Treat their Cushing’s Syndrome.

Help restore their vitality.
What is Cushing’s syndrome?

Cushing’s syndrome is one of the most common endocrine disorders, occurring mostly in middle-aged and older dogs and is associated with an overproduction of cortisol. Cushing’s syndrome is also referred to as hyperadrenocorticism (hyper=excess, adreno=adrenal gland, corticism=cortisol level) or more plainly, an excess of cortisol produced by the adrenal glands.

Cortisol is produced by the adrenal glands, two small glands located in the abdomen, next to each kidney. A hormone called ACTH controls the production and release of cortisol from the adrenal glands. ACTH itself is produced by the pituitary gland, a pea-sized gland located at the base of the brain.

The concentration of cortisol in the blood of healthy animals varies greatly as the body’s demand for cortisol fluctuates. For example, during a period of stress or illness, the production of cortisol by the adrenal glands is increased. Once this period of stress has passed, the cortisol concentration in the blood returns back to normal again.

Cortisol overproduction

In dogs with Cushing’s syndrome, there is a chronic overproduction of cortisol over weeks and months. Although the concentration of cortisol in the blood of a dog with Cushing’s also fluctuates greatly, it tends to be, on average, much higher than in healthy dogs. The excessive amount of cortisol released into the bloodstream has a harmful effect on the function of many organs and the body’s metabolism.
What causes Cushing’s syndrome?

Cushing’s syndrome will usually occur as a result of a tumor - often benign – in the pituitary gland (most common) or the adrenal gland (less common). Regardless of the cause, a dog suffering from Cushing’s syndrome will develop a combination of clinical signs which may initially be confused with signs associated with the normal aging process.

Most dog’s with Cushing’s syndrome (80 - 85%) have a benign tumor of the pituitary gland. The tumor cells produce large amounts of the hormone ACTH, which in turn stimulates the adrenal glands to overproduce cortisol.

In 15 - 20% of cases, Cushing's syndrome is caused by a tumor of one (or very rarely both) of the adrenal glands, which produces excessive amounts of cortisol.

Irrespective of the cause of Cushing’s syndrome, the result is always the same - more cortisol is produced than actually needed by the body. This results in the slow development of a combination of clinical signs that are commonly associated with Cushing’s syndrome.

Recognizing the signs of Cushing’s syndrome

Cushing’s syndrome occurs mainly in older dogs. Lethargy (decreased energy levels), hair loss, pot-bellied appearance, chronic skin disease, changes in behavior, frequent urination and a ravenous appetite are some of the most noticeable signs. Many of these symptoms are very similar to those associated with the normal aging process and occur slowly over many months, making it difficult to recognize as a disease process versus “normal” aging.

The most noticeable signs of Cushing’s syndrome include:
- Excessive urination with possible incontinence
- Large water intake
- Ravenous appetite
- Excessive panting, even at rest
- Muscle wastage and weakness
- Frequent urinary tract infections (cystitis)
- Pot-bellied appearance
- Lethargy
- Hair loss, thin skin and recurrent skin infections

Not all dogs will react to the overproduction of cortisol seen with Cushing’s syndrome in the same way, therefore your dog will likely not display all of these signs. Always discuss any changes in energy, behavior, water intake or appetite with your veterinarian.

If you become concerned with your dog’s health you should consult your veterinarian immediately.
Diagnosing Cushing’s syndrome

Your veterinarian may initially suspect Cushing’s syndrome based on the outward appearance of your dog and the symptoms you are noticing at home. The diagnosis of Cushing’s requires a series of blood tests, urine tests and sometimes an abdominal ultrasound to look at the adrenal glands and other internal organs.

Generally, your veterinarian will start the diagnostic process with a chemistry panel, complete blood count (CBC), a urinalysis and possibly a urine cortisol:creatinine ratio (UCCR) to assess the overall health of your dog. If the results of these preliminary tests are consistent with Cushing’s and there are no other concerns, your veterinarian will then begin testing that is specifically directed at examining your dog’s cortisol production and the adrenal glands.

There is not one specific test that can identify Cushing’s 100% of time in the dog. So the diagnosis often involves multiple tests. The two tests that are most commonly used to confirm a diagnosis of Cushing’s are called the low-dose dexamethasone suppression (LDDS) test and the ACTH stimulation test. It may be necessary to perform both tests.

The LDDS test requires your dog to stay at the veterinary hospital for at least 8 hours. The veterinarian will take three separate blood samples to measure the cortisol levels every 4 hours after giving an injection of dexamethasone. This test measures your dog’s ability to respond to the dexamethasone and lower their cortisol levels. Dogs with Cushing’s syndrome have difficulty lowering their cortisol in response to the injection. The LDDS test may also help identify whether your dog has a pituitary or an adrenal tumor.

