



# Phenobarbital

Phenobarbital is an effective antiepileptic drug used in dogs and cats.<sup>1-3</sup>

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## Overview

⚠ Many adverse events associated with phenobarbital (PB) use in dogs and cats are transient; others are acceptably managed with appropriate client education.<sup>1,3</sup>

⚠ Hepatotoxicity can develop in dogs treated chronically with PB<sup>3-6</sup> but

- Is avoidable with diligent therapeutic monitoring
- May be reversible with prompt drug withdrawal and supportive therapy

⚠ Early recognition and treatment are key in resolving any complication that may arise.

## Adverse Events

⚠ Adverse events are more commonly observed in dogs than in cats.<sup>2,3</sup>

⚠ Common acute and transient

adverse behavioral effects include sedation, hyperexcitability, and restlessness.

- Signs resolve in most patients within 2 weeks of starting therapy.<sup>1,3</sup>
  - Improvement may result from induction of PB biotransformation over time.

⚠ Frequently reported chronic and persistent side effects are polydipsia, polyuria, and polyphagia.

- Can be intolerable to some owners, requiring changing the antiepileptic drug (AED)<sup>1,3</sup>

⚠ In dogs, subacute-to-chronic treatment is often associated with subclinical laboratory abnormalities, including<sup>3,7</sup>

- Decreased total and free thyroxine concentrations
- Mild-to-moderate elevations in ALP and, to a lesser extent, ALT

## Toxicities & Severe Reactions

⚠ Hepatotoxicity

- Most common clinically significant, severe complication associated with PB<sup>3,4,8</sup>
- Risk factors include
  - Chronic PB use
  - Serum PB concentrations >35 µg/mL (151 µmol/L)
  - Concurrent therapy with other hepatotoxic drugs (see **Warnings**)
- May result in irreversible and fatal hepatic failure
- Clinical signs
  - Abdominal effusion
  - Anorexia
  - Icterus and pigmenturia
  - Marked sedation and ataxia
  - Vomiting/diarrhea
- Laboratory abnormalities
  - Elevated bile acid concentrations
  - Low serum albumin (hypoalbuminemia)

**Hepatotoxicity is the most common clinically significant, severe complication associated with phenobarbital therapy.**

## Avoid use of phenobarbital in patients with preexisting hepatic disease.

- Increased serum PB concentration without dose escalation
- Moderate-to-marked elevations in ALP and ALT

- ⚠ Blood dyscrasia<sup>3,5</sup>
  - Rare idiosyncratic reaction that usually develops within several months of therapy
  - Clinical signs
    - Anorexia
    - Fever
    - Lethargy
    - Splenomegaly
    - Spontaneous hemorrhage
  - Laboratory abnormalities
    - Neutropenia
    - Thrombocytopenia
    - Anemia
- ⚠ Superficial necrolytic dermatitis<sup>8</sup>
  - Multifocal dermatopathy characterized by erythema and papules that progress to erosions
    - Predilection for footpads, mucocutaneous junctions, and axillary and inguinal regions

- Can develop with chronic PB administration
- Often associated with laboratory, ultrasonographic, and histopathologic evidence of hepatic disease
  - Overt clinical hepatic failure is rare.

- ⚠ Dyskinesia<sup>6</sup>
  - Rare reaction defined by abnormal, involuntary, repetitive muscle movements that distort or impair voluntary motions

### Treatment Monitoring & Precautionary Measures<sup>3-6</sup>

- ⚠ CBC, serum chemistry panel, and urinalysis should be performed before PB therapy is initiated.
- ⚠ After steady-state PB concentrations are confirmed (at approximately 2 weeks), monitor serum PB concentrations, serum chemistry panel findings, and serum

bile acids q6mo in patients on chronic PB therapy.

- ⚠ Serious hepatotoxicity requires
  - Prompt PB discontinuation
  - Appropriate symptomatic and supportive care
    - Fluids
    - Gastric protectants
    - Dietary and nutraceutical hepatic support
    - Management of hepatic encephalopathy or coagulopathy (if present)
    - Other measures as indicated
- ⚠ Acute PB withdrawal may precipitate seizures.
  - Consider loading with additional AED (eg, potassium bromide).
- ⚠ Hepatotoxicity, myelosuppression, and dyskinesia may be reversible with prompt recognition and treatment.

### Warnings<sup>3,4</sup>

- ⚠ Avoid PB use in patients with preexisting hepatic disease.



## WORDS OF CAUTION

PEER REVIEWED

### Perform CBC, serum chemistry panel, and urinalysis before initiating therapy.

- ⚠ Risk for clinically significant liver dysfunction may increase when PB is administered with other hepatotoxic drugs.
- ⚠ May potentiate sedative effects of CNS depressants (eg, anti-histamines, benzodiazepines, narcotics)
- ⚠ Hepatic or intestinal P450 activities induced by PB may result in drug interactions by increasing drug metabolism, resulting in
  - Reduced blood concentrations and therapeutic efficacy (eg, cyclosporine, doxycycline, zonisamide, mitotane)
  - Increased active metabolites of parent compound, thus potentiating therapeutic effects or causing toxic effects (eg, acetaminophen)

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Methimazole Risks



#### Caution

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

#### Indications

SENTINEL SPECTRUM® (milbemycin oxime/lufenuron/praziquantel) is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*; for the prevention and control of flea populations (*Ctenocephalides felis*); and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Taenia pisiformis*, *Echinococcus multilocularis* and *Echinococcus granulosus*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

#### Dosage and Administration

SENTINEL SPECTRUM should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 4.55 mg/lb (10 mg/kg) lufenuron, and 2.28 mg/lb (5 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes.

Dosage Schedule				
Body Weight	Milbemycin Oxime per chewable	Lufenuron per chewable	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	46 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	115 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	230 mg	114 mg	One
50.1 to 100 lbs.	23.0 mg	460 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables			

To ensure adequate absorption, always administer SENTINEL SPECTRUM to dogs immediately after or in conjunction with a normal meal.

SENTINEL SPECTRUM may be offered to the dog by hand or added to a small amount of dog food. The chewables should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole. Care should be taken that the dog consumes the complete dose, and treated animals should be observed a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, re-dosing is recommended.

#### Contraindications

There are no known contraindications to the use of SENTINEL SPECTRUM.

#### Warnings

Not for use in humans. Keep this and all drugs out of the reach of children.

#### Precautions

Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Prior to administration of SENTINEL SPECTRUM, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. SENTINEL SPECTRUM is not effective against adult *D. immitis*.

Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Do not use in puppies less than six weeks of age.

Do not use in dogs or puppies less than two pounds of body weight.

The safety of SENTINEL SPECTRUM has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime and lufenuron alone.

#### Adverse Reactions

The following adverse reactions have been reported in dogs after administration of milbemycin oxime, lufenuron, or praziquantel: vomiting, depression/lethargy, pruritus, urticaria, diarrhea, anorexia, skin congestion, ataxia, convulsions, salivation, and weakness.

To report suspected adverse drug events, contact Novartis Animal Health at 800-637-0281 or the FDA at 1-888-FDA-VETS.

Manufactured for: Novartis Animal Health U.S. Inc.  
Greensboro, NC 27408, USA

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