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PRESCRIPTION ANIMAL REMEDY
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING
FOR ANIMAL TREATMENT ONLY

Pexion®

100 mg Tablets for Dogs
400 mg Tablets for Dogs

Boehringer Ingelheim

Active constituent:
100 mg tablet contains 100 mg imepitoin.
400 mg tablet contains 400 mg imepitoin.

Statement of Claim
Imepitoin is an antiepileptic agent for use as an aid in the treatment of idiopathic epilepsy in dogs.

Action
Imepitoin is a centrally acting antiepileptic drug which acts as a low affinity partial agonist of the benzodiazepine receptor. Imepitoin potentiates the $GABA_A$ receptor-mediated inhibitory effects on the neurons and thereby prevents seizures. In addition, imepitoin has a weak calcium channel blocking effect which may contribute to its anticonvulsive properties. Imepitoin differs from high affinity benzodiazepine receptor agonists (e.g. diazepam), as the lower binding affinity of imepitoin results in superior safety in long term use.

In seizure models, imepitoin was effective against different seizure types. In addition, imepitoin was effective in anxiety models and in stress-related agitation models. In laboratory animals with brain insults, imepitoin was effective in preventing the development of epilepsy. Imepitoin was also shown to exert neuroprotective benefits in a model of ischemia-induced neurodegeneration.

Long term use of imepitoin does not induce pharmacoresistance (drug tolerance) and cessation of therapy does not result in withdrawal symptoms. Imepitoin has a low interaction potential with centrally acting pharmaceuticals. Imepitoin treatment does not need to be discontinued if general anaesthesia is required, however recovery periods may be longer than usual.

In patients with drug resistant epilepsy, imepitoin can be combined with phenobarbital. The anticonvulsant activity is potentiated and the combination treatment is well tolerated.

In patients where phenobarbital preparations are to be replaced by imepitoin, the potential of phenobarbital to cause withdrawal symptoms should be considered.

If emergency treatment is required to interrupt a status epilepticus, a short acting full benzodiazepine agonist (e.g. diazepam) can be administered or general anaesthesia can be initiated. The efficacy of Pexion in dogs with status epilepticus and cluster seizures has not been investigated. Therefore, Pexion should not be used as a primary treatment in dogs with cluster seizures and status epilepticus.

Pharmacokinetic Properties
Imepitoin is well absorbed (> 92%) after oral administration. At 30 mg/kg without food, peak blood concentrations are attained rapidly with a Tmax of around 2 hours. The plasma protein binding of imepitoin in dogs is low (60 to 70%), therefore, no interaction with highly protein bound compounds is expected. Imepitoin is rapidly cleared from blood with an elimination half-life of approximately 1.5 to 2 hours. Imepitoin is extensively metabolised prior to elimination. The majority of imepitoin and its metabolites are excreted via the faecal route so that no accumulation is expected in renally impaired dogs.

DIRECTIONS FOR USE
Contraindications
This product is contraindicated in dogs that have demonstrated hypersensitivity to imepitoin.
This product is contraindicated in dogs with severely impaired hepatic function, severe renal or severe cardiovascular disorders.

Precautions
Use during reproduction, pregnancy or lactation should be based on a benefit/risk assessment by the veterinarian.
Careful consideration should be given before deciding to switch a stabilized dog onto imepitoin from a different treatment. When transition between different antiepileptic therapies is medically required, this should be done gradually and with appropriate clinical supervision.

Side Effects
The following mild and generally transient adverse reactions have been observed in pre-clinical and clinical studies (in order of decreasing frequency): polyphagia (increased appetite) at the beginning of the treatment, also hyperactivity (much more active than usual), polyuria (increased urine production), polydipsia (increased thirst), somnolence (drowsiness), hypersalivation (increased saliva production), emesis (vomiting), ataxia (loss of coordination), apathy, diarrhoea, prolapsed nictitating

membrane (visible third eyelid), decreased sight and sensitivity to sound. A mild elevation in plasma creatinine and cholesterol levels has been observed in dogs treated with imepitoin; however these did not exceed the normal reference ranges and were not associated with any clinically significant observations or events.

Dosage and Administration
Give orally at an initial dose rate of 10 mg imepitoin per kg bodyweight twice daily, approximately 12 hours apart. The dose can be increased up to 30 mg/kg bodyweight twice daily if required. Tablets can be administered with or without food, although studies suggest superior absorption in fasted dogs. The timing of tablet administration in relation to feeding should be kept consistent. The required dose will vary between dogs and will depend on the severity of the disorder. The recommended initial dose of imepitoin is 10 mg per kg bodyweight twice daily.

Initiate therapy using the bodyweight in kg and the dosing table below. If seizures are not adequately reduced following a minimum of 1 week of treatment at the current dose the supervising veterinarian should re-assess the dog. Assuming that Pexion is well tolerated by the dog, the dose can be increased by 50 to 100% increments up to a maximum dosage of 30 mg per kg administered twice daily.

Each tablet can be halved for appropriate dosing according to the individual bodyweight of the dog. Use any divided tablet at the next administration time.

Suggested number of tablets (to be given twice daily) for initiation of treatment:

Bodyweight (kg)	Number of tablets	
	100 mg tablet	400 mg tablet
5.0	½	
5.1 - 10.0	1	
10.1 - 15.0	1 ½	
15.1 - 20.0		½
20.1 - 40.0		1
40.1 - 60.0		1 ½
Over 60		2

General Directions
Before commencing treatment with Pexion, an appropriate diagnostic investigation should be conducted to rule out causes of seizures that may require other treatments; that is, to confirm the diagnosis of idiopathic epilepsy.

Because of the nature of epilepsy, the pharmacological response to Pexion may vary. Some dogs will be free of seizures, in other dogs a reduction of the number of seizures will be observed, whilst others may be non-responders. In non-responders, an increase in seizure frequency may be observed. Should seizures not be adequately controlled, further diagnostic measures and other antiepileptic treatment should be considered.

No loss of anticonvulsant efficacy (tolerance development) during continuous treatment of 4 weeks was observed in experimental studies lasting 4 weeks.

Overdose
Pexion has a high margin of safety in dogs.

In cases of repeated overdose with 5 times the highest recommended dose, neurologic and gastrointestinal-related effects have been noted. At such doses, the signs are not usually life threatening and generally disappear within 24 hours if symptomatic treatment is given. Neurologic effects may include ataxia (unsteadiness), loss of righting reflex (loss of balance), decreased activity, eyelid closure, lacrimation (excessive tears), dry eye (inadequate tears), and nystagmus (unusual eye movement). Gastrointestinal effects may include salivation, vomiting and white material (tablet residues) in faeces.

SAFETY DIRECTIONS
Wash hands after use.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766 (0800 POISON)

Additional User Safety
Harmful if swallowed. May irritate the eyes. Avoid contact with eyes.

Disposal
Dispose of empty container by wrapping with paper and putting in garbage.

Storage
Store below 30°C (room temperature).

Presentation
High density polyethylene bottle of 100 or 250 tablets with a child resistant closure and a desiccant canister.
Not all pack sizes may be marketed.

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APVMA Approval No.:
67812/56906, 67813/56907.

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See www.foodsafety.govt.nz for registration conditions.