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Pexion 100 mg tablets for dogs, Pexion 400 mg tablets for dogs

Species: Dogs

Therapeutic indication:Pharmaceuticals: Neurological preparations: Others

Active ingredient: Imepitoin

Product: Pexion® 100 mg tablets for dogs, Pexion® 400 mg tablets for dogs

Product index: Pexion

Incorporating:

Presentation

White, oblong, half-scored tablets with embedded logo “I 01” (100 mg) or “I 02” (400 mg) on one side. The tablet can be divided into equal halves. One tablet contains either 100 mg imepitoin or 400 mg imepitoin.

Excipients:

Qualitative composition of excipients and other constituents

Lactose monohydrate

Cellulose microcrystalline

Hypromellose

Magnesium stearate

Sodium starch glycolate

Uses

NOAH Compendium

For the reduction of the frequency of generalised seizures due to idiopathic epilepsy in dogs for use after careful evaluation of alternative treatment options.

For the reduction of anxiety and fear associated with noise phobia in dogs.

Dosage and administration

Idiopathic Epilepsy

Oral administration at a dose range of 10 mg to 30 mg imepitoin per kg bodyweight twice daily, approximately 12 hours apart. Each tablet can be halved for appropriate dosing according to the individual bodyweight of the dog. Any remaining half-tablet should be used for the next dose.

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. If seizures are not adequately reduced following a minimum of 1 week of treatment at the current dose the supervising veterinary surgeon should re-assess the dog. Assuming that the veterinary medicinal product 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.

Bioavailability is greater when administered to fasted dogs. The timing of tablet administration in relation to feeding should be kept consistent.

Number of tablets (to be given twice daily) for initiation of epilepsy treatment:

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

Noise phobia

Oral administration at a dose of 30 mg imepitoin per kg bodyweight twice daily, approximately 12 hours apart. Each tablet can be halved for appropriate dosing according to the individual bodyweight of the dog.

Initiate therapy 2 days prior to the day of the expected noise event and continue through the noise event using the bodyweight in kg and the dosing table below.

Bioavailability is greater when administered to fasted dogs. The timing of tablet administration in relation to feeding should be kept consistent.

Number of tablets (to be given twice daily) for noise phobia treatment:

	Number of tablets
Bodyweight (kg)	**100 mg**
2.5 - 3.9	1
4 - 5.9	1½
6 - 7.9	2
8 - 10.9	3
11 - 15.9	
16 - 22.9	
23 - 29.9	
30 -36.9	
37 - 43.9	
44 - 49.9	
50 - 55.9	
56 - 71.9	
72 -80	

Contra-indications, warnings, etc

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Do not use in dogs with severely impaired hepatic function, severe renal or severe cardiovascular disorders.

Special Warnings

Idiopathic epilepsy

The pharmacological response to imepitoin may vary and efficacy may not be complete. On treatment, some dogs will be free of seizures, in other dogs a reduction of the number of seizures will be observed, whilst others will be non-responders. For this reason, careful consideration should be given before deciding to switch a stabilized dog onto imepitoin from a different treatment. 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. When transition between different antiepileptic therapies is medically required, this should be done gradually and with appropriate clinical supervision.

The efficacy of the veterinary medicinal product in dogs with status epilepticus and cluster seizures has not been investigated. Therefore, imepitoin should not be used as primary treatment in dogs with cluster seizures and status epilepticus.

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

No definitive conclusions can be drawn on the effectiveness of imepitoin as an add-on therapy to phenobarbital, potassium bromide and/or levetiracetam from the limited studies available (see section **Interaction with other medicinal products and other forms of interaction**).

Noise phobia

Efficacy for reduction of anxiety and fear associated with noise phobia has not been tested in dogs younger than 12 months.

Up to 2 days of pre-treatment may be necessary to achieve optimal anxiolytic efficacy in dogs with noise phobia. See section “Dosage for each species, route(s) and method of administration”.

Special precautions for use in animals

Special precautions for safe use in the target species:

The safety of the veterinary medicinal product has not been tested in dogs weighing less than 2 kg or in dogs with safety concerns such as renal, liver, cardiac, gastrointestinal or other disease.

Anxiolytic drugs acting at the benzodiazepine receptor site, such as imepitoin, may lead to disinhibition of fear-based behaviours. The veterinary medicinal product may therefore result in an increase or decrease in aggression levels.

In dogs with a history of aggression problems, a careful benefit-risk evaluation should be made prior to treatment. This evaluation may include consideration of inciting factors or situations associated with previous aggressive episodes. Prior to initiating treatment in these cases, behaviour therapy or referral to a behaviour specialist should be considered. In these dogs, additional measures to mitigate the risk of aggression problems should be implemented as appropriate before treatment is initiated.

