



What is Cushing's Syndrome?

TECHNICAL BROCHURE



WHAT IS CUSHING'S SYNDROME?

Hyperadrenocorticism, or *Cushing's syndrome*, is one of the most commonly diagnosed canine endocrine disorders. Cushing's syndrome is usually seen in older dogs and can be either spontaneous or iatrogenic.

The signs of Cushing's syndrome in dogs arise due to an excess of circulating glucocorticoids, particularly cortisol. Cortisol is a hormone produced in the cortex of the adrenal glands. The normal function of cortisol is to help the body respond to stress and change, and also to prepare the body for the fight or flight response. Cortisol mobilizes nutrients, modifies the body's response to inflammation, stimulates the liver to raise the blood sugar, and helps control the amount of water in the body.

There Are Two Forms of Spontaneous Cushing's Syndrome:

a) Pituitary-dependent hyperadrenocorticism (PDH)

This is the most common form of the disease (80% to 85% of spontaneous cases), and it often occurs as the result of a benign tumor of the pituitary gland. This tumor causes the pituitary gland to produce large amounts of ACTH.

b) Adrenal-dependent hyperadrenocorticism (ADH)

This form of the disease is less common (15% to 20% of spontaneous cases), and occurs when a tumor producing large amounts of cortisol develops in one, or sometimes both, of the adrenal glands.



For Technical Support, please contact Dechra Veterinary Products at 866-933-2472.
www.VETORYL.com

Diagnosing Cushing's Syndrome

Excess levels of glucocorticoids in the body cause a range of clinical signs that include:

- Polydipsia
- Polyuria
- Polyphagia
- Hypertension
- Pot belly
- Thinning of the skin
- Hair loss
- Recurrent skin diseases
- Lethargy
- Excessive panting

Other less common clinical signs include heat intolerance, seborrhea, comedones, hyperpigmentation, calcinosis cutis, bruising, testicular atrophy, failure to cycle, clitoral hypertrophy, and facial paralysis! Any of these signs can be very distressing for owners.

Signs of Cushing's syndrome are very similar to normal aging, and this can make it particularly difficult to diagnose. Several tests that involve analysis of the blood or urine are available to aid in the confirmation of a diagnosis. However, because cortisol levels in the blood of both normal dogs and dogs with hyperadrenocorticism fluctuate greatly throughout the day, a diagnosis cannot be confirmed by simply measuring the concentration of cortisol in the blood.

There are a number of diagnostic tests for Cushing's syndrome available, including the ACTH Stimulation Test, Low-Dose Dexamethasone Suppression Test, and Urinary Cortisol:Creatinine Ratio.



What Are the Treatment Options for Dogs with Cushing's Syndrome?

If it can be determined that there is a tumor of the adrenal gland, surgical removal of the tumor is an option, although the risks of this procedure can be high. However, it is not usually possible to remove pituitary gland tumors (the most frequent cause of Cushing's syndrome).

The alternative to surgery is medical management. While other oral medications exist, such as selegiline hydrochloride and mitotane, the only licensed treatment available for both pituitary-dependent hyperadrenocorticism (PDH) and adrenal-dependent hyperadrenocorticism (ADH) in dogs in the United States and 20 European countries is VETORYL®. VETORYL Capsules contain the active ingredient trilostane.

Although the daily administration of VETORYL does not offer a medical cure for Cushing's syndrome, it may allow the disease to be managed successfully, greatly enhancing the dog's vitality and quality of life.

More information about these tests can be obtained by contacting Dechra Technical Support.

What Are VETORYL® Capsules, and How Do They Work?

VETORYL Capsules contain the active ingredient trilostane. Trilostane blocks the excessive production of cortisol by reversibly inhibiting the action of the enzyme 3-β hydroxysteroid dehydrogenase. While treatment with trilostane significantly reduces serum cortisol concentrations, it has not been found to reduce basal aldosterone significantly.^{2,3}

Starting Dose

VETORYL Capsules should be administered orally once daily in the morning with food. Administration with food will significantly increase the rate and extent of absorption of VETORYL.

