CI 6012-2

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Mysoline® (primidone) *Anticonvulsant*

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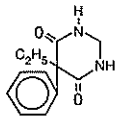
(primidone)
Anticonvulsant

Rx Only

DESCRIPTION

Chemical name: 5-ethyldihydro-5-phenyl-4,6 (1H, 5H)-pyrimidinedione.
Structural formula:



Mysoline* (primidone) is a white, crystalline, highly stable substance, M.P. 279-284° C. It is poorly soluble in water (60 mg per 100 mL at 37° C) and in most organic solvents. It possesses no acidic properties, in contrast to its barbiturate analog.

Mysoline 50 mg and 250 mg tablets contain the following inactive ingredients: Microcrystalline Cellulose, NF; Lactose, USP; Methylcellulose, USP; Sodium Starch Glycolate, NF; Talc, USP; Sodium Lauryl Sulfate, NF; Magnesium Stearate, NF; Water, USP, Purified.

Mysoline 250 mg tablets also contain Yellow Iron Oxide, NF.

* Registered trademark of Xcel Pharmaceuticals, Inc.

ACTIONS

Mysoline raises electro- or chemoshock seizure thresholds or alters seizure patterns in experimental animals. The mechanism(s) of primidone's antiepileptic action is not known.

Primidone per se has anticonvulsant activity as do its two metabolites, phenobarbital and phenylethylmalonamide (PEMA). In addition to its anticonvulsant activity, PEMA potentiates the anticonvulsant activity of phenobarbital in experimental animals.

INDICATIONS

Mysoline, used alone or concomitantly with other anticonvulsants, is indicated in the control of grand mal, psychomotor, and focal epileptic seizures. It may control grand mal seizures refractory to other anticonvulsant therapy.

CONTRAINDICATIONS

Primidone is contraindicated in:
1) patients with porphyria and
2) patients who are hypersensitive to phenobarbital (see **ACTIONS**).

WARNINGS

The abrupt withdrawal of antiepileptic medication may precipitate status epilepticus.

The therapeutic efficacy of a dosage regimen takes several weeks before it can be assessed.

Usage in Pregnancy

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

Recent 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 diphenylhydantoin 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 leading to birth defects, e.g., genetic factors or the epileptic condition itself, may be more important than drug therapy. The 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 disorders 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.

Neonatal hemorrhage, with a coagulation defect resembling vitamin K deficiency, has been described in newborns whose mothers were taking primidone and other anticonvulsants. Pregnant women under anticonvulsant therapy should receive prophylactic vitamin K_1 therapy for one month prior to, and during, delivery.

PRECAUTIONS

The total daily dosage should not exceed 2 g. Since Mysoline therapy generally extends over prolonged periods, a complete blood count and a sequential multiple analysis-12 (SMA-12) test should be made every six months.

In Nursing Mothers

There is evidence that in mothers treated with primidone, the drug appears in the milk in substantial quantities. Since tests for the presence of primidone in biological fluids are too complex to be carried out in the average clinical laboratory, it is suggested that the presence of undue somnolence and drowsiness in nursing newborns of Mysoline-treated mothers be taken as an indication that nursing should be discontinued.

ADVERSE REACTIONS

The most frequently occurring early side effects are ataxia and vertigo. These tend to disappear with continued therapy, or with reduction of initial dosage. Occasionally, the following have been reported: nausea, anorexia, vomiting, fatigue, hyperirritability, emotional disturbances, sexual impotency,

diplopia, nystagmus, drowsiness, and morbilliform skin eruptions. Granulocytopenia, agranulocytosis, and red-cell hypoplasia and aplasia, have been reported rarely. These and, occasionally, other persistent or severe side effects may necessitate withdrawal of the drug. Megaloblastic anemia may occur as a rare idiosyncrasy to Mysoline and to other anticonvulsants. The anemia responds to folic acid without necessity of discontinuing medication.

DOSAGE AND ADMINISTRATION

Adult Dosage

Patients 8 years of age and older who have received no previous treatment may be started on Mysoline according to the following regimen using either 50 mg or scored 250 mg Mysoline tablets:

Days 1 to 3: 100 to 125 mg at bedtime.

Days 4 to 6: 100 to 125 mg b.i.d.

Days 7 to 9: 100 to 125 mg t.i.d.

Day 10 to maintenance: 250 mg t.i.d.

For most adults and children 8 years of age and over, the usual maintenance dosage is three to four 250 mg Mysoline tablets daily in divided doses (250 mg t.i.d. or q.i.d.). If required, an increase to five or six 250 mg tablets daily may be made but daily doses should not exceed 500 mg q.i.d.

INITIAL: ADULTS AND CHILDREN OVER 8

KEY: ●=50 mg tablet; ⬤=250 mg tablet

DAY	1	2	3	4	5	6
AM				●●	●●	●●
NOON						
PM				●●	●●	●●

DAY	7	8	9	10	11	12
AM	●●	●●	●●	⬤	Adjust to Maintenance	
NOON	●●	●●	●●	⬤		
PM	●●	●●	●●	●●	●●	●●

Dosage should be individualized to provide maximum benefit. In some cases, serum blood level determinations of primidone may be necessary for optimal dosage adjustment. The clinically effective serum level for primidone is between 5 to 12 µg/mL.

In Patients Already Receiving Other Anticonvulsants

Mysoline should be started at 100 to 125 mg at bedtime and gradually increased to maintenance level as the other drug is gradually decreased. This regimen should be continued until satisfactory dosage level is achieved for the combination, or the other medication is completely withdrawn. When therapy with Mysoline alone is the objective, the transition from concomitant therapy should not be completed in less than two weeks.

Pediatric Dosage

For children under 8 years of age, the following regimen may be used:

Days 1 to 3: 50 mg at bedtime.

Days 4 to 6: 50 mg b.i.d.

Days 7 to 9: 100 mg b.i.d.

Day 10 to maintenance: 125 mg t.i.d. to 250 mg t.i.d.

For children under 8 years of age, the usual maintenance dosage is 125 to 250 mg three times daily or, 10 to 25 mg/kg/day in divided doses.

HOW SUPPLIED

Mysoline Tablets

Each square-shaped, scored, yellow tablet, identified by "MYSOLINE 250" and an embossed M, contains 250 mg of primidone, in bottles of 100 (NDC 66490-691-10) and 1,000 (NDC 66490-691-11).

Also available in a unit-dose package of 100 (NDC 66490-691-81).

Each square-shaped, scored, white tablet, identified by "MYSOLINE 50" and an embossed M, contains 50 mg of primidone, in bottles of 100 (NDC 66490-690-10) and 500 (NDC 66490-690-50).

The appearance of these tablets is a trademark of Xcel Pharmaceuticals, Inc.

Store at room temperature, approximately 25° C (77° F).

Dispense in a tight, light-resistant container as defined in the USP.

Distributed By:

Xcel Pharmaceuticals

San Diego, CA 92122

Xcel Pharmaceuticals

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