Mild behavioural or muscular signs may be observed in dogs upon abrupt termination of treatment with imepitoin.

The claim for the treatment of noise phobia is based on a pivotal field study which investigated a 3 day course of treatment for a noise event associated with fireworks. Longer treatment durations for noise phobia should be at the benefit-risk assessment of the veterinarian. Consideration should be given to use of a behavioural modification programme.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Ingestion of this veterinary medicinal product may cause dizziness, lethargy and nausea.

In case of accidental ingestion especially by a child, seek medical advice immediately and show the package leaflet or the label to the physician.

To prevent accidental ingestion of tablets, the cap of the bottle should be replaced immediately after withdrawing the required number of tablets for one administration.

Special precautions for the protection of the environment:

Not applicable.

Adverse reactions:

Dogs:

Idiopathic epilepsy

Very common	Ataxia1, somnolence1
(>1 animal / 10 animals treated):	Emesis1
	Increased appetite1,2
Common	Hyperactivity1
(1 to 10 animals / 100 animals treated):	Apathy1, anorexia1, polydipsia1
	Disorientation1
	Hypersalivation1, diarrhoea1
	Polyuria1
Uncommon	Agression3
(1 to 10 animals / 1,000 animals treated):	
Rare	Increased sensitivity to sound3
(1 to 10 animals / 10,000 animals treated):	Anxiety3
	Elevated Creatinine4
Very rare	Elevated blood urea nitrogen (BU
(<1 animal / 10,000 animals treated, including isolated reports):	Prolapse of the nictitating memb

1 Mild and generally transient.

2 At the beginning of treatment.

3 Potentially treatment related. It may also be present during the preictal or postictal period or as behaviour changes which occur as part of the disease itself.

4 Mild; however generally not exceeding normal reference ranges and not associated with any clinically significant observations or events.

Noise phobia

Very common	Ataxia1, 2
(>1 animal / 10 animals treated):	Increased appetite1,2
Common	Emesis2
(1 to 10 animals / 100 animals treated):	Aggression2
Uncommon	Hyperactivity2
(1 to 10 animals / 1,000 animals treated):	Somnolence2
	Hypersalivation2

1 Transient. Occurred early in the treatment course. In more than half of the dogs that experienced ataxia during a clinical trial the signs resolved spontaneously within 24 hours in spite of continued treatment and in half of the remaining dogs within 48 hours.

2 Most events are transient, resolving during or shortly after the end of the treatment course.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

Pregnancy and lactation

The use of the veterinary medicinal product is not recommended in female dogs during pregnancy and lactation.

Fertility:

Do not use in male breeding animals (see section **Symptoms of overdose (and where applicable, emergency procedures and antidotes)).**

Interaction with other medicinal products and other forms of interaction

The veterinary medicinal product has been used in combination with phenobarbital, potassium bromide and/or in a small number of cases with levetiracetam and no harmful clinical interactions were observed (see section “Special warnings”).

Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In case of repeated overdose of up to 5 times the highest recommended dose of 30 mg imepitoin per kg bodyweight, central nervous system (CNS) effects, gastrointestinal-related effects and reversible prolongation of the QT interval have been noted. At such doses, the symptoms are not usually life-threatening and generally resolve within 24 hours if symptomatic treatment is given.

These CNS effects may include loss of righting reflex, decreased activity, eyelid closure, lacrimation, dry eye and nystagmus.

At 5 times the recommended dose, decreased bodyweight may be observed.

In male dogs administered 10 times the upper recommended therapeutic dose, diffuse atrophy of seminiferous tubules in the testes and associated decreased sperm counts were seen. See also section **Use during pregnancy, lactation or lay**.

Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

Not applicable.

Withdrawal periods

Not applicable.

Pharmaceutical precautions

Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

Nature and composition of immediate packaging

Pack sizes of high-density polyethylene bottle each containing 30, 100 or 250 tablets with a child resistant closure.

Not all pack sizes may be marketed.

Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

Legal category

Legal category:POM-V

Packaging quantities

Pack sizes of 1 high-density polyethylene bottle each containing of 30, 100 or 250 tablets with a child resistant closure. Not all pack sizes may be marketed.

Further information

PHARMACOLOGICAL INFORMATION

ATCvet code: QN03AX90.

Pharmacodynamics

Imepitoin is a centrally acting substance with anxiolytic and antiepileptic properties which

crosses the blood brain barrier without involvement of active transport or active clearance, resulting in immediate equilibrium between plasma and brain. Here it acts as a low affinity partial agonist of the benzodiazepine receptor.

The anxiolytic effect of imepitoin is mediated via the GABAA receptor. Imepitoin also inhibits seizures via potentiation of the GABAA receptor-mediated inhibitory effects on the neurons and in addition, imepitoin has a weak calcium channel blocking effect which may contribute to its anticonvulsive properties.