Recommended starting dosages are outlined below. Ideally, the starting dose to aim for is 1.0 to 3.0 mg/lb (2.2 to 6.7 mg/kg) once a day based on body weight and capsule size.

Table 1: Starting dose

WEIGHT RANGE (POUNDS)	WEIGHT RANGE (KG)	STARTING DOSE (MG) ONCE DAILY
≥3.8 to <10	≥1.7 to <4.5	10
≥10 to <22	≥4.5 to <10	30
≥22 to <44	≥10 to <20	60
≥44 to <88	≥20 to <40	120 (2 x 60 mg)
≥88 to <132*	≥40 to <60*	180 (3 x 60 mg)

*Dogs over 132 pounds (60 kg) should be administered the appropriate combination of capsules.



ONCE TREATMENT HAS STARTED, THE OWNER SHOULD BE ADVISED TO MONITOR THE DOG'S DEemeanOR, APPETITE, AND WATER INTAKE. IF THE DOG SHOWS ANY SIGNS OF ILLNESS, ADVISE THE OWNER TO STOP TREATMENT AND CONTACT HIS OR HER VETERINARIAN IMMEDIATELY.

This information is more thoroughly explained in the dog owner information sheet, included in each carton of VETORYL Capsules.

Monitoring Efficacy of the Treatment

The efficacy of treatment is assessed by collectively monitoring:

- Clinical improvement
- Blood cortisol with an ACTH stimulation test
- Biochemistry profile (particularly electrolytes, urea, and creatinine)

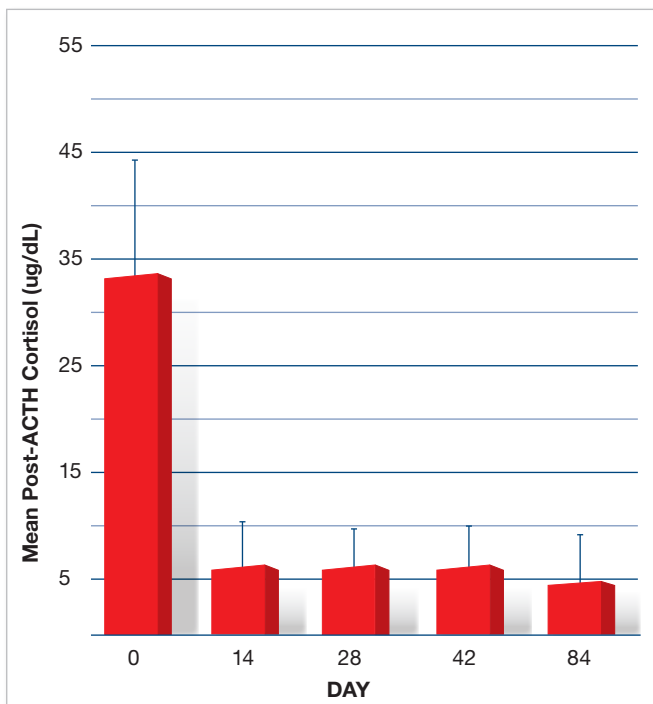
Before starting treatment, cases should be screened for the presence of primary hepatic disease and renal insufficiency, as VETORYL is contraindicated in both of these situations.

Blood Cortisol Monitoring With an ACTH Stimulation Test

A positive response to therapy is regarded as an improvement in clinical signs and a post-ACTH serum cortisol concentration of between 1.45 µ/dL and 9.1 µ/dL (40-250 nmol/L). The ACTH stimulation test should be performed 4-6 hours after dosing with VETORYL® Capsules. Standard advice is to obtain the initial blood sample at 4 hours post dosing. After the administration of VETORYL Capsules, cortisol remains most significantly suppressed for 2-8 hours (data on file).

Treatment should be monitored with an ACTH stimulation test at 2 weeks, 4 weeks, and 12 weeks after starting therapy (or 10-14 days following any dose change), and thereafter every 3 months. Once VETORYL treatment begins, the post-ACTH serum cortisol concentration should decrease significantly during the first 9-12 days of treatment, and should remain suppressed while treatment continues.

