PRIMIDONE - primidone tablet
NCS HealthCare of KY, Inc dba Vangard Labs

PRIMIDONE TABLETS, USP
Revised 06/09
Rx only

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

![Chemical Structure](image)

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.

Each tablet, for oral administration, contains 250 mg primidone. In addition, each tablet contains the following inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium starch glycolate, and stearic acid.

CLINICAL PHARMACOLOGY
Primidone 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 AND USAGE
Primidone, used alone or concomitantly with other anticonvulsants, are 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 CLINICAL PHARMACOLOGY).

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.

Suicidal Behavior and Ideation
Antiepileptic drugs (AEDs), including Primidone Tablets, 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, and/or any unusual changes in mood or behavior.

Table 1 shows absolute and relative risk by indication for all evaluated AEDs.
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 Primidone Tablets or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families 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.

Usage in Pregnancy
To provide information regarding the effects of in utero exposure to primidone, physicians are advised to recommend that pregnant patients taking Primidone Tablets enroll in the North American Antiepileptic Drug (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/.

The effects of primidone 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 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 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 K1 therapy for one month prior to, and during, delivery.

PRECAUTIONS
The total daily dosage should not exceed 2 g. Since primidone 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 primidone-treated mothers be taken as an indication that nursing should be discontinued.
Information for Patients

Suicidal Thinking and Behavior
Patients, their caregivers, and families should be counseled that AEDs, including Primidone Tablets, 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.

Patients should be encouraged to enroll in the NAAED 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 Usage in Pregnancy section).

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 primidone 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 primidone according to the following regimen using either 50 mg or scored 250 mg primidone 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 primidone 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.

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.

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<td>KEY: ● = 50 mg tablet; ● = 250 mg tablet</td>
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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 5-12 µg/mL.

In patients already receiving other anticonvulsants
Primidone 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 primidone alone is the objective, the transition from concomitant therapy should not be completed in less than two weeks.
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, 10-25 mg/kg/day in divided doses.

HOW SUPPLIED
Primidone Tablets, USP 250 mg are supplied as: white, round, scored tablets; debossed “WW 484” on one side of the tablet, and scored on the other side of the tablet, and are available in:

- Blistercards of 30 tablets.

Store at 20-25°C (68-77°F) [See USP Controlled Room Temperature].
Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.
Manufactured by
West-ward Pharmaceutical Corp.
Eatontown, NJ 07724
Rev. June 2009

PRINCIPAL DISPLAY PANEL
Primidone Tablets,
USP 250mg