

Lysodren Tablets

(mitotan)

Lysodren (mitotane) is used for the medical treatment of Cushing's Disease (pituitary-dependent hyperadrenocorticism) in dogs. It has also been used for the palliative treatment of adrenal carcinoma in humans and dogs.

Dosage and Administration:

Dogs: For medical treatment of pituitary-dependent hyperadrenocorticism (bilateral adrenal hyperplasia):

- **Initial therapy:** 50 mg/kg divided twice a day, PO with food.
- Do not give glucocorticoids, but owner should have a small supply of prednisolone. Give until one of the following occurs:
 - Polydipsic dogs consume less than 60 ml/kg/day of water.
 - Dogs with excellent appetite takes 10-30 minutes longer than before mitotane therapy to consume meals (feed two small meals twice daily).
 - Dog vomits, is listless, or has diarrhea.
 - If dog develops GI upset 3-4 days after starting therapy, evaluate and either temporarily halt therapy or divide dosage further.
- After 8-9 days of therapy, the dog should be evaluated. Repeat the following tests: ACTH response test, BUN, serum sodium and potassium blood levels.
- If the dog has responded clinically, stop mitotane until ACTH response test can be evaluated. If the response test yields normal or high cortisol values, mitotane is continued (generally for 3-7 days). Repeat ACTH response test every 7-10 days until a low post-ACTH cortisol level is obtained. Most dogs respond during 7-10 days and nearly all respond by the 16th day of therapy.

Maintenance therapy:

- Dogs who have responded to mitotane within 10 days of initiation receive 25 mg/kg every 7 days. Recheck ACTH response every 1-3 months. Those taking longer than 10 days to respond receive 50 mg/kg weekly in 2-3 divided dosages.
- If ACTH-stimulated cortisol levels begin to increase, mitotane dosage should be increased. Dogs with recurrent signs and symptoms of PDH or post ACTH cortisol values of >5 micrograms/dl, should undergo daily therapy as outlined above. These animals should also be evaluated for other conditions (e.g., renal disease, diabetes mellitus). Should anorexia and listlessness be seen with low plasma cortisol levels, reduce dosage.

Contraindications and Precautions:

Mitotane is contraindicated in patients known to be hypersensitive to it. Patients with concurrent diabetes mellitus may have rapidly changing insulin requirements during the initial treatment period. These animals should be closely monitored until they are clinically stable. Dogs with preexisting renal or hepatic disease should receive the drug with caution and with more intense monitoring.

Some veterinarians recommend giving prednisolone at 0.2 mg/kg/day during the initial treatment period

(0.4 mg/kg/day to diabetic dogs) to reduce the potential for side effects from acute endogenous steroid withdrawal. Other clinicians have argued that routinely administering steroids masks the clinical markers that signify when the endpoint of therapy has been reached and must be withdrawn 2-3 days before ACTH stimulation tests can be done. Since in adequately observed patients, adverse effects requiring glucocorticoid therapy may only be necessary in 5% of patients, the benefits of routine glucocorticoid administration may not be warranted.