Changes in Post-ACTH Serum Cortisol Concentration Associated with VETORYL Treatment⁴



Biochemistry Profile

Biochemical parameters should be measured at 2 weeks, 4 weeks, and 12 weeks after starting therapy (or 10-14 days following any dose change), and thereafter every 3 months. Particular attention should be paid to changes in the serum concentration of electrolytes, urea, and creatinine.

PARAMETER	EXPECTED BIOCHEMICAL CHANGES IN DOGS ON VETORYL TREATMENT
Alkaline Phosphatase	Decrease but may not return to reference range
Alanine Aminotransferase	Decrease but may not return to reference range
Cholesterol	Decrease but may not return to reference range
Sodium	May decrease slightly but should remain within reference range
Potassium	May increase slightly but should remain within reference range
Urea	May increase slightly but should remain within reference range
Creatinine	May increase slightly but should remain within reference range
Red Blood Cells	May decrease slightly but should remain within reference range



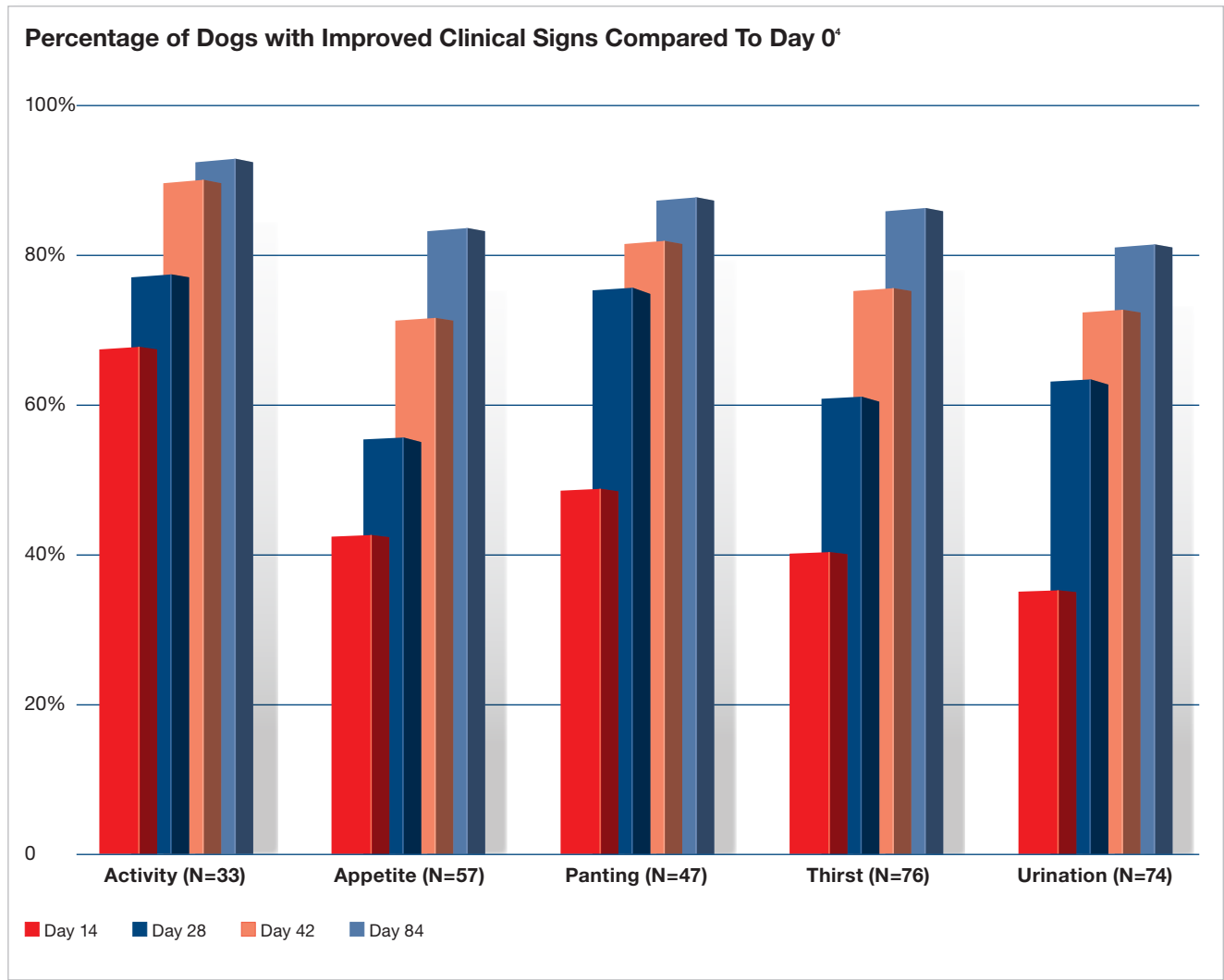
Expected Changes in Clinical Signs of Hyperadrenocorticism

