unusual changes in behavior or mood

How can I watch for early symptoms of suicidal thoughts and actions?

- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled.

Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

Do not stop ethosuximide capsules without first talking to a healthcare provider.

- Stopping ethosuximide capsules suddenly can cause serious problems.
- Stopping a seizure medicine suddenly in a patient who has epilepsy can cause seizures that will not stop (status epilepticus).

Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

What are ethosuximide capsules?

Ethosuximide capsules are a prescription medicine used to treat absence (petit mal) seizures.

Who should not take ethosuximide capsules?

Do not take ethosuximide capsules if you are allergic to succinimides (methsuximide or ethosuximide), or any of the ingredients in ethosuximide capsules. See the end of this Medication Guide for a complete list of ingredients in ethosuximide capsules.

What should I tell my healthcare provider before taking ethosuximide capsules?

Before you take ethosuximide capsules, tell your healthcare provider if you:

- have had liver problems
- have or had depression, mood problems or suicidal thoughts or behavior
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if ethosuximide capsules can harm your unborn baby. Tell your healthcare provider right away if you become pregnant while taking ethosuximide capsules. You and your healthcare provider should decide if you should take ethosuximide capsules while you are pregnant.
- if you become pregnant while taking ethosuximide capsules, talk to your healthcare provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic drugs during pregnancy. You can enroll in this registry by calling 1-888-233-2334.
- are breast-feeding or plan to breast-feed. It is not known if ethosuximide can pass into breast milk. You and your healthcare provider should decide how you will feed your baby while you take ethosuximide capsules.

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of ethosuximide capsules. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ethosuximide capsules?

Store ethosuximide capsules at room temperature, between 20°–25°C (68°–77°F).

Keep ethosuximide capsules and all medicines out of the reach of children.

General information about ethosuximide capsules

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ethosuximide capsules for a condition for which it was not prescribed. Do not give your medicine to other people, even if they have the same condition. It may harm them.

This Medication Guide summarizes the most important information about ethosuximide capsules. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ethosuximide capsules that is written for healthcare professionals.

For more information, go to www.versapharm.com or call 1-800-548-0700.

What are the ingredients in ethosuximide capsules?

Active ingredient: ethosuximide

Inactive ingredients: Polyethylene glycol 400, NF; FD&C yellow No. 6; FD&C red No. 3; gelatin, NF; glycerin, USP; and sorbitol.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Rx only
Coded 2076
Revised Feb 2014

Manufactured by: Swiss Caps AG, Kirchberg, Switzerland

Distributed by: VersaPharm, Incorporated
1775 W. Oak Parkway, Marietta, GA 30062

70010425
DISCLAIMER

All labeling reflected on this website is for informational and promotional purposes only. It is not intended to be used by healthcare professionals or patients for the purpose of prescribing or administering these products. Questions regarding the current content of product labeling should be directed to Akorn's Customer Service department at 800.932.5676.