Clinical trials in epilepsy

In a European field trial that compared the efficacy of imepitoin to phenobarbital in 226 dogs with newly diagnosed idiopathic epilepsy, 45% of cases from the imepitoin group and 20% from the phenobarbital group were excluded from the efficacy analysis for reasons that included failure to respond to treatment. In the remaining dogs (64 dogs for Pexion and 88 dogs for phenobarbital), the following clinical results were observed: Mean frequency of generalised seizures was reduced from 2.3 seizures per month in the imepitoin group and from 2.4 seizures per month in the phenobarbital group to 1.1 seizures per month in both groups after 20 weeks of treatment. The difference between imepitoin and phenobarbital groups in the seizure frequency per month after treatment (adjusted for baseline difference) was 0.004, 95% CI [-0.928, 0.935]. During the evaluation phase of 12 weeks, the proportion of generalised seizure-free dogs was 47% (30 dogs) in the imepitoin group and 58% (51 dogs) in the phenobarbital group.

The safety of both treatments was evaluated in the full analysis data set (or safety data set, i.e. 116 animals in the imepitoin group and 110 animals in the phenobarbital group). Increasing doses of phenobarbital were associated with increasing levels of the liver enzymes ALT, AP, AST, GGT, and GLDH. In comparison, none of the five enzymes increased with increasing doses of imepitoin. A slight increase in creatinine values compared to baseline was observed in the imepitoin-treated dogs. However, the upper limit of the confidence interval for creatinine remained within the reference range at all visits. Additionally, fewer adverse events were noted for polyuria (10% vs 19% of dogs),

polydipsia (14% vs 23%) and marked sedation (14% vs 25 %) when comparing imepitoin to phenobarbital. Please refer to section 3.6 of the SPC for further details of adverse events.

In a US field trial that compared the efficacy of imepitoin at a fixed dose of 30 mg/kg twice daily to a placebo in 151 dogs with idiopathic epilepsy during a treatment period of 84 days, the proportion of generalized seizure-free dogs was 21% (21 dogs out of 99; 95 % CI [0.131; 0.293]) in the imepitoin group and 8% (4 dogs out of 52; 95% CI [0.004; 0.149]) in the placebo group. 25% of dogs did not respond to the treatment with imepitoin (same or increased frequency of seizures).

Pharmacokinetic particulars

Absorption

Pharmacokinetic studies indicate that imepitoin is well absorbed (> 92 %) after oral administration and that no pronounced first pass effect occurs. After oral administration of imepitoin tablets at 30 mg/kg without food, peak blood concentrations are attained rapidly with a Tmax of around 2 hours, a Cmax of about 18 µg/ml. Co-administration of imepitoin tablets with food, reduces the total AUC by 30% but produces no significant change in Tmax and Cmax. Gender-specific differences do not occur.

Distribution

Dose linearity occurs over the therapeutic dose range of imepitoin. Imepitoin has a relatively high volume of distribution (579 to 1548 ml/kg). The *in-vivo* plasma protein binding of imepitoin in dogs is low (60 to 70%). No interaction with highly protein bound compounds is therefore expected. No accumulation of imepitoin in plasma occurs after repeated administration, once steady state is reached.

Metabolism

Imepitoin is extensively metabolised prior to elimination. Metabolite profiles in urine and faeces revealed four major inactive metabolites which are formed by oxidative modification.

Elimination

Imepitoin is rapidly cleared from blood (Cl = 260 to 568 ml/hours/kg) with an elimination half-life of approximately 1.5 to 2 hours. The majority of imepitoin and its metabolites are excreted via the faecal route rather than the urinary route so that no major change in pharmacokinetics and no accumulation is expected in renally impaired dogs.

Marketing Authorisation Holder (if different from distributor)

Boehringer Ingelheim Vetmedica GmbH

Marketing Authorisation Number

UK(GB): Vm 04491/5040 (100mg)

UK(GB): Vm 04491/5041 (400mg)

NOAH Compendium

UK(NI): EU/2/12/147/001 100 tablets (100 mg)

UK(NI): EU/2/12/147/002 250 tablets (100 mg)

UK(NI): EU/2/12/147/003 100 tablets (400 mg)

UK(NI): EU/2/12/147/004 250 tablets (400 mg)

UK(NI): EU/2/12/147/005 30 tablets (400 mg)

UK(NI): EU/2/12/147/006 30 tablets (100 mg)

Significant changes

GTIN

GTIN description: Pexion 100 mg tablets for dogs - 5012917030068

GTIN: Pexion 400 mg tablets for dogs - 5012917030075