

NUTRAMAX LABORATORIES, INC.

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DENOSYL®

Nutramax Labs.

(S-Adenosylmethionine)

FROM THE MAKERS OF COSEQUIN®

Sold only through veterinarians

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 is available in three strengths: as an enteric-coated 90 mg, 225 mg, and 425 mg tablet of active S-Adenosylmethionine. Because S-Adenosylmethionine is extremely sensitive to moisture, tablets are individually sealed in specialized moisture-resistant blister packs.

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

Pharmacokinetics

In a pharmacokinetic study with fasted dogs given Denosyl, peak plasma levels were recorded within 4 hours of administration.¹ A pharmacokinetic study in fasted cats showed peak plasma levels at 2-4 hours post Denosyl administration.^{7,11}

Safety

Denosyl demonstrates an exceptionally wide margin of safety. Oral acute toxicity studies in rats indicated an LD50 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}

Administration as a Nutritional Supplement

Because the tablet must be kept intact to prevent destruction by stomach acid, administration range is based on the nearest whole-tablet. 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 tablet size or combination of sizes.

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. For those owners who have difficulty administering tablets to their pets, Denosyl[®] tablet(s) may be disguised in a small bite of food. Studies

have shown that, in many cases, tablets or capsules given as a “dry swallow” do not pass into the stomach in cats but may become lodged in the esophagus. It is recommended for pet owners to administer 3-6 cc of water immediately following any tablet administration to speed passage of the tablet into the stomach.^{12,13} Denosyl 90 mg tablets are ideal for cats because of their small size. If the pet is to receive more than one tablet daily, the total number of tablets may be divided between morning and evening for ease of administration. For example, a daily administration of three tablets could be divided into two tablets in the morning and one tablet in the evening.

FELINE AND CANINE DENOSYL DAILY* ADMINISTRATION GUIDE

For Cats and Small Dogs

Body Weight		90 mg Denosyl
Pounds	Kilograms	
Up to 12	Up to 5.5	One tablet

For Medium Dogs

Body Weight		225 mg Denosyl
Pounds	Kilograms	
13 to 34	6 to 15.5	One tablet

For Large Dogs

Body Weight		425 mg Denosyl
Pounds	Kilograms	
35 to 65	16 to 29.5	One tablet
66 to 120	30 to 54.5	Two tablets
Over 120	Over 54.5	Three tablet

*The number of tablets can be gradually reduced or increased at any time depending on the pet's needs. Many pets are maintained long-term on every-other-day or every-third-day administration.

Storage

Store in a cool dry place not to exceed 86° F. Keep tablets in original blister pack until used. Tablets are sensitive to moisture and extreme heat and should not be split or crumbled.

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Any questions or comments?

Call toll-free 1-800-925-5187

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02-1001-07

FOR CATS and SMALL DOGS	90 mg - 30 stabilized tablets	01-1007-01
FOR MEDIUM DOGS	225 mg - 30 stabilized tablets	01-1008-01
FOR LARGER DOGS	425 mg - 30 stabilized tablets	01-1014-02

NAC No.: 12910121