

Vetmedin FAQs

Q *What is Vetmedin?*

A Vetmedin is a cardiac medication that falls into an entirely new class of therapy. As an 'inodilator' Vetmedin has a dual mode of action; positive inotropy and balanced systemic vasodilation. The two modes of action work in a complimentary way to increase cardiac output while decreasing both preload and afterload.

Q *What is the dose of Vetmedin?*

A Vetmedin has a licensed dosage range of 0.1-0.3 mg/kg BID. The recommended target dose is 0.25 mg/kg BID, to be administered one hour prior to feeding (or 2-3 hours after eating).

Q *How do I appropriately dose Vetmedin in dogs weighing under 4 kg?*

A The smallest sized Vetmedin capusle is 1.25 mg and, based on the dose range of 0.3-0.6 mg/kg divided twice per day, would over-dose dogs weighing under 5 kg if given twice per day. While Vetmedin does have a wide safety margin, accurate dosing is ideal. Therefore consider diluting the contents of the capusle in 2 - 4 mls of distilled water to administer 1/2 the volume every 12 hours. Alternatively mix approximately 1/2 the contents of the capsule in a small amount of food/treat (the small amount of food will not interfere with bioavailability) and then administer the remaining amount 12 hours later.

Q *Can I use Vetmedin with other cardiac medications?*

A Yes. There are no known adverse interactions with any other cardiac medication. However, the concurrent use of a calcium channel blocker or beta blocker may decrease their or Vetmedin's efficacy.

Q *Should diuretics always be used as an adjunct to Vetmedin therapy?*

A Vetmedin is indicated for the treatment of congestive heart failure. Complete therapy for congestive heart failure includes the use of a diuretic. In some cases the dose of diuretic can be reduced when an animal is treated with Vetmedin.

Q *At what stage of heart disease should I prescribe Vetmedin?*

A All studies to date have demonstrated patient benefits from improvements in quality of life, survival, or both when Vetmedin was begun at the first signs of congestive heart failure due to either mitral valve disease or DCM. As a general rule of thumb, when a diuretic is required to treat CHF, it is beneficial to begin Vetmedin as well.

Q *Some of my clients simply cannot afford triple therapy of a diuretic, Vetmedin, and an ACE inhibitor. If my clients can only afford dual therapy, which products should I recommend?*

A Because of their complimentary and anticipated synergistic modes of action, triple therapy (as outlined above) is currently considered to be the best therapeutic option for treating canine CHF due to mitral valve disease or DCM. Generally, once pet owners see the benefits from this therapeutic protocol, costs become less of a concern. However, if dual therapy remains the only option, a diuretic and Vetmedin appear to provide the best therapeutic choice and this is supported by a number of studies comparing Vetmedin to an ACE inhibitor for treating canine CHF due to mitral valve disease. Regardless, the

underlying heart disease will progress and mandate the use of triple therapy at some stage.

Q *What are the possible side effects of Vetmedin?*

A A moderate positive chronotropic (i.e., tachycardia) effect and vomiting/diarrhea may occur in rare cases. These effects are dose dependant and may be avoided by reducing the dose. In the majority of cases, dogs tolerate Vetmedin without any adverse effects.

Q *Some previous positive inotropes have been associated with decreased life span. Does Vetmedin decrease life expectancy?*

A No. Unlike other positive inotropes, Vetmedin's unique mode of action does not lead to an increase in oxygen consumption in the already failing heart. Increasing oxygen consumption depletes energy stores and results in a decreased life span. Vetmedin appears to increase force of contraction without increased myocardial oxygen consumption.

Q *Why isn't Vetmedin (pimobendan) used in people?*

A Pimobendan has been licensed for use in people in Japan since 1996.

Q *How does Vetmedin make myocardial function more economical?*

A By increasing the sensitivity of myocardial cells to preexisting calcium. Vetmedin increases myocardial contractility without increasing intracellular calcium. Energy is required to remove intracellular calcium for relaxation. Because Vetmedin does not increase calcium levels within the cell there is no additional energy required to remove this calcium.

Q *How is Vetmedin different from digoxin?*

A The failing heart has been shown to have impaired calcium management so that the increase in intracellular calcium brought about by digoxin actually increases energy consumption and oxygen requirements. This may also lead to impaired relaxation and arrhythmias. Vetmedin does not lead to an increase in intracellular calcium ions and therefore does not increase oxygen demand. Vetmedin does not impair relaxation. To date, no studies have demonstrated an increase in arrhythmias.

