

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

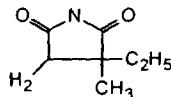
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DRAFT FINAL PRINTED LABELING

Ethosuximide Syrup

DESCRIPTION

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



NOV 22 2000

Each teaspoonful (5 mL), for oral administration, contains 250 mg ethosuximide, USP. Also contains citric acid, FD&C Red No. 40, FD&C Yellow No. 6, cherry-raspberry flavoring, glycerin, purified water, saccharin sodium, sodium benzoate, sodium citrate, and sucrose. Sodium hydroxide may be used for pH adjustment. The pH range is 5.0 to 6.5.

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, including some with fatal outcome, have been reported to be associated with the use of ethosuximide; therefore, periodic blood counts should be performed.

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: The effects of ethosuximide in human pregnancy and nursing infants are unknown.

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.

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 methodologic 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 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.

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.

Pregnancy: See WARNINGS section.

ADVERSE REACTIONS

Gastrointestinal System: Gastrointestinal symptoms occur frequently and include anorexia, vague gastric upset, nausea and vomiting, cramps, epigastric and abdominal pain, weight loss, and diarrhea.

Hemopoietic System: Hemopoietic complications associated with the administration of ethosuximide have included leukopenia, agranulocytosis, pancytopenia, aplastic anemia, 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, and pruritic erythematous rashes.

Miscellaneous: Other reactions reported have included myopia, vaginal bleeding, swelling of the tongue, gum hypertrophy, and hirsutism.

DOSAGE AND ADMINISTRATION

Ethosuximide Syrup 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 coexist with absence (petit mal). The *optimal* dose for most pediatric patients is 20 mg/kg/day.

HOW SUPPLIED

Ethosuximide Syrup is supplied as:

NDC 0121-0670-16 1 pint (474 mL) bottles, and NDC 0121-0670-05 (unit dose cups of 5 mL, 10 cups per tray). Each 5 mL of syrup contains 250 mg ethosuximide in a cherry-raspberry flavored base.

Store below 30°C (86°F).

Protect from freezing and light.

Rx ONLY

 **Pharmaceutical
Associates, Inc.**
Greenville, SC 29605

R 6/00

NOV 22 2000

Delivers 5 mL
NDC 0121-0670-05
ETHOSUXIMIDE
SYRUP
250 mg/5 mL
FOR INSTITUTIONAL USE ONLY
Usual Dosage: See insert
Expiration Date and Lot No.
Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605

Delivers 5 mL
NDC 0121-0670-05
ETHOSUXIMIDE
SYRUP
250 mg/5 mL
FOR INSTITUTIONAL USE ONLY
Usual Dosage: See insert
Expiration Date and Lot No.

Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605

NDC 0121-0670-16

Ethosuximide Syrup

250 mg / 5 mL

Each 5 mL contains:
Ethosuximide, 250 mg.

Rx ONLY

1 Pint (474 mL)

pai Pharmaceutical
Associates, Inc.
Greenville, SC 29605

USUAL DOSAGE: *Initially, 1 or 2 teaspoonfuls, increased gradually according to the patient's response. The optimal dose is 20 mg/kg/day. See package insert for complete prescribing information.*

NOV 22 2000

Delivers 5 mL
NDC 0121-0670-05
ETHOSUXIMIDE
SYRUP
250 mg/5 mL
FOR INSTITUTIONAL USE ONLY
Usual Dosage: See insert
Expiration Date and Lot No.

Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605

PHARMACIST: Dispense in a tight, light-resistant container with a child-resistant closure as defined in the USP.
**Store below 30°C (86°F).
Protect from freezing and light.**
WARNING: Keep this and all medications out of the reach of children.

11/22/00

ETHOSUXIMIDE SYRUP
250 mg/5 mL 10 x 5 mL
NOV 22 2000

Usual Dosage: See Insert.

10 x 5 mL

- This unit-dose package is not child-resistant.
Store at controlled room temperature,
15° - 30°C (59° - 86°F).

Rx ONLY

PHARMACEUTICAL ASSOCIATES, INC., GREENVILLE, SC 29605

NDC 0121-0670-05
ETHOSUXIMIDE SYRUP
250 mg/5 mL

Usual Dosage: See Insert.

10 x 5 mL

- This unit-dose package is not child-resistant.
Store at controlled room temperature,
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Rx ONLY

PHARMACEUTICAL ASSOCIATES, INC., GREENVILLE, SC 29605

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PHARMACEUTICAL ASSOCIATES, INC., GREENVILLE, SC 29605

Tray Label

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