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Vetmedin[®]

1.25 mg chewable tablets for dogs
5 mg chewable tablets for dogs

Marketing authorization holder

Rhone Ma Malaysia Sdn Bhd (200001023279),
Lot 18A & 18B, Jalan 241, Seksyen 51A,
46100 Petaling Jaya,
Selangor, Malaysia

Manufacturer responsible for batch release:

BI Promeco S.A. de C.V.
Calle Maiz 49, Barrio Xaltocan
Del. Xochimilco
C.P. 16090, Mexico City,
Mexico

Statement of the active substance and other ingredients

Active substance:
Pimobendan 1.25mg
Pimobendan 5mg

Chewable tablet

1.25 mg: Oblong, scored, mottled brown tablets with fine white spots, embossed with Boehringer Ingelheim logo and P01.

5 mg: Oval, scored, mottled brown tablets with fine white spots, embossed with Boehringer Ingelheim logo and P03.

The tablet can be divided into equal parts.

Indication

For the treatment of canine congestive heart failure originating from dilated cardiomyopathy or valvular insufficiency (mitral and/or tricuspid valve regurgitation).

(See also section "Dosage, routes and method of administration").

For the treatment of dilated cardiomyopathy in the preclinical stage (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter) in Doberman Pinschers following echocardiographic diagnosis of cardiac disease.

For the treatment of dogs with myxomatous mitral valve disease (MMVD) in the preclinical stage (asymptomatic with a systolic mitral murmur and evidence of increased heart size) to delay the onset of clinical symptoms of heart failure (see section "Special warnings" and "Special precautions for use in animals").

Contraindications

Vetmedin is not to be used in hypertrophic cardiomyopathies or in diseases in which an improvement in cardiac output cannot be achieved for functional or anatomical reasons (e.g. aortic stenosis). Since Vetmedin is metabolized mainly via the liver, it should not be used in dogs with severe impairment of liver function (see also section on use during pregnancy, lactation or lay).

Adverse Reactions

In rare cases a slight positively chronotropic effect (rise in heart rate) and vomiting can occur. However, these effects are dose-dependent and can be avoided by reducing the dose. In rare cases transient diarrhea, anorexia or lethargy have been observed. In rare cases, an increase in mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease. Although a relationship with pimobendan has not been clearly established, in very rare cases, signs of effects on primary haemostasis (petechiae on mucous membranes, subcutaneous haemorrhages) may be observed during treatment. These signs disappear when the treatment is withdrawn.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports)

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

Target species

Dog

Dosage for each species, route(s) and method of administration

Do not exceed the recommended dosage.

Determine the bodyweight accurately before treatment to ensure correct dosage.

The dose should be orally administered and within the dose range of 0.2 mg to 0.6 mg pimobendan/ kg bodyweight, divided into two daily doses. The preferable daily dose is 0.5 mg/kg bodyweight, divided into two daily doses (0.25 mg/kg bodyweight each). Each dose should be given approximately 1 hour before feeding.

This corresponds to:

One 1.25 mg chewable tablet in the morning and one 1.25 mg chewable tablet in the evening for a bodyweight of 5 kg.

One 5 mg chewable tablet in the morning and one 5 mg chewable tablet in the evening for a bodyweight of 20 kg.

Chewable tablets can be halved at the score line provided, for dosage accuracy according to the bodyweight. Vetmedin chewable tablets may also be combined with a diuretic, e.g. furosemide.

Pimobendan may be attenuated by the concurrent use of a β -adrenergic blocker or a calcium channel blocker.

Withdrawal

Not applicable

Special Storage Precautions

Keep out of the sight and reach of children.

Do not store above 30°C

Keep the container tightly closed in order to protect from moisture.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and bottle after EXP. The expiry date refers to the last day of that month.

Use any divided tablet at the next administration time.

Special warnings

The product has not been tested in cases of asymptomatic DCM in Dobermans with atrial fibrillation or sustained ventricular tachycardia.

The product has not been tested in cases of asymptomatic myxomatous mitral valve disease in dogs with significant supraventricular and/or ventricular tachyarrhythmia.

Special precautions for use**Special precautions for use in animals**

The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus.

For use in the "preclinical stage" of dilated cardiomyopathy (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter), a diagnosis should be made by means of a comprehensive cardiac examination (incl. echocardiographic examination and possibly Holter monitoring).

For use in the preclinical stage of myxomatous mitral valve disease (stage B2, according to ACVIM consensus: asymptomatic with mitral murmur $\geq 3/6$ and cardiomegaly due to myxomatous mitral valve disease), a diagnosis should be made by means of a comprehensive physical and cardiac examination which should include echocardiography or radiography where appropriate. (See also "Pharmacodynamic properties").

Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan (see also section on adverse reactions).

The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

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

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

Wash hands after use.

