

# Tolerability

**The most common side-effects in dogs on treatment with Vetoryl® are vomiting, diarrhoea, anorexia, weakness and lethargy.**

## Acute withdrawal of circulating glucocorticoids

A small percentage of dogs may develop “corticosteroid withdrawal syndrome” or hypocortisolaemia within 7-10 days of starting Vetoryl treatment due to acute withdrawal of circulating glucocorticoids<sup>1</sup>. Clinical signs are very similar to and must be differentiated from an early Addisonian crisis by performing an ACTH stimulation test and by measuring serum sodium and potassium concentrations. Corticosteroid withdrawal syndrome responds to stopping treatment with Vetoryl for seven

days and restarting at a lower dose. This should allow for a more gradual reduction in the dog’s serum cortisol concentration.

Treatment of hyperadrenocorticism and the resultant reduction in endogenous cortisol concentration could lead to the unmasking of previously suppressed immune-mediated, inflammatory (e.g. arthritis, atopy) or neoplastic diseases. Subclinical renal dysfunction may also be unmasked following treatment.

## Hypoadrenocorticism

Clinical signs associated with iatrogenic hypoadrenocorticism include weakness, lethargy, anorexia, vomiting and diarrhoea.

In a published study of 78 dogs treated with trilostane, it was reported that only two dogs (2.6%) became Addisonian while on treatment<sup>2</sup>. This low incidence of hypoadrenocorticism compares very favourably with a reported incidence of 5-17% in dogs treated with mitotane<sup>3</sup>.

There is no specific antidote for trilostane. Treatment should be withdrawn and supportive therapy, including corticosteroids, correction of electrolyte imbalances and fluid therapy may be indicated depending on the clinical signs.

Any iatrogenic adrenocortical insufficiency is usually quickly reversed following cessation of treatment. However in a small percentage of dogs, effects may be prolonged.

## Adrenal necrosis

There are very few histopathologically confirmed cases of adrenal necrosis secondary to Vetoryl treatment published in the literature<sup>4,5</sup>. There is no conclusive evidence to link trilostane to the induction of adrenal necrosis.

A combination of different events may predispose hyperadrenocorticoid dogs to adrenal necrosis: chronic oversuppression of cortisol production, elevated plasma ACTH levels, thromboembolism and a secondary insult, for example endotoxaemia.

Dogs on Vetoryl treatment have been shown to have high circulating levels of ACTH due to reduced negative feedback of cortisol on the pituitary gland. A recently published paper supports the hypothesis that the adrenal gland lesions seen in dogs with hyperadrenocorticism treated with trilostane are caused by an increased concentration of endogenous ACTH<sup>6</sup>.

## Overdose

Overdose may lead to signs of hypoadrenocorticism (lethargy, anorexia, vomiting, diarrhoea, cardiovascular signs and collapse). There were no mortalities following chronic administration at 3x the maximum recommended dose to healthy dogs, however mortalities may be expected if higher doses are administered to dogs with hyperadrenocorticism.

## Contraindications, special precautions and drug interactions

### Concurrent diabetes mellitus and hyperadrenocorticism

The presence of diabetes mellitus and hyperadrenocorticism together requires specific monitoring. Hyperadrenocorticism can cause insulin resistance, which leads to overt diabetes mellitus in some dogs. Even if the cortisol levels are successfully reduced it is unlikely that diabetes mellitus will fully resolve. It should also be noted that diabetes mellitus is a metabolically stressful illness and therefore cortisol levels and responses to ACTH stimulation and low dose dexamethasone suppression tests may be increased – leading to false positive diagnoses of hyperadrenocorticism in uncontrolled or poorly controlled diabetic dogs.

### Primary hepatic disease and renal insufficiency

Trilostane has been demonstrated to be excreted primarily in the faeces of the rat, indicating biliary excretion as the major metabolic pathway. In the monkey, trilostane is excreted in equal amounts in the faeces and urine. It is therefore particularly important to screen cases for primary hepatic disease and renal insufficiency as the product is contraindicated in these cases.

### ACE inhibitors and potassium - sparing diuretics

The risk of hyperkalaemia developing should be considered if trilostane is used in conjunction with ACE inhibitors (e.g. benazepril, enalapril or ramipril) or potassium-sparing diuretics (e.g. spironolactone) since both drugs have an anti-aldosterone effect.

<sup>1</sup> Greco, D.S., Behrend, E.N. (1995). Corticosteroid withdrawal syndrome. Kirk's Current Veterinary Therapy XII, ed J Bornaguria, WB Saunders, 413

<sup>2</sup> Neiger, R. *et al* (2002) Trilostane treatment of 78 dogs with pituitary-dependent hyperadrenocorticism *Veterinary Record* **150**: 799-804

<sup>3</sup> Kintzer, P.P., Peterson, M.E. (1991) Mitotane treatment of 200 dogs with pituitary - dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine* **5**: 182-190

<sup>4</sup> Chapman *et al* (2004) Adrenal necrosis in a dog receiving trilostane for the treatment of hyperadrenocorticism *Journal of Small Animal Practice* **45**: 307-310

<sup>5</sup> Reusch *et al* (2007) Histological evaluation of the adrenal glands of seven dogs with hyperadrenocorticism treated with trilostane *Veterinary Record* **160**: 219-224

<sup>6</sup> Burkhardt *et al* (2011) ACTH, but not trilostane, causes severe adrenal haemorrhage, vacuolization and apoptosis in rats. *Domestic Animal Endocrinology* **40**: 155-164

VETORYL: Vetoryl contains Trilostane

Dechra Veterinary Products A/S, Mekuvej 9, 7171 Uldum, Denmark

Dechra Veterinary Products A/S is a trading business of Dechra Pharmaceuticals PLC

[www.dechra.com](http://www.dechra.com)



For more details:

Phone: +971 6 539 5443  
WhatsApp: +971 6 539 5443  
Email: [sales@thevet.group](mailto:sales@thevet.group)  
[www.thevet.group](http://www.thevet.group)

**the veterinary group**  
DELIVERING EXCELLENCE



THE VETERINARY GROUP LLC



THE VETERINARY GROUP LLC



THE VETERINARY GROUP LLC