For the ACTH stimulation test, blood is taken to measure cortisol before and after your dog is given a synthetic version of the hormone ACTH. This test assesses how well your dog’s adrenal glands control the production of cortisol. You will need to leave your dog at the veterinary hospital for a few hours or for the day to perform the ACTH stimulation test.

In addition to the low-dose dexamethasone test and the ACTH stimulation test your veterinarian may also elect to perform an abdominal ultrasound to evaluate the adrenal glands, the liver and other vital organs.
The importance of treatment

Daily administration of VETORYL Capsules can greatly reduce the clinical signs associated with Cushing’s syndrome, helping to restore your dog’s vitality. Clinical studies demonstrated that daily treatment with VETORYL Capsules resulted in decreased thirst, decreased frequency of urination, decreased panting, and improvement of appetite and activity. Activity levels began to show improvement within 14 days of treatment.

The overproduction of cortisol has a negative impact on your dog’s body and if left untreated your dog runs a greater risk of developing other serious conditions such as:

- Diabetes mellitus (high blood sugar levels)
- High blood pressure
- Inflammation of the pancreas (pancreatitis)
- Inflammation and infection of the gallbladder (mucocele formation)
- Infections of the kidneys and urinary tract
- High levels of protein in the urine that can lead to kidney damage
- Chronic infections of the skin and ears
- Pulmonary thromboembolism (blood clots in the lung)

Management of Cushing’s syndrome

Cushing’s syndrome cannot typically be cured with medication, but it can be successfully managed. VETORYL® Capsules, which are the only FDA-approved treatment for use in dogs with pituitary or adrenal tumors, contain the active ingredient trilostane. Trilostane reduces the production of cortisol by the adrenal glands. However, it does not directly treat the tumor itself.

Treatment with VETORYL Capsules

Now that your dog has started treatment, you should soon notice some marked improvements. It is important that you follow the instructions given by your veterinarian.

Your dog will begin VETORYL Capsules at the recommended starting dose based on its body weight. You should then make an appointment for your dog to return to the veterinary hospital after 10-14 days. It may be necessary for your veterinarian to adjust the dosage of VETORYL Capsules. Every dosage change should be followed by blood tests 10-14 days later. Your veterinarian will assess your dog’s response to VETORYL Capsules by:

- Looking for improvement in clinical signs
- Performing blood tests to evaluate response to treatment

In most cases you can expect to see decreased thirst, frequency of urination and panting, and improvement of appetite and activity within the first few weeks. Other clinical signs, especially changes to the hair, skin and their pot-bellied appearance may take 3 to 6 months to improve.

The results of routine blood tests, including electrolytes, and an ACTH stimulation test are used to assess the effectiveness of VETORYL Capsules at 10-14 days, 4 weeks and 12 weeks after starting your dog on treatment, and every 3 months thereafter.
Continuous care

Your dog should be closely monitored in the early stages of therapy so the dose of VETORYL Capsules can be adjusted to meet your dog’s specific needs. This also helps to minimize the risk of side-effects or complications that could be harmful to your dog.

Quick Reference guide

Answers to some questions you may have about VETORYL Capsules.

Why do I have to give VETORYL Capsules every day?
The active ingredient in VETORYL Capsules is a medicine called trilostane. Trilostane is a short-acting medicine which needs to be given every day to control the disease. Most dogs need to be given VETORYL Capsules every day for life.

How do I give VETORYL Capsules to my dog?
Give VETORYL Capsules with a meal in the morning so they can be effectively absorbed. Administration in the morning is critical so your veterinarian can perform the monitoring test at the appropriate time after dosing.

How long will it take for my dog to improve on treatment?
The clinical signs of Cushing’s such as lethargy, increased drinking, eating and urination improve quickly, often within the first two weeks of treatment. Skin changes and hair loss can take up to 3 to 6 months to improve.

Will I need to revisit my veterinarian?
Yes. It is important that your dog revisits your veterinarian for assessment and monitoring tests at 10-14 days, 4 weeks and 12 weeks after starting VETORYL Capsules, and thereafter every 3 months. If your dog becomes sick or ill at any time while on VETORYL Capsules, stop giving them to your dog and consult your veterinarian as soon as possible.

VETORYL Capsules are well-tolerated by most dogs. If your dog develops any signs of illness while on VETORYL Capsules including lethargy, vomiting, diarrhea, weakness, an extremely reduced appetite or anorexia, stop giving VETORYL Capsules immediately and contact a veterinarian as soon as possible.