Advice to doctors: accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

Use during pregnancy and lactation:

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or foetotoxic effects. However, these studies have shown evidence of maternotoxic and embryotoxic effects at high doses, and have also shown that pimobendan is excreted into milk. The safety of the product has not been assessed in pregnant or nursing bitches. Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction:

In pharmacological studies no interaction between the cardiac glycoside strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by the calcium antagonists verapamil and diltiazem and by the β -antagonist propranolol.

Overdose:

In the case of overdose, a positive chronotropic effect, vomiting, apathy, ataxia, heart murmurs or hypotension may occur. In this situation, the dosage should be reduced and appropriate symptomatic treatment should be initiated.

In prolonged exposure (6 months) of healthy beagle dogs at 3 and 5 times the recommended dose, mitral valve thickening and left ventricular hypertrophy were observed in some dogs. These changes are of pharmacodynamic origin.

Pharmacological Properties

Pharmacotherapeutic group: Cardiac stimulants excl. cardiac glycosides, phosphodiesterase inhibitors ATCvet Code: QC01CE90

Pharmacodynamic properties:

Pimobendan, a benzimidazole-pyridazinone derivative has a positive inotropic action and possesses pronounced vasodilator properties.

The positive inotropic effect of pimobendan is mediated by two mechanisms of action: increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase III. Thus the positive inotropism is triggered neither by an action similar to that of the cardiac glycosides nor sympathomimetics.

The vasodilator effect arises from inhibition of phosphodiesterase III.

By combining these mechanisms of action, a cardioprotective effect is achieved. This is manifested by better neuroendocrine regulation of the heart, improved haemodynamics (e.g. positive lusitropy) and a partial reversal of progressive morphological changes to the heart, which leads to a reduction in heart size.

When used in cases of symptomatic valvular insufficiency in conjunction with furosemide the product has been shown to improve the quality of life and extend life expectancy in treated dogs. When used in a limited number of cases of symptomatic dilated cardiomyopathy in conjunction with furosemide, enalapril and digoxin, the product has been shown to improve the quality of life and to extend life expectancy in treated dogs.

In a randomized and placebo controlled study in 363 dogs with preclinical myxomatous mitral valve disease, the median time to onset of clinical signs of heart failure or cardiac death/euthanasia was extended by approximately 15 months in dogs receiving pimobendan. Additionally, there was a reduction in the heart size of dogs treated with pimobendan in the preclinical stage of myxomatous mitral valve disease. Furthermore, overall survival time was prolonged by approximately 170 days in all dogs receiving pimobendan independent of their cause of death (cardiac death/ euthanasia and noncardiac death/ euthanasia). Dogs in the pimobendan group spent a longer time in the study (347.4 patient years) than those in the placebo group (267.7 patient years) resulting in a lower rate of occurrence of clinical symptoms of the myxomatous mitral valve disease or congestive heart failure and its sequelae.

In a randomized and placebo controlled study including Doberman Pinschers with preclinical dilated cardiomyopathy (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter following echocardiographic diagnosis), the time to onset of congestive heart failure or sudden death was extended and survival time was prolonged among dogs administered pimobendan.

Additionally, there was a reduction in the heart size of dogs treated with pimobendan in the preclinical stage of dilated cardiomyopathy. Efficacy evaluation is based on data from 19 (of 39) and 25 (of 37) dogs that reached the primary efficacy endpoint in the pimobendan and the placebo group, respectively.

Pharmacokinetic particulars:**Absorption:**

After oral administration of pimobendan the absolute bioavailability is 60-63%. Since simultaneous or previous food intake reduces the bioavailability, pimobendan should be administered about 1 hour before feeding.

Distribution:

The volume of distribution is 2.6 l/kg, indicating that pimobendan. The mean plasma protein binding is 93%.

Metabolism:

The compound is demethylated by oxidation to the major active metabolite (UD-CG212).

Further metabolic steps are phase II conjugates of UD-CG212, such as glucuronides and sulphates.

Elimination:

The plasma elimination half-life of pimobendan is 0.4 ± 0.1 hours, which corresponds to the high clearance of 90 ± 19 ml/min/kg and the short mean residence of 0.5 ± 0.1 hours.

The most significant active metabolite is eliminated with a plasma elimination half-life of 2.0 ± 0.3 hours. Almost the entire dose is eliminated in the faeces.

Incompatibilities:

None known

Shelf life:

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

Use any divided tablet at the next administration time.

Pack sizes:

1.25 mg: Cardboard box containing 50 or 100 tablets in a polyethylene bottle, closed with a polypropylene child-resistant screw cap.

5 mg: Cardboard box containing 50 tablets in a polyethylene bottle, closed with a polypropylene child-resistant screw up.

Not all pack sizes may be marketed.

Date of revision:

DD/MM/YYYY

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