First recheck at 14 days⁴

- Owners should have noticed that the dog is drinking less and urinating less
- The animal should be less ravenous and excessive panting should have decreased
- Lethargy is another clinical sign of Cushing's syndrome that rapidly responds to treatment; even at the first 14-day check many owners have noticed their dogs are more active

Re-examination at 12 weeks⁴

- At day 84 after starting treatment with VETORYL Capsules, 80% of the dogs were considered treatment successes
- At day 84, the percentage of dogs showing improvements in activity, appetite, thirst, urination, and panting ranged from 81% to 93%
- In 93% of dogs, improvement in clinical assessments were noted at day 84





Treatment prior to VETORYL

Photographs courtesy of Carlos Mellan, DVM, PhD



Following 3 months of treatment with VETORYL



Following 9 months of treatment with VETORYL

Drug Interactions

If a dog has previously been treated with mitotane, its adrenal function will have been reduced. Experience in the field suggests that mitotane therapy should be stopped for at least a month (or until the clinical signs of hyperadrenocorticism start to recur) and treatment with VETORYL Capsules should not be started until the post-ACTH serum cortisol is $>9.1 \mu\text{g/dL}$ ($>250 \text{ nmol/L}$). Close monitoring of adrenal function is advised, as these dogs may be more susceptible to the effects of trilostane.

The risk of hyperkalemia developing should be considered if trilostane is used in conjunction with potassium-sparing diuretics or ACE inhibitors (i.e., drugs that interfere with aldosterone production).

VETORYL Capsules were administered concurrently with a variety of medications that are commonly dispensed to middle-aged and geriatric dogs. The most commonly dispensed concurrent medications include heartworm prophylaxis, flea and tick treatments, routine vaccinations, antimicrobials, levothyroxine, non-steroidal anti-inflammatories, and joint supplements.

The product insert, which is located on the last page of this brochure, is where you can locate full product disclosure.

References

- (1) Reusch CE (2005). Hyperadrenocorticism. *Textbook of Veterinary Internal Medicine*, 6th Ed., Ed SJ Ettinger, EC Feldman pp. 1592-1612.
- (2) Sieber-Ruckstuhl NS, Boretti FS, Wenger M, Maser-Gluth C and Reusch CE (2006). Cortisol, aldosterone, cortisol precursor, androgen and endogenous ACTH concentrations in dogs with pituitary-dependant hyperadrenocorticism treated with trilostane. *Domestic Animal Endocrinology*. 31 (1): 63-75.
- (3) Wenger M, Sieber-Ruckstuhl NS, Muller C, Reusch CE (2004). Effect of trilostane on serum concentrations of aldosterone, cortisol and potassium in dogs with pituitary-dependent hyperadrenocorticism. *Am J Vet Res*. 65 (9):1245-50.
- (4) Data on file at Dechra Veterinary Products: US Field Study.

Clinical signs of Cushing's syndrome that rapidly respond to treatment include lethargy and excessive thirst, urination, and panting.



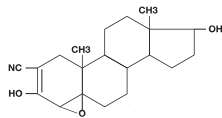
Adrenocortical suppressant for oral use in dogs only.

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

DESCRIPTION:

VETORYL Capsules are available in 3 sizes (10, 30 and 60 mg) for oral administration based on body weight. Trilostane (4a, 5a-epoxy-17 β -hydroxy-3-oxoandrostane-2a-carbonitrile) is an orally active synthetic steroid analogue that selectively inhibits 3 β -hydroxysteroid dehydrogenase in the adrenal cortex, thereby inhibiting the conversion of pregnenolone 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.

