

Hyperadrenocorticism in dogs – treatment options, monitoring and control



Basically, the following options are available for the treatment of hyperadrenocorticism in dogs: For Cushing's disease, an ACTH-secreting tumour of the pituitary gland, it is hypophysectomy and radiotherapy. For Cushing's syndrome, i.e. hyperadrenocorticism of adrenal origin, adrenalectomy may be considered. Medical treatment with Vetoryl is possible for both causes of the disease. Although treatment is not curative, in many cases it provides sufficient control of the symptoms, an improvement in the quality of life and a prolonged lifespan.

Mode of action and pharmacological properties of Vetoryl

The active substance is trilostane, an

anticorticosteroid. Trilostane selectively and reversibly inhibits the 3-beta-hydroxysteroid dehydrogenase enzymatic system and thus decreases, dose dependent, the synthesis of cortisol, corticosterone and aldosterone in the adrenal cortex.

After the administration of trilostane, maximum plasma concentrations are reached within ½ an hour to 2 ½ hours. Excretion occurs rapidly in the urine, metabolites are excreted in the bile after conjugation. Baseline values are reached after 6 to 12 hours. The substance is fat-soluble and is therefore best administered together with food.

In dogs, the active substance is approved for the treatment of pituitary- as well as adrenal-dependent hyperadrenocorticism.

Starting Vetoryl treatment

Therapy may only be started after a definite diagnosis has been made and other medical conditions have been ruled out. Vetoryl should not be given to dogs with primary liver disease or kidney disease. It is recommended to perform an initial “check” with the ACTH stimulation test before administering the first tablet.

Treatment is started with an initial dose of about 2 mg/kg body weight, preferably in the morning with the food. If this dosage does not sufficiently control the symptoms, it can be increased by up to 50% and administered in 2 daily doses in the morning and the evening.

The aim of this treatment is to reduce the symptoms as much as possible in the long run and thus help the dog to have a better quality of life and a longer lifespan. The treatment plan and monitoring are used to find the right dosage and to minimise the risk of an overdose, especially at the beginning of treatment, as well as to adjust the dosage of Vetoryl if necessary.

Monitoring

Most dogs respond quickly to the treatment and symptoms significantly improve within 10 days. Food and fluid intake are reduced, panting and restlessness improve. Within a month, fluid intake should have normalised and the dog should show a normal behaviour. It takes 3 to 6 months until the abdominal girth decreases, muscles increase and hair growth is visible.

During therapy, other diseases may become apparent, and other pre-existing conditions, such as arthritis or allergic diseases, might first become symptomatic as a result of the treatment of hyperadrenocorticism. Dogs with hyperadrenocorticism have an increased risk of pancreatitis, also during treatment with Vetoryl.

Options for monitoring

Components of therapy monitoring comprise observation by the owner, clinical examination results, laboratory findings and checking the current adrenal function.

Standard laboratory checks include a complete blood count, liver and kidney parameters as well as electrolytes. Various tests can be used to check the current adrenal function:

1. ACTH stimulation test

As trilostane is acting as synthesis inhibitor a high dose of ACTH activates the residual adrenal reserve to the maximum, which can be measured as post-stimulation cortisol concentration. For a long time, the test was the standard approach for therapy monitoring. It is time-consuming and cost-intensive and, in the past, had long been limited by the fact that there was no synthetic ACTH available. For some time now, synthetic ACTH has been available as tetracosactide under the trade name Cosacthen. Performing an ACTH stimulation test is recommended in all patients before starting Vetoryl treatment, and as the first test about 10 to 14 days after starting treatment. It is also recommended at every follow-up examination in dogs that are very anxious or which also suffer from other diseases, and if an overdose of Vetoryl is suspected.

Test procedure:

A baseline sample is taken and, immediately afterwards, 5 µg/kg (equivalent to 0.02 ml/kg) of ACTH is administered by intravenous or intramuscular injection. 60 to 90 minutes later, the 2nd sample is collected and the cortisol level is determined in both samples.

