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

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\[
\text{O} \quad \text{N}
\]  
\[
\text{C}_7 \text{H}_{11} \text{N}_2 \text{O}_2 \quad \text{MW 141.17}
\]
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Each teaspoonful (5 mL) for oral administration, contains 250 mg ethosuximide, USP. Also contains artificial raspberry flavor, citric acid, ethyl maltol, FD&C Red No. 40, FD&C Yellow No. 6, glyc erin, purified water, saccharin sodium, sodium benzoate, sodium citrate, and sucrose.

**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.

**CONTRAINDICATIONS**

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 symptoms of infection (e.g., sore throat, fever) develop, blood counts should be considered at that point.

Effects on Liver and Kidneys

Ethosuximide has been reported to induce 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 alert 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 any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI: 1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In these trials, which had a median duration of 12 weeks, the estimated incidence rate of suicidal behavior or ideation among 27,683 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 thinking or behavior for every 500 patients treated. There were four suicides in drug-treated patients in the trials treated with ethosuximide, and none in patients on placebo, 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 after starting drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed.

The risk of suicidal thoughts or behavior was generally consistent among AEDs in the drug class when they were administered to all AEDs used for any indication. The risk did not vary substantially by age (5-100 years) in the clinical trials analyzed. Table 1 shows absolute and relative risk by indication for all evaluated AEDs.

### Table 1: Risk by indication for antiepileptic drugs in the pooled analysis

| Indication | Placebo Patients Drug Patients Relative Risk Incidence of Events Incidence of Events in Drug Patients/Placebo Patients Relative Risk Difference: Drug Patients/Placebo Patients | Risk Difference: Drug Patients/Placebo Patients |
|------------|--------------|--------------------------------|-----------------------------------------------|------------------------------------------------|
| Epilepsy   | 1.0          | 3.4                           | 3.5                                          | 2.4                                               |
| Psychiatric | 5.7          | 8.5                           | 1.5                                          | 2.9                                               |
| Other      | 1.0          | 1.8                           | 1.9                                          | 0.9                                               |
| Total      | 2.4          | 4.3                           | 1.8                                          | 1.9                                               |

The relative risk for 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.

Anyone considering prescribing ethosuximide or any other AED must carefully weigh the potential risks and benefits of its use. The physician should be alert to this possibility.

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 there are also the more commonly prescribed anticonvulsants, less systematic or anecdotal reports suggest a possible similar association with the use of all antiepileptic drugs.

**Usage in Pregnancy**

Ethosuximide crosses the placenta. There are, however, no adequate and well-controlled studies in pregnant women. The physician should be alert to the possibility of possible risk to the fetus to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI: 1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In these trials, which had a median duration of 12 weeks, the estimated incidence rate of suicidal behavior or ideation among 27,683 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 thinking or behavior for every 500 patients treated. There were four suicides in drug-treated patients in the trials treated with ethosuximide, and none in patients on placebo, but the number is too small to allow any conclusion about drug effect on suicide.

**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 the dosage, or when decreasing the dosage or discontinuing treatment. Abrupt withdrawal of anticonvulsant medication may precipitate exacerbation (petit mal) status.

**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.

**ADVERSE REACTIONS**

**Body As A Whole**

Allergic reaction. Drug Reaction with Eosinophilia

**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, and specific supportive measures. Hemodialysis may also 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 teaspoonful (250 mg) per day; for patients 6 years of age and older, 2 teaspoonfuls (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 consist with absence (petit mal) status. The usual dose for most pediatric patients is 20 mg/kg/day.

**HOW SUPPLIED**

Ethosuximide oral solution, USP 250 mg/5 mL is supplied in bottles of 16 fl. oz. NDC 61748-024-16. Each 5 mL of oral solution contains 250 mg ethosuximide in a raspberry flavored base.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from freezing and light.

Dispense in a tight, light-resistant container with a child-resistant closure.
Before you take ethosuximide oral solution, tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Taking ethosuximide oral solution with certain other medicines can cause side effects or affect how well they work. Do not start or stop other medicines without talking to your healthcare provider.

Know the medicines you take. Keep a list of them with you to show your healthcare provider and pharmacist when you get a new medicine.

How should I take ethosuximide oral solution?

• Take ethosuximide oral solution exactly as prescribed. Your healthcare provider will tell you how much ethosuximide oral solution to take.
• Your healthcare provider may change your dose. Do not change your dose of ethosuximide oral solution without talking to your healthcare provider.
• If you take too much ethosuximide oral solution, call your healthcare provider or your local Poison Control Center right away.

What should I avoid while taking ethosuximide oral solution?

• Do not drink alcohol or take other medicines that make you sleepy or dizzy while taking ethosuximide oral solution without first talking to your healthcare provider. Ethosuximide oral solution taken with alcohol or medicines that cause sleepiness or dizziness may make your sleepiness or dizziness worse.
• Do not drive, operate heavy machinery, or do other dangerous activities until you know how ethosuximide oral solution affects you. Ethosuximide oral solution can slow your thinking and motor skills.

What are the possible side effects of ethosuximide oral solution?

• See “What is the most important information I should know about ethosuximide oral solution?”

Ethosuximide oral solution may cause other side effects, including:

• Serious allergic reactions. Call your healthcare provider right away if you have any of these symptoms:
  • skin rash
  • hives
  • sores in your mouth
  • itching or peeling skin
  • changes in thinking, mood, or behavior. Some patients may get abnormally suspicious thoughts, hallucinations (seeing or hearing things that are not there), or delusions (false thoughts or beliefs).
• Grand mal seizures can happen more often or become worse Call your healthcare provider right away, if you have any of the symptoms listed above.

The most common side effects of ethosuximide oral solution include:

• nausea or vomiting
• indigestion, stomach pain
• diarrhea
• weight loss
• loss of appetite
• hiccups
• fatigue
• dizziness or lightheadedness
• intolerance when walking
• headaches
• loss of concentration

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 oral solution. 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 oral solution?

• Store ethosuximide oral solution at 20º to 25ºC (68 º to 77 ºF). Preserve in tight containers. Protect from freezing and light.

Keep ethosuximide oral solution and all medicines out of the reach of children.

General information about ethosuximide oral solution

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

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