

# Neurosyn™

## Primidone

### Description

Primidone 5-ethylidihydro-5, phenyl-4,6(1H,-5H)-pyrimidine-dione is a white crystalline substance, and is a pyrimidine derivative. Studies of chronic administration of primidone indicate it can metabolize into two active metabolites, phenobarbital and phenylethylmalonamide (PEMA).

Neurosyn™ acts upon the central nervous system to raise the seizure threshold, hence its value as an anticonvulsant, whether the seizure is induced electrically or is a symptom of a primary disease process.

### Features

High degree of safety when used as directed.

Tablets may be administered whole or crushed and mixed with food.

Convulsion suppression with no gastrointestinal irritation.

250 mg scored tablets.

### Benefits

Safe and efficacious.

Convenient administration methods.

Few side effects.

Accurate dosing.

### Advantages

Neurosyn is veterinary labeled primidone used as an anticonvulsant only for dogs.

### Administration

Use in dogs only at a rate of 25 mg per pound of body weight per day. Tablets may be administered whole or crushed and mixed with food. When convulsions are frequent, the daily dosage should be given at one time. Reduction in dosage should always be made gradually and treatment should never be discontinued abruptly.

### Precautions

**Do not use in felines.** Primidone appears to have specific neurotoxicity in cats.

In long-term therapy using primidone there is the possibility of serum alkaline phosphatase (SAP) elevation to slightly above normal. When primidone therapy is discontinued, SAP should return to normal unless the elevation is caused by other abnormal conditions, such as bone disease, healing fractures or pregnancy.

### Uses

Use only in dogs to treat idiopathic epilepsy, epileptiform convulsions, virus encephalitis, distemper, hardpad disease.

### Warning

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Keep out of reach of children.

For use in animals only.

### Product Information

Name	Code	Size
Neurosyn™	682-515	100's
	682-535	1000's

### Highlights

- Safe and effective.
- Scored tablets.
- No gastrointestinal irritation.



NADA 117-689, Approved by FDA

## Neurosyn™ Tablets

(primidone)

**Caution:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**Description:** Primidone 5-ethylidihydro-5-phenyl-4,6 (1H,-5H)-pyrimidinedione is a white crystalline substance, and is a pyrimidine derivative. Studies of chronic administration of primidone indicate it can metabolize into two active metabolites, phenobarbital and phenylethylmalonamide (PEMA).<sup>1 2 3</sup>

Although primidone is less potent than phenobarbital as a general CNS depressant, primidone is more potent than phenobarbital in the protection of animals against maximal seizures induced by both electroshock and pentylenetetrazole.<sup>4 5 10</sup> As indicated above, primidone may undergo a somewhat complex metabolism involving the production of phenobarbital and the practitioner should take this into consideration if administering other drugs such as other antiepileptics concurrently.

Primidone acts upon the central nervous system to raise the seizure threshold, hence its value as an anticonvulsant, whether the seizure is induced electrically or is a symptom of a primary disease process.

**Indications:** Use only in dogs to treat:

### Idiopathic Epilepsy

Archibald<sup>6</sup> has reported on the use of primidone in the treatment of idiopathic epilepsy in dogs previously treated with other anticonvulsants without success. In this experience, primidone was found to be an effective agent completely controlling the convulsions in most of the cases studied and reducing the number and severity of seizures in the remaining small percentage.

### Epileptiform Convulsions

Clinically, these convulsions are similar to those of true epilepsy. Primidone may be useful as symptomatic treatment of these convulsions of unknown etiology.

### Virus Encephalitis, Distemper, Hardpad Disease Which Occurs as a Clinically Recognizable Lesion in Certain Entities in Dogs.

Primidone provides an effective means of controlling convulsions associated with infectious neuropathies such as virus encephalitis, distemper or hardpad disease. Supplementation of therapy with primidone is recommended as soon as diagnosis is made. Oliver and Hoerlin (1965), reported that primidone has been the most effective agent in the dog for the control of seizures associated with post distemper convulsions. Clinical experience has revealed that once the seizure of a dog cannot be controlled with primidone, none of the other anticonvulsants is likely to do any better.<sup>7</sup> However, it must be borne in mind that primidone does not correct the primary causes of these disorders, but is a valuable adjunct to therapy, making possible control of seizures without hypnosis or interference with proper nutrition.

The initial dose of primidone is gradually increased until optimum control of convulsions is achieved, and the dosage level necessary to establish this effect is usually maintained.

Primidone has not proved useful in the treatment of chorea.