Evaluation:

The aim is a baseline cortisol concentration of >18 ng/ml and a concentration of <73 ng/ml after stimulation. If the baseline cortisol level is <18 ng/ml, an overdose of Vetoryl is suspected.

2. Baseline cortisol

Determination of baseline cortisol, together with other vital signs and laboratory parameters, may be suitable for assessing the dose of Vetoryl in an otherwise healthy dog.

Test procedure:

At the time when Vetoryl has its maximum effect, i.e. 2 to 5 hours after capsule administration, a blood sample is taken to determine the cortisol level.

Evaluation:

A baseline cortisol level of <18 ng/ml may indicate an overdose. It is recommended to perform an ACTH stimulation test. A baseline cortisol level of >18 ng/ml is good if clinical improvement of symptoms can be observed. If 28 days after starting treatment no clinical improvement is seen and the baseline cortisol is high, other causes of symptoms must be ruled out and the dose of Vetoryl should then be increased cautiously.

3. Vetoryl therapy monitoring by means of pre-pill cortisol determination and 2x pre-pill cortisol determination

For the pre-pill cortisol determination, baseline cortisol is determined before the capsule is administered. Comparative studies have shown a good correlation between the pre-pill levels and the values

of the ACTH stimulation test. To minimise stress-related influences on cortisol levels, a second pre-pill cortisol determination can be performed approximately one hour after the first one. This method is not suitable for anxious, aggressive and otherwise ill dogs.

Procedure:

The dog does not receive Vetoryl on the day of the examination. At the time the capsule is usually administered +/- 1 hour, the first sample is taken and about an hour later, the second sample is collected, after which the dog receives the Vetoryl capsule. The first blood collection should be done immediately after arrival at the practice prior to any other measures.

Evaluation:

Cortisol levels between 14 and 50 ng/ml are preferred.

4. Pre-pill and post-pill cortisol determination (Vetoryl therapy monitoring)

To assess the dose of Vetoryl, this test may be used as an alternative to the ACTH stimulation test. Dosage changes should not be made too early in the course of the treatment. It is therefore advisable not to perform this test until the second follow-up appointment about 28 days after starting treatment. It is unsuitable for clinically ill and anxious dogs.

Procedure:

The first blood sample is collected just like it is done for the determination of the pre-pill level. Immediately afterwards, the dog is given the usual dose of Vetoryl with the usual meal. The second sample is taken 3 hours after capsule administration. The cortisol concentration is determined in both samples.

Evaluation:

Baseline cortisol levels between 14 and 50 ng/ml are preferred, and after capsule administration, levels should be between 14 and 23 ng/ml.

Tips for successful treatment

Owner compliance is an essential part of successful treatment. The dog must regularly be presented to the practice and its condition must be re-evaluated. Concomitant diseases have to be recognised at an early stage and treated adequately.

Treatment needs to be started with a low dose. Increase in dosage must be gradual. Large dogs need less Vetoryl. Sometimes, the dosage can be reduced again; in certain situations, Vetoryl must even be temporarily discontinued and treatment restarted. Pre-Vetoryl cortisol is a suitable method for routine checks but cannot always replace the ACTH stimulation test. For anxious and aggressive dogs, dogs with signs of an illness and if an overdose of Vetoryl is suspected, the ACTH stimulation test remains the test of choice.

Dose adjustments must always be based on the clinical picture. The given reference values do not necessarily indicate the appropriate cortisol concentration for every dog.

Unit conversion made easy:

$$1 \mu\text{g/dl} = 1000 \text{ ng}/100 \text{ ml} = 10 \text{ ng/ml} (\times 10)$$

$$1 \text{ ng/ml} = 0.001 \mu\text{g}/0.01 \text{ dl} = 0.1 \mu\text{g/dl} (: 10)$$

For cortisol, the following still applies:

$$\mu\text{g/dl} \times 27.59 = \text{nmol/l}$$

$$\text{nmol/l} \times 0.036 = \mu\text{g/dl}$$

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