As with all drugs, side effects may occur. In field studies and post-approval experience, the most common side effects reported were: anorexia, lethargy/depression, vomiting, diarrhea, elevated liver enzymes, elevated potassium with or without elevated sodium, elevated BUN, decreased Na/K ratio, hypoadrenocorticism, weakness, elevated creatinine, shaking, and renal insufficiency. In some cases, death has been reported as an outcome of these adverse events. VETORYL Capsules are not for use in dogs with primary hepatic or renal disease, or in pregnant dogs. Refer to the prescribing information for complete details or visit www.Dechra-US.com.
Do:

• Give VETORYL Capsules in the morning with food, so they can be effectively absorbed. Administration in the morning is critical so your veterinarian can perform the monitoring test at the appropriate time after dosing.

• Take your dog back to your veterinarian for regular monitoring.

• Note your dog’s weight, water consumption, appetite and frequency of urination so you can monitor its improvement once treatment starts. Contact your veterinarian if you have any concerns.

• Contact your veterinarian immediately if your dog stops eating, drinking or urinating or becomes unwell while on Vetoryl.

• Wash your hands after handling VETORYL Capsules.

• Book follow up appointments with your veterinarian every three months so your dog’s progress and health can be assessed.

• You might like to consider taking a photo before you start treatment - improvements such as hair regrowth or the loss of a pot-belly occur gradually so are less noticeable on a daily basis.

Don’t:

• Don’t give on an empty stomach. Food is critical to ensure the optimum absorption of VETORYL Capsules.

• Don’t split or open the capsules.

• Give a double dose if you have forgotten a dose before. Consult your veterinarian.

• Handle VETORYL Capsules if you are pregnant, or planning to become pregnant.

• Change the daily dosage without consulting your veterinarian.

Ensure you continue giving your dog the prescribed dose of VETORYL Capsules even if you notice dramatic physical improvements. VETORYL Capsules will help block the production of cortisol and the associated symptoms, but they will not cure the disease.

Monitoring is extremely important and regular examinations and blood tests performed by your veterinarian will ensure your dog continues to get the best possible care.
Adrenocortical suppressant for oral use in dogs only.

**CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.**

**DESCRIPTION:** VETORYL ® Capsules are available in 4 sizes (10, 30, 60 and 120 mg) for oral administration based on body weight. Trilostane (4,5-epoxy-17-hydroxy-3-oxocort-20-ene) is an active metabolite of the synthetic steroid amastanone which selectively inhibits 3-hydroxysteroid dehydrogenase in the adrenal cortex; thereby inhibiting the conversion of progrenosterone to progesterone. This inhibition blocks production of glucocorticoids and to a lesser extent, mineralocorticoids and sex hormones while steroid precursor levels increase.

The structural formula is:

**INDICATIONS:**
VETORYL Capsules are indicated for the treatment of pituitary-dependent hyperadrenocorticism in dogs. VETORYL Capsules are indicated for the treatment of hyperadrenocorticism due to adrenocortical tumor in dogs (see PRECAUTIONS: ANIMAL SAFETY). Complete information is available in the full prescribing information for VETORYL Capsules.

**CONTRAINDICATIONS:**
Do not use VETORYL in dogs that have demonstrated hypersensitivity to trilostane. Do not use if radiographic examination reveals the presence of a normal, functioning adrenal gland. Do not use in dogs that have demonstrated signs consistent with hyperadrenocorticism at any dose of VETORYL (unless the signs are consistent with secondary hypoadrenocorticism). Do not use in dogs that have demonstrated signs consistent with hypoadrenocorticism (glucocorticoids and mineralocorticoids) after the acute presentation. Additional adverse reactions were reported in 3 dogs. The most common of these included diarrhea (31 dogs), lethargy (20 dogs), inappetence/anorexia (27 dogs), vomiting (28 dogs), musculoskeletalalterations (lameness, worsening of degenerative joint disease) (25 dogs), constipation (20 dogs), dehydration (17 dogs), polydipsia/polyuria (17 dogs), incontinence (17 dogs), shaking, muscle tremors, convulsions, weight gain (15 dogs), weight loss (10 dogs), and ataxia (9 dogs). In some cases, death has been reported as an outcome of the adverse events listed above. For a cumulative listing of adverse reactions for trilostane reported to the CVM see: http://www.fda.gov/ADEreports. This listing includes adverse reactions reported to VETORYL Capsules reporting for a variety of conditions considered to be unrelated to or to have an unknown relationship with administration of trilostane. Listings by active ingredient may represent more than one brand name. To report suspected adverse events for VETORYL Capsules, contact Dechra Veterinary Products at (866) 933-2472.

**PRECAUTIONS:**

**STORAGE INFORMATION:**
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.