### Precautions: Do not use in feline species.

Primidone appears to have a specific neurotoxicity in cats.

In long-term therapy using primidone there is the possibility of Serum Alkaline Phosphatase (SAP) elevation to slightly above normal. When primidone therapy is discontinued SAP should return to normal unless the elevation was caused by other abnormal conditions, such as bone disease, healing fractures or pregnancy.

**Dosage and Administration:** Usual daily dosage—25 mg/lb of body weight (55 mg/kg of body weight).

Tablets may be administered whole, or crushed and mixed with food. When convulsions are frequent, the dosage should be divided and administered at intervals. When convulsions occur only every few days, or less often, daily dosage should be given at one time.<sup>10</sup>

Reduction in dosage should always be made gradually and treatment should never be discontinued abruptly.

**Adverse Reactions:** Primidone is well tolerated at effective therapeutic levels. Side reactions such as staggering and drowsiness occur infrequently and usually disappear with adjustment in dosage.

Potential side effects of primidone are polydipsia, polyuria and polyphagia.

Hepatic dysfunction has been reported in a small percentage of dogs maintained on chronic primidone therapy, alone or in combination with other primary anticonvulsants (phenytoin and phenobarbital).

Biochemical monitoring (including measurements of serum gamma glutaryl transferase activity, bile acid concentration, and BSP retention) of patients prior to commencement of and at regular intervals during primidone therapy may identify early hepatic injury or intercurrent hepatic disease, which may be indications for dosage adjustments to the minimum required to control seizures. The risk of potential hepatotoxicity appears to be small relative to the risk associated with intractable seizures, and may be an idiosyncratic reaction related to individual susceptibility to the drug.

The activity of drug metabolizing enzymes can be inhibited by certain compounds, such as chloramphenicol. Concurrent administration of chloramphenicol and primidone (or the other primary anticonvulsants) may result in accumulation of the anticonvulsant drug and clinical signs of toxicity (sedation, ataxia, prolonged anesthesia).

Several investigators have successfully treated megaloblastic anemia associated with long-term primidone with folic acid, vitamin B-12 and iron.<sup>89</sup>

**How Supplied:** Each primidone tablet contains 250 mg of primidone (scored), in bottles of 100 and 1,000.

#### **Bibliography:**

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4. Bogue, J.Y. and H.C. Carrington, "The Evaluation of 'Mysoline' a New Anticonvulsant Drug," *Br. J. Pharmacol.* 8:230, 1953.
5. Goodman, L.S., E.A. Swineyard, W.C. Brown, D.O. Schiffman, M.S. Grewal and E.L. Bliss, "Anticonvulsant Properties of 5-phenyl-5-ethylhexahydropyrimidine-4, 6-dione (Mysoline), a New Anti-epileptic," *J. Pharmacol. Exp. Ther.* 108:428, 1953.
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9. Reynolds, E.H., I. Chanarin, G. Milner and D.M. Matthews, "Anticonvulsant Therapy, Folic Acid and Vitamin B-12 Metabolism and Mental Symptoms," *Epilepsia*. 7(1966): 261–270.
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682503L-00-0002

**Indications:** For the control of convulsions associated with idiopathic epilepsy, epileptiform convulsions, virus encephalitis, distemper and hardpad disease that occurs as a clinically recognizable lesion in certain disease entities in dogs. Primidone has not proved useful in treatment of chorea.

**Warning:** For use only in dogs.

**Precautions:** Do not use in feline species, as primidone appears to have a specific neurotoxicity in cats.

# Neurosyn™

(primidone)  
250 mg Tablets

Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

NADA 117-689, Approved by FDA

**Net Contents:  
1000 Tablets**

682503L-00-0002  
Code 682535

**Each Tablet Contains:** 250 mg of primidone.

**Dosage and Administration:** Usual daily dosage—25 mg/lb of body weight (55 mg/kg). Tablets may be administered whole or crushed and mixed with food. When convulsions are frequent, the daily dosage should be divided and administered at intervals. Reduction in dosage should be made gradually and never be discontinued abruptly.

Keep out of reach of children. For use in animals only.

Refer to folded label attached to this container and read carefully before use.

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**Boehringer Ingelheim  
Vetmedica, Inc.**  
St. Joseph, MO 64506 U.S.A.



**Boehringer Ingelheim Vetmedica, Inc.**

2621 North Belt Highway • St. Joseph, MO 64506-2002

Information 800-325-9167 • Sales Service 800-325-9167 • Fax 816-236-2717

[www.bi-vetmedica.com](http://www.bi-vetmedica.com)