Adverse reactions/new clinical findings were seen in both treatment groups and were not statistically different in CHF, the therapy of CHF; or both. The following adverse reactions/new clinical findings are listed according to body system and are not in order that the positive inotropic effect of pimobendan may be attenuated by the concomitant use of a β-adrenergic blocker or a calcium channel blocker.

Effectiveness: In a double-masked, multi-site, 56-day field study, 363 dogs with modified NYHA Class II or IV CHF due to AVI or DCM were randomly assigned to either the active control (enalapril) or VETMEDIN (pimobendan) treatment group. Of the 359 dogs, 52% were male and 48% were female; 72% were spayed or neutered, and 28% were in intact male. The VETMEDIN group had a slightly lower mean age and weight compared to the active control group.

The safe use of VETMEDIN has not been established in dogs with asymptomatic heart disease (See Animal Safety). Pimobendan caused an exaggerated hemodynamic response in dogs with CHF, which resulted in a more than 20% decrease in cardiac output at the end of the first month of therapy. The maximum number of non-escape VEs recorded either at baseline or in a control group dog was 20 at 25 and 20, and in one dog from each of the 1X and 5X groups at Week 20. None of the dogs had clinical signs associated with these escape responses. Treatment was associated with small differences in mean platelet counts (decreased in the 1X and 5X groups), potassium (increased in the 5X group), and mean blood glucose in glucose curves (increased in the 1X and 3X groups), and these differences were within the normal range. Three 1X and one 5X group dogs had mild elevations of alkaline phosphatase (less than two times normal). Loose stools and vomiting were infrequent, and were not associated with any treatment-related adverse drug reactions.

Storage Information: Store at 20° to 25°C (68° to 77°F), excursions permitted between 15° and 30°C (59° and 86°F).

How Supplied: VETMEDIN® (pimobendan) Chewable Tablets: Available as 1.25, 2.5, and 5 mg oblong half-scored chewable tablets - 50 tablets per bottle.

Animal Safety: In a laboratory study, VETMEDIN did not cause, by absorption, any of the signs of hyperthyroidism observed in healthy Beagles per treatment group at a total of (1), 3, and 5 times the recommended dosage for 8 months. See Table 2 for cardiac pathology results. The cardiac pathology/histopathology noted in the 3X and 5X dose groups included non-caseating granulomatous and interstitial myocardial infiltrate rich in macrophages and associated chronic inflammation, and focal myocardial injury in normal heart dogs, and is associated with the metabolism of pimobendan to these agents. None of the dogs developed signs of heart failure and there was no mortality.

Table 1: CHF Death and New Arrhythmias in the 56-Day Field Study

Table 2: Effectiveness Results for the 56-Day Field Study

Animal Safety: Safety Data Sheet (SDS), or for technical assistance, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about VETMEDIN, contact the FDA at 1-888-FDA-VETS or online at http://www.fda.gov/vets or call 1-800-359-9276.

Clinical Pharmacology: Pimobendan is oxidatively demethylated to a pharmacologically active metabolite which is then conjugated with sulfaic or glucuronic acid and excreted mainly via feces. The mean extent of protein binding of pimobendan and the pharmacologically active metabolite in dog plasma is ~90%. Following a single oral administration of 0.25 mg/kg body weight of pimobendan, the maximal mean ± (SD) plasma concentrations (Cmax) of pimobendan and the active metabolite were 0.30 (0.76) mg/l and 3.68 (1.11) mg/l, respectively. Individual Dog Cmax values for pimobendan and the active metabolite were observed 1 to 4 hours post-dose (mean: 2 and 3 hours, respectively). The total drug concentration of pimobendan was approximately 90% 15 mg/l, and the terminal elimination half-life of pimobendan and the active metabolite were approximately 0.5 hours and 2 hours, respectively. Plasma levels of pimobendan and active metabolite were below quantifiable levels by 6 hours and 8 hours after oral administration, respectively. The steady-state volume of distribution of pimobendan is 2.6 l/kg indicating that the drug is readily distributed into tissues. Food decreased the bioavailability of an aqueous solution of pimobendan, but the effect of food on the pharmacokinetic parameters of strength, VETMEDIN and tablets is unknown.

In normal dogs instrumented with left ventricular (LV) catheters, the average LV end-diastolic volume and LV end-systolic volume (in mL) were 159±67 and 23±10, respectively. Dogs in the chronic heart failure group were instrumented with LV catheters and an LV end-diastolic pressure and aortic pressure catheter. The maximum number of non-escape VEs recorded either at baseline or in a control group dog was 20 at 25 and 20, and in one dog from each of the 1X and 5X groups at Week 20. None of the dogs had clinical signs associated with these escape responses. Treatment was associated with small differences in mean platelet counts (decreased in the 1X and 3X groups), and maximum blood glucose in glucose curves (increased in the 1X and 3X groups), and these differences were within the normal range. Three 1X and one 5X group dogs had mild elevations of alkaline phosphatase (less than two times normal). Loose stools and vomiting were infrequent, and were not associated with any treatment-related adverse drug reactions.

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