Q *Does the use of Vetmedin increase the risk for cardiac arrhythmias and sudden death?*

A No. As discussed in the previous question, Vetmedin's unique mode of action as a calcium sensitizer appears to avoid this side-effect common to other positive inotropes. Additionally, Vetmedin causes coronary vasodilatation and improves cardiac relaxation during diastole, all of which improve myocardial blood flow. Published veterinary studies to date have not demonstrated any potential to cause arrhythmias.

Q *Can Vetmedin use result in hypotension, whether used alone or in conjunction with other vasodilators?*

A Vasodilators may cause excessive afterload reduction resulting in hypotension and reduced organ perfusion, as evidenced biochemically by increases in urea and/or creatinine. This is the reason that manufacturers of pure vasodilators (e.g., ACE I) recommend that renal values and electrolytes be tested approximately 1 week postinitiation of therapy. However, this has not been reported as a concern with

Vetmedin, whether used on its own or in conjunction with ACEIs or diuretics, likely because of its dual mode of action as both a balanced vasodilator and positive inotrope.

Q *Do I have to be concerned about toxicity?*

A Any drug has the potential, if used improperly, to cause toxicity. However, the margin of safety for Vetmedin is very wide. An oral LD₅₀ could not be established in dogs for humane reasons because vomiting occurs at extremely high doses. Unlike other positive inotropes, there are no toxic adverse effects associated with chronic administration.

Q *Why is it not necessary to monitor renal function while on Vetmedin treatment?*

A Although Vetmedin is a vasodilator, it also increases cardiac output, so reducing the risk of impaired renal vascular perfusion. Vetmedin's mode of action also does not directly interfere with renal blood flow autoregulation, as can occur with other cardiac medications.

Q *Can Vetmedin be used to control heart rate?*

A Vetmedin has no direct chronotropic effects in most patients. If tachycardia is secondary to poor cardiac output then this may normalize with Vetmedin.

Q *Can Vetmedin be used with Metacam?*

A Congestive heart failure is a relative contraindication to the use of any NSAID; however, if the patient is stable with normal renal function, Metacam use can be considered based on the needs of the individual patient. No formal drug interaction studies have been performed but clinical experience would suggest that the concurrent use of these products is not a problem. As with any situation where there are concurrent illnesses, it is always good practice to titrate the Metacam to the lowest daily dose that controls the clinical signs associated with osteoarthritis.

Q *Can Vetmedin be used in pregnant or lactating animals?*

A Even at elevated doses in lab animals, pimobendan had no effect on fertility and no embryotoxic effects. No information is available specifically on the safety of Vetmedin in pregnant or lactating bitches. Therefore, Vetmedin should only be used in these animals if the therapeutic benefit outweighs the potential risk.

Q *How does Vetmedin affect the cycle of heart failure?*

A The decrease in cardiac output associated with the failing heart results in the initiation of compensatory mechanisms (sympathetic nervous system and the renin-angiotensin-aldosterone system [RAAS]). The primary aim of these mechanisms is to maintain blood pressure. In the short term these compensatory mechanisms are beneficial but in the long term they result in further progression of heart failure. By increasing cardiac output and providing balanced peripheral vasodilatation, Vetmedin reduces the stimulus for these compensatory changes, thereby interrupting the vicious cycle of heart failure.

Q *Can I use Vetmedin to delay the onset of clinical heart failure for dogs with mitral valve disease that are clinically asymptomatic (i.e., occult disease)?*

A The answer to this question is not known and Vetmedin's current label indication is for the treatment of clinical heart failure. Currently, there is no licensed cardiac medication

(including ACE I) that has been shown to be effective in slowing the progression of heart disease due to mitral valve insufficiency to overt heart failure.

Q *Can I use Vetmedin in a dog with indications of renal disease?*

A Yes. Vetmedin increases cardiac output and does not interfere with renal perfusion, hence it may actually improve serum biochemical renal values if they are elevated due to pre-renal azotemia, which is common in situations of lowered cardiac output. However, as Vetmedin is minimally excreted by the kidneys, even pre-existing renal disease is not a contraindication to its use.

Q *Can I use Vetmedin in a dog with indications of liver disease?*

A Vetmedin has no adverse effect on liver function. However, it is metabolized almost completely by the liver so impaired liver function may affect drug metabolism and excretion. In dogs with evidence of liver disease please contact the Boehringer Ingelheim Canada technical service team (800-567-1885) before using Vetmedin.