Denosyl® Chewable Tablets

(S-Adenosylmethionine)

Denosyl, a nutritional supplement, is the pure and stabilized salt of S-Adenosylmethionine for veterinary use only. It is the only brand researched in U.S. trials for veterinary use in dogs and cats. Denosyl chewable tablets are liver flavored and available as scored 225 mg tablets. While S-Adenosylmethionine is sensitive to moisture, the specific NMXSS75™ S-Adenosylmethionine found in Denosyl chewable tablets has been manufactured to maintain stability.

Background

S-Adenosylmethionine is an endogenous molecule synthesized by cells throughout the body and is formed from the amino acid methionine and ATP. It is an essential part of three major biochemical pathways: transmethylation, transsulfuration and aminopropylation. As part of these pathways, S-Adenosylmethionine is essential to all cells and is particularly important in hepatocytes because of their central role in metabolism. A deficiency of S-Adenosylmethionine, therefore, may initiate or contribute to abnormalities of cellular structure and function in the liver as well as many other body tissues.

Conversely, exogenous administration of S-Adenosylmethionine has been shown to result in improvements in hepatocellular function in both *in vivo* and *in vitro* studies, without cytotoxicity or significant side effects.[1-9] Precursors of S-Adenosylmethionine do not have similar effects. Administration of methionine to animals with decreased liver function may not increase hepatic S-Adenosylmethionine levels and may be toxic.[6] The best way to increase S-Adenosylmethionine levels in the body is by direct supplementation with S-Adenosylmethionine.

Purpose

Denosyl has been shown to increase hepatic glutathione levels in cats and dogs.[1,7] Glutathione is a potent antioxidant that protects hepatic cells from toxins and death. A study found that low liver glutathione concentrations are common in dogs and cats with decreased hepatobiliary function.[10] Denosyl is recommended to improve hepatic glutathione levels in patients to help maintain and protect liver function. Denosyl may also be used in other areas of tissue oxidant injury and RBC fragility caused by certain toxins or drugs which are related to reduced glutathione concentrations.[6] Denosyl, however, goes beyond increasing glutathione levels and has been shown to protect liver cells from cell death[2,8] and may be useful in cell regeneration.[6] A study has also shown that Denosyl may improve bile flow in cats.[5] Recently, S-Adenosylmethionine has also been shown beneficial in maintaining brain health as a neuro protector in dogs.

Pharmacokinetics

In a pharmacokinetic study with fasted dogs given the chewable tablet versus the enteric coated Denosyl® tablet, bioavailability was found to be comparable between the two formulations. The time course of uptake, however, was significantly more rapid and consistent with the chewable tablet compared to the enteric coated tablet.[11]

Safety

Denosyl demonstrates an exceptionally wide margin of safety. Oral acute toxicity studies in rats indicated an LD_{50} greater than 4,640 mg/kg.[6] Clinically healthy dogs administered 20 mg/kg/day of Denosyl for 6 weeks and clinically healthy cats administered Denosyl at 2 times the recommended daily amount for 113 days remained healthy with no adverse effects from administration of Denosyl.[1,7]

See reverse side for administration table

Administration as a Nutritional Supplement

The chart below is provided as a guide for administration. Daily administration may also be calculated based on 20 mg/kg of body weight and rounded to the closest 1/2 tablet size.

For optimal absorption, tablets should be given on an empty stomach, at least one hour before feeding, as the presence of food decreases the absorption of S-Adenosylmethionine.

Denosyl® 225 mg tabs	
Weight (lbs.)	**# of tablets daily**
Up to 6	1/4
7 to 15	1/2
16 to 30	1
31 to 45	1 1/2
46 to 60	2
61 to 75	2 1/2
76 to 90	3
91 to 105	3 1/2
Over 105	4

Storage

Store in a cool dry place, not to exceed 86º F. Keep bottle closed with desiccant inside when not removing tablets. Tablets are sensitive to moisture and extreme heat.

REFERENCES

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11. Data on file. Nutramax Laboratories, Inc., Edgewood, MD 21040, USA 2008.

Any questions or comments?
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