Cardiac drug for oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Use only as directed.

It is a violation of Federal law to use this product in the United States in a manner inconsistent with its labeling.

Conditionally approved by FDA pending a full demonstration of effectiveness under application number 14110427.

Description: VETMEDIN®-CA1 (pimobendan) is supplied as oblong half-scored chewable tablets containing 1.25 or 5 mg pimobendan per tablet. Pimobendan is 2-[4-(5-yl)-5-methyl-3(2H)-pyridazinone]. A non-sympathomimetic, non-glycoside inotropic drug with vasodilatory properties. Pimobendan exhibits a stimulatory myocardial effect by a dual mechanism of action consisting of an increase in calcium sensitivity of cardiac myofibrils and inhibition of phosphodiesterase (Type III). Pimobendan exhibits vasodilatory activity by inhibiting phosphodiesterase activity III activity. The chemical name of pimobendan is 4,5-dihydro-6-(2-((methylamino)methyl)-1H-benzimidazol-5-yl)-5-methyl-3(2H)-pyridazinone. The structural formula of pimobendan is: 

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\text{CH}_3\text{C}_6\text{H}_4\text{N}=\text{N}-\text{N}=\text{N}\text{C}_6\text{H}_4\text{N}=\text{N}-\text{N}=\text{N}\text{C}_6\text{H}_4\text{N}=\text{N}-\text{N}=\text{N}\text{C}_6\text{H}_4\text{N}=\text{N}-\text{N}=\text{N} \]

If only radiographic examination is possible, cardiomyopathy may be diagnosed in cases where contractility is normal or slightly reduced (LV/SLA) \( \geq 0.7 \). If radiographic cardiomyopathy does not meet both criteria, echocardiography should be performed prior to the initiation of therapy with VETMEDIN–CA1.

VETMEDIN–CA1 has not been evaluated in dogs other than those with cardiomegaly.

The safety of VETMEDIN–CA1 has not been established in dogs with asymptomatic heart disease or with other diseases other than MMVD. The use of VETMEDIN–CA1 has not been evaluated in dogs younger than 6 months of age, dogs with congenital diseases, other than mitral valve disease, dogs with serious metabolic diseases, dogs used for breeding, or pregnant and lactating bitches.

Adverse Reactions: In a controlled multi-center field study, 363 dogs with preclinical MMVD (Stage B2 MMVD, 2019 ACVIM Consensus Statement) received 3 mg pimobendan (VETMEDIN–CA1) or a placebo control tablets (n=181) for up to 1563 days. The control group was continued until the development of congestive heart failure (CHF). Adverse reactions were seen in both treatment groups with many findings associated with the progression of MMVD and comorbidity consistent with the age of the treated dogs.

The median time to the primary endpoint (development of left-sided CHF or death of heart failure) was 38% longer in the VETMEDIN–CA1 group. Despite the longer duration of the study, the incidence of reported adverse reactions was similar between treatment groups. Cough was the most frequently reported adverse reaction (12% in the VETMEDIN–CA1 group). Clinical findings common to cases in MMVD and the incidence was similar between treatment groups. Lethargy, inappetence, tachycardia, sweating, tremors, and syncope may also be associated with the progression of MMVD and were reported in the control group. All individual values for these variables were within the normal range. None of these events were associated with adverse reactions to pimobendan (VETMEDIN–CA1).

Mortality rate, regardless of reason, prior to CHF was similar between the VETMEDIN–CA1 and the control group. All animals that died from CHF were in the control group. A total of 363 dogs across various breeds were randomized to treatment. The result population included 362 dogs with effective enrollment, including a systolic heart murmur grade of ≥3/6 and evidence of cardiomegaly, including a VHS ≥105, and echocardiographic evidence of left atrial hypertrophy or dilatation.

Indications: VETMEDIN–CA1 (pimobendan) is indicated for the delay of onset of congestive heart failure in dogs with moderate or severe mitral valve disease (MMVD) (2019 ACVIM Consensus Statement).