DOSAGE AND ADMINISTRATION:

Always provide the Client Information Sheet with prescription. The starting dose for the treatment of hyperadrenocorticism in dogs is 1.0-3.0 mg/lb (2.2-6.7 mg/kg) once a day based on body weight and capsule size (see Table 1). VETORYL Capsules should be administered with food.

Table 1: Starting dose

Weight range (pounds)	Weight range (kg)	Starting dose (mg) ONCE DAILY
≥3.8 to <10	≥1.7 to <4.5	10
≥10 to <22	≥4.5 to <10	30
≥22 to <44	≥10 to <20	60
≥44 to <88	≥20 to <40	120 (2 x 60 mg)
≥88 to <132*	≥40 to <60*	180 (3 x 60 mg)

*Dogs over 132 pounds (60 kg) should be administered the appropriate combination of capsules.

After approximately 10-14 days at this dose, re-examine the dog and conduct a 4-6 hour post-dosing ACTH stimulation test. If physical examination is acceptable, take action according to Table 2.

Table 2: Action at 10-14 day evaluation

Post-ACTH serum cortisol		Action
µg/dL	nmol/L	
<1.45	<40	Stop treatment. Re-start at decreased dose
1.45 to 5.4	40 to 150	Continue on same dose
>5.4 to 9.1	>150 to 250	EITHER: Continue on current dose if clinical signs are well controlled OR: Increase dose if clinical signs of hyperadrenocorticism are still evident*
>9.1	>250	Increase initial dose

*Combinations of capsule sizes should be used to slowly increase the once daily dose.

Individual dose adjustments and close monitoring are essential.

Re-examine and conduct an ACTH stimulation test 10-14 days after every dose alteration. Care must be taken during dose increases to monitor the dog's clinical signs and serum electrolyte concentrations. Once daily administration is recommended. However, if clinical signs are not controlled for the full day, twice daily dosing may be needed. To switch from once daily to twice daily dosing, increase the total daily dose by 1/3 to 1/2 and divide the total amount into two doses given 12 hours apart.

Long-Term Monitoring

Once an optimum dose of VETORYL Capsules has been reached, re-examine the dog at 30 days, 90 days and every 3 months thereafter. At a minimum, this monitoring should include a thorough history and physical examination, ACTH stimulation test (conducted 4-6 hours after VETORYL Capsule administration), and serum biochemical tests (with particular attention to electrolytes, renal and hepatic function). A post-ACTH stimulation test resulting in a cortisol of <1.45 µg/dL (<40 nmol/L), with or without electrolyte abnormalities, may precede the development of clinical signs of hyperadrenocorticism. Good control is indicated by favorable clinical signs as well as post-ACTH serum cortisol of 1.45-9.1 µg/dL (40-250 nmol/L).

If the ACTH stimulation test is <1.45 µg/dL (<40 nmol/L) and/or if electrolyte imbalances characteristic of hyperadrenocorticism (hyperkalemia and hyponatremia) are found, VETORYL Capsules should be temporarily discontinued until recurrence of clinical signs consistent with hyperadrenocorticism and test results return to normal (1.45-9.1 µg/dL or 40-250 nmol/L). VETORYL Capsules may then be re-introduced at a lower dose.

Owners should be instructed to stop therapy and contact their veterinarian immediately in the event of adverse reactions or unusual developments.

CONTRAINDICATIONS:

The use of VETORYL Capsules is contraindicated in dogs that have demonstrated hypersensitivity to trilostane.

Do not use VETORYL Capsules in animals with primary hepatic disease or renal insufficiency.

Do not use in pregnant dogs. Studies conducted with trilostane in laboratory animals have shown teratogenic effects and early pregnancy loss.

WARNINGS:

In case of overdosage, symptomatic treatment of hyperadrenocorticism with corticosteroids, mineralocorticoids and intravenous fluids may be required.

