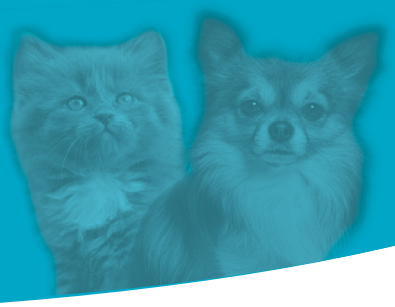
Phenobarbital Utilization with the VETSCAN® VS2

Michelle Larsen, DVM



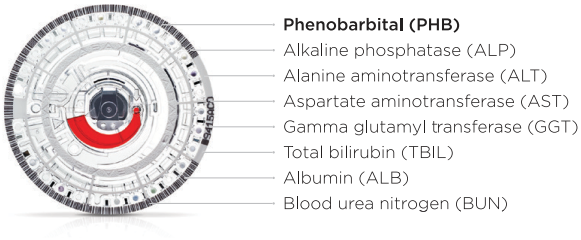
Introduction

Phenobarbital (PHB) often serves as a first line medication for the treatment of primary seizures in dogs and cats.[1] It is a long-acting, barbiturate medication and a popular choice due to efficacy, availability, cost, dosing convenience, and safety when dosed and monitored appropriately. Seizures are controlled in 70% of dogs and most cats with PHB monotherapy.[2]

PHB takes 2-3 weeks to achieve blood steady state levels in dogs and cats.

VETSCAN® Phenobarbital Profile

The VETSCAN Phenobarbital Profile used with the VETSCAN VS2 Chemistry Analyzer provides comprehensive evaluation of the PHB level, alongside analytes that screen for hepatotoxicity to provide ideal, comprehensive patient monitoring.



Advantages of the VETSCAN Phenobarbital Profile

- Cost effective test that evaluates both PHB and liver values simultaneously.
- Immediately and thoroughly evaluate a patient receiving PHB medication when run with a complete blood count.
- Immediate monitoring and titration of PHB for in-clinic client discussion and improved client compliance.

Mechanism of Action

PHB stabilizes neurons by acting on the GABA receptors. This increases the seizure threshold and reduces the spread of seizure activity.

Pharmacokinetics

PHB has a long half-life, and it takes 2-3 weeks to achieve blood steady state levels in dogs and cats.[3]

Hepatotoxicty can be avoided in an otherwise healthy patient when phenobarbital is dosed within the therapeutic range.

Beginning PHB Therapy

An initial database should be performed prior to starting chronic PHB medication. PHB levels should be evaluated once steady state levels are achieved.

- This is generally recommended at 14 and 28 days initially.
- An appropriate starting dose is 2.5 mg/kg orally every 12 hours.[2]

Monitoring PHB Therapy[2]

1. PHB levels should be tested 2 weeks after starting treatment or 2 weeks after any change in dose or dosing frequency.[2]
2. Routinely perform PHB levels every 6 months along with a full liver panel and complete blood count to screen for bone marrow suppression and hepatotoxicity.[2]
3. Re-test PHB levels whenever 2 or more seizures occur between scheduled PHB evaluations.[2]

PHB Monitoring Best Practices

- Drug levels should be obtained at the same time relative to the time the medication was administered for each sampling.[2]
- While peak and trough levels have been discussed in past literature, trough levels are often sufficient for monitoring at 6-12 month intervals.
- Trough levels are recommended at baseline and if the patient has breakthrough seizures.[5]
- Over time, PHB may induce hepatic microsomal enzymes increasing its own elimination and warranting a higher dose to maintain therapeutic levels.[2]

Conclusion

Once properly diagnosed and evaluated, control to minimize seizures can be accomplished with the use of anti-epileptic drugs. The VETSCAN Phenobarbital Profile provides comprehensive clinical diagnostic monitoring of patient PHB level along with important relevant chemistry values on a single panel. Use of the VETSCAN Phenobarbital Profile allows PHB to be used to prevent seizures, safely and effectively.

