Phenobarbital (Phenobarbitone)

(Epiphen (d), Epityl (d), Phenoleptil (d), Soliphen (d), Phenobarbital*) POM-V, POM CD SCHEDULE 3

- **Formulations**

Oral: 12.5 mg, 30 mg, 50 mg, 60 mg, 100 mg tablets; 4% (40 mg/ml) oral solution. Injectable: 15 mg/ml, 30 mg/ml, 60 mg/ml, 200 mg/ml solutions (phenobarbital sodium BP).

- **Action**

Thought to mediate its antiepileptic effect through affinity for the $GABA_A$receptor, resulting in a GABA-ergic effect; GABA being the major inhibitory mammalian neurotransmitter with prolonged opening of the chloride channel. Phenobarbital also blocks the AMPA receptor, inhibiting release of the excitatory neurotransmitter glutamate. This combined potentiation of GABA and inhibition of glutamate leads to reduced neuronal excitability.

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- **Use**
    - Phenobarbital and imepitoin are the initial medications of choice for the management of epileptic seizures due to idiopathic epilepsy in dogs. The choice of initial medication is guided by patient requirements: phenobarbital is more efficacious, while imepitoin has a more rapid onset of action than phenobarbital (does not need to achieve a steady state), does not require the determination of serum concentrations and has a less severe adverse effect profile.
    - Also authorized for the management of epileptic seizures due to structural brain disease in dogs.
    - Used for the management of epileptic seizures in cats, although not authorized.
    - Phenobarbital may also be used in dogs in combination with propranolol and a behaviour modification programme for the control of fears and anxieties, especially those with a large physiological component which may be antagonizing the condition through biofeedback processes.

Phenobarbital is rapidly absorbed after oral administration in dogs; maximal plasma concentrations reached within 4–8 hours. Wide range of elimination half-life (40–90 hours) in dogs. Steady state serum concentrations are not reached until 7–10 days after treatment is initiated and the full clinical effect of a dose cannot be ascertained until this point. Serum concentrations should be determined once a steady state has been reached; if <15 µg (micrograms)/ml, the dose should be increased accordingly. If seizures are not adequately controlled, the dose may be increased up to a maximum serum concentration of 45 µg/ml. Plasma concentrations above this level are associated with increased hepatotoxicity. Blood samples for serum concentration determination should be collected at the same time of day relative to the time of dose administration in dogs on higher daily doses, but timing is not normally important in dogs on a total daily dose of <8 mg/kg. For accuracy of dosing, dogs <4 kg should commence therapy with the oral solution. With chronic therapy, induction of the hepatic microsomal enzyme system results in a decreased half-life, particularly during the first 6

months of therapy in dogs. As a result, the dose may need to be increased. Phenobarbital levels should be assessed every 6–12 months. Any termination of phenobarbital therapy should be performed gradually (recommended protocol: reduce the dose by 25% of the original dose each month).

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- **DOSES**
    - **Dogs**
        - Initial therapy: 1–2.5 mg/kg p.o. q12h (authorized dose). However, in one study only 40% of dogs started on this dose achieved therapeutic serum concentrations. Therefore, initial dose recommendation is usually 2.5–3 mg/kg p.o. q12h. Incremental modifications of the initial dose, based on serum concentrations, are essential.
        - Emergency management of status epilepticus or severe cluster seizures in dogs that have not been receiving maintenance phenobarbital: aim for a total loading dose of 18–24 mg/kg, followed by a maintenance dose of 2–3 mg/kg q12h. The loading dose is given as an initial 12 mg/kg slow i.v. and then after 20 minutes, two further doses of 4–6 mg/kg slow i.v. 20 minutes apart. Always wait 20 minutes before giving additional doses as CNS levels take 20 minutes to respond, and do not administer if the dog is excessively sedated or has evidence of respiratory depression. Higher doses may be required in very small dogs.
        - Emergency management in dogs that have been receiving maintenance phenobarbital: 4–6 mg/kg i.v. or i.m. to increase the blood levels slightly in case these were subtherapeutic. Always take a serum sample for phenobarbital level determination first, before giving the top-up dose.
        - Control of fear and anxiety: 2–3 mg/kg p.o. q12h with propranolol also at 2–3 mg/kg p.o. q12h.
    - **Cats**
        - Initial therapy: 1.5–3 mg/kg p.o. q12h.
        - Emergency management: doses as for dogs.