Stage B2 preclinical mitral valve disease (MMVD) refers to dogs with asymptomatic MMVD that have moderate murmurs due to mitral regurgitation and cardiomegaly.

Dosage and Administration: Always provide the Client Information Sheet with each prescription. VETMEDIN–CA1 should be administered orally at a total daily dose of 0.23 mg/lb (0.5 mg/kg) divided into two administrations approximately 12 hours apart (i.e., morning and evening). The tablets are scored, and the calculated dosage should be provided to the nearest half tablet increment.

Contraindications: Do not administer VETMEDIN–CA1 in cases of hypertrophic cardiomyopathy, aortic stenosis, or any other clinical condition where an augmentation of cardiac output is inappropriate for functional or anatomical reasons.

Do not administer VETMEDIN–CA1 to dogs with Stage A or B1 preclinical MMVD (2019 ACVIM Consensus Statement) due to the risk of cardiac pathology associated with exaggerated hemodynamic responses to use of VETMEDIN–CA1.

Warnings: User Safety Warnings: Not for use in humans. Keep VETMEDIN–CA1 in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Animal Safety Warnings: Keep VETMEDIN–CA1 in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose. A 1X and 5X clinical dose was administered, over a 6-month period of time, pimobendan caused an exaggerated hemodynamic response in the normal dog heart, which was associated with cardiac pathology (See Target Animal Safety).

Precautions: VETMEDIN–CA1 should be used only in dogs with preclinical MMVD that have a moderate or loud mitral murmur due to mitral regurgitation and cardiomegaly (Stage B2 MMVD, 2019 ACVIM Consensus Statement). A diagnosis of MMVD should be made by means of a comprehensive physical, hematochemical and echocardiographic examination which should include radiography and electrocardiography.

Stage B2 cardiomegaly is diagnosed based on meeting all three of the following criteria:

- Radiographic left heart shadow score (VHS) \( \geq 10.5 \), and
- Echocardiographic left atrium/ventricle ratio (LA/Ao ratio) \( \geq 1.5 \), and
- Echocardiographic left ventricular internal diastolic diameter normalized to body weight (LVDDN) \( \geq 17 \).

Echocardiographic examination is recommended in all cases to determine the extent and severity of the disease. If therapy is initiated prior to the development of cardiomegaly, treated dogs are at risk for cardiac pathology associated with exaggerated hemodynamic responses to VETMEDIN–CA1.

Reasonable Expectation of Effectiveness: A reasonable expectation of effectiveness may be demonstrated by the absence and the increase in the number of patients with normal systolic blood pressures, the time to the primary endpoint, and the incidence of adverse reactions in the control group. Any increase in the incidence of cardiomegaly, left atrial endocardial thickening, or murmurs grade of ≥3/6 and evidence of cardiomegaly, including a VHS ≥105, and echocardiographic evidence of left atrial hypertrophy or dilatation should be considered as evidence that VETMEDIN–CA1 may be effective.

Contraindications: VETMEDIN–CA1 is contraindicated in dogs with the presence of severe renal and hepatic disease, as well as any condition that will interfere with the metabolism and excretion of pimobendan. Concomitant use of a non-cardiac cause of death, prior to treatment with VETMEDIN–CA1.

Storage Information: Store at 20° to 25°C (68° to 77°F) except as permitted between 10° and 30°C (between 50° and 86°F).

How Supplied: VETMEDIN–CA1 (pimobendan) Chewable Tablets: Available as 1.25 and 5 mg oblong half-scored chewable tablets - 5 tablets per bottle.

NDC 0019-4410-01 - 12.5 mg - 50 tablets per bottle

NDC 0019-4410-05 - 5 mg - 50 tablets per bottle

References:


3. Boehringer Ingelheim Animal Health USA Inc. Duluth, GA 30096

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