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PHB levels should be tested:

- 2 weeks after starting treatment or 2 weeks after any change in dose or dosing frequency
- Every 6 months along with a full liver panel and complete blood count
- Whenever 2 or more seizures occur between scheduled PHB evaluations[2]

Reported Adverse Effects

Side effects can include sedation, ataxia, polyphagia, weight gain, polyuria and polydipsia (PU/PD), hepatotoxicity, bone marrow suppression and hyper-excitability.[2]

- Hepatotoxicty is usually avoided in an otherwise healthy patient when dosed within the therapeutic range.[4]
- Sedation and ataxia typically subside after the first 10-21 days of therapy.[2]
- Owners should be warned to refrain from over feeding their pet due to the side effect of polyphagia.
- In addition, PHB increases the biotransformation of drugs metabolized by the liver, decreasing the effects of many medications that may be administered concurrently.
- Drugs that inhibit microsomal enzymes may dramatically inhibit the metabolism of PHB, resulting in higher and potentially hepatotoxic levels.

PHB and Hypothyroidism[2]

In dogs, PHB at therapeutic doses may decrease serum T4 and fT4 concentrations into a range consistent with hypothyroidism.[2] A delayed increase in TSH occurs as fT4 and T4 concentrations decline, while usually staying within the reference interval.[8] Evidence for this effect on thyroid hormones in cats has not been demonstrated. If there is concern for primary hypothyroidism, it is recommended to discontinue use of PHB to determine if the patient is truly hypothyroid, or if it is secondary to PHB usage. It may take up to 4 weeks after discontinuing PHB for fT4 and T4 levels to return to normal.[8]

Phenobarbital Drug Interactions

Listed below are more commonly used medications that may require higher doses in an animal on PHB due to microsomal p450 enzyme induction.[6] This list includes, but is not limited to the following medications:

- Corticosteroids
- Some antibiotics, including doxycycline
- Certain heart medications
- Metronidazole
- Mitotane
- Clomipramine
- Ketoconazole

Commonly used drugs inhibit microsomal enzymes and therefore may lead to increased PHB blood concentrations +/- hepatotoxicity.[2] This list includes, but is not limited to the following medications:

- Chloramphenicol
- Tetracycline
- Cimetidine and Ranitidine

Note: The p450 microsomal enzyme inducer is not reported in cats.[7]

References/Citations:

1. Ettinger SJ, Feldman EC, Côté E. Textbook of Veterinary Internal Medicine: Diseases of the Dog and the Cat. 8th ed. St. Louis: Chapter 35, p. 142 Elsevier; 2017. **2.** Nelson RW, Couto CG. Small Animal Internal Medicine. 4th ed. St. Louis: Elsevier; pages 1042-1043. 2009. **3.** Shell L. Maintenance Anticonvulsant or Antiepileptic Therapy - Pharmacology - Veterinary Manual. Merck Manual: Veterinary Manual. http://www.merckvetmanual.com/pharmacology/systemic-pharmacotherapeutics-of-the-nervous-system/maintenance-anticonvulsant-or-antiepileptic-therapy. Accessed April 28, 2017. **4.** Therapeutic ranges may differ depending on the manufacturer of laboratory equipment. Ranges specific to the VETSCAN VS2 can be found in the package insert for the VETSCAN® Phenobarbital Profile. **5.** Willard, Michael and Tvedten, Harold. Small Animal Clinical Diagnosis by Laboratory Methods. 5th Edition. p. 393. **6.** Trepanier L. Top ten drug interactions in dogs and cats (Proceedings). dvm360.com. http://veterinarycalendar.dvm360.com/top-ten-drug-interactions-dogs-and-cats-proceedings?id=&sk=&date=&%0A%09%09%09&pageID=2. Published 2010. Accessed April 28, 2017. **7.** Truhaut R, Ferrando R, Graillot C, Gak JC, Fourlon C, Moraillon R. [Induction of cytochrome P 450 by phenobarbital in cats]. C R Acad Sci Hebd Seances Acad Sci D. 1978;286(4):371-373. **8.** Feldman, Edward et al. Canine & Feline Endocrinology, 4th Edition, p.116, 2015.

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