Phenobarbital

Phenobarbital is an effective antiepileptic drug used in dogs and cats.[1-3]

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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.[1,3]

⚠ Hepatotoxicity can develop in dogs treated chronically with PB[3-6] 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.[2,3]

⚠ Common acute and transient adverse behavioral effects include sedation, hyperexcitability, and restlessness.
- Signs resolve in most patients within 2 weeks of starting therapy.[1,3]
  —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)[1,3]

⚠ In dogs, subacute-to-chronic treatment is often associated with subclinical laboratory abnormalities, including[3,7]
- 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[3,4,8]
- 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[3,5]
- 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[8]
- 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[6]
- Rare reaction defined by abnormal, involuntary, repetitive muscle movements that distort or impair voluntary motions

Treatment Monitoring & Precautionary Measures[3-6]

⚠ 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[3,4]

⚠ Avoid PB use in patients with preexisting hepatic disease.

AED = antiepileptic drug, PB = phenobarbital

MORE ▶

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, antihistamines, 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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