Angiotensin-converting enzymes (ACE) inhibitors should be used with caution with VETORYL Capsules, as both drugs have aldosterone-lowering effects which may be additive, impairing the patient's ability to maintain normal electrolytes, blood volume and renal perfusion. Potassium sparing diuretics (e.g. spironolactone) should not be used with VETORYL Capsules, as both drugs have the potential to inhibit aldosterone, increasing the likelihood of hyperkalemia.

HUMAN WARNINGS:

Keep out of reach of children. Not for human use.

Wash hands after use. Do not empty capsule contents and do not attempt to divide the capsules. Do not handle the capsules if pregnant or if trying to conceive. Trilostane is associated with teratogenic effects and early pregnancy loss in laboratory animals. In the event of accidental ingestion/overdose, seek medical advice immediately and take the labeled container with you.

PRECAUTIONS:

Hyperadrenocorticism can develop at any dose of VETORYL Capsules. In some cases, it may take months for adrenal function to return and some dogs never regain adequate adrenal function.

A small percentage of dogs may develop corticosteroid withdrawal syndrome within 10 days of starting treatment. This phenomenon results from acute withdrawal of circulating glucocorticoids; clinical signs include weakness, lethargy, anorexia, and weight loss. These clinical signs should be differentiated from an early hypoadrenocortical crisis by measurement of serum electrolyte

concentrations and performance of an ACTH stimulation test. Corticosteroid withdrawal syndrome should respond to cessation of VETORYL Capsules (duration of discontinuation based on the severity of the clinical signs) and restarting at a lower dose.

Mitotane (o,p'-DDD) treatment will reduce adrenal function. Experience in foreign markets suggests that when mitotane therapy is stopped, an interval of at least one month should elapse before the introduction of VETORYL Capsules. It is important to wait for both the recurrence of clinical signs consistent with hyperadrenocorticism, and a post-ACTH cortisol level of >9.1 µg/dL (>250 nmol/L) before treatment with VETORYL Capsules is initiated. Close monitoring of adrenal function is advised, as dogs previously treated with mitotane may be more responsive to the effects of VETORYL Capsules.

The use of VETORYL Capsules will not affect the adrenal tumor itself. Adrenalectomy should be considered as an option for cases that are good surgical candidates.

The safe use of this drug has not been evaluated in lactating dogs and males intended for breeding.

ADVERSE REACTIONS:

The most common adverse reactions reported are poor/reduced appetite, vomiting, lethargy/dullness, diarrhea, and weakness. Occasionally, more serious reactions, including severe depression, hemorrhagic diarrhea, collapse, hypoadrenocortical crisis or adrenal necrosis/rupture may occur, and may result in death.

In a US field study with 107 dogs, adrenal necrosis/rupture (two dogs) and hypoadrenocorticism (two dogs) were the most severe adverse reactions in the study. One dog died suddenly of adrenal necrosis, approximately one week after starting trilostane therapy. One dog developed an adrenal rupture, believed to be secondary to adrenal necrosis, approximately six weeks after starting trilostane therapy. This dog responded to trilostane discontinuation and supportive care.

Two dogs developed hypoadrenocorticism during the study. These two dogs had clinical signs consistent with hypoadrenocorticism (lethargy, anorexia, collapse) and post-ACTH cortisol levels of ≤0.3 µg/dL. Both dogs responded to trilostane discontinuation and supportive care, and one dog required continued treatment for hypoadrenocorticism (glucocorticoids and mineralocorticoids) after the acute presentation.

Additional adverse reactions were observed in 93 dogs. The most common of these included diarrhea (31 dogs), lethargy (30 dogs), inappetence/anorexia (27 dogs), vomiting (28 dogs), musculoskeletal signs (lameness, worsening of degenerative joint disease) (25 dogs), urinary tract infection (UTI)/hematuria (17 dogs), shaking/shivering (10 dogs), otitis externa (8 dogs), respiratory signs (coughing, congestion) (7 dogs), and skin/coat abnormality (seborrhea, pruritus) (8 dogs).

Five dogs died or were euthanized during the study (one dog secondary to adrenal necrosis, discussed above, two dogs due to progression of pre-existing congestive heart failure, one dog due to progressive central nervous system signs, and one dog due to cognitive decline leading to inappropriate elimination). In addition to the two dogs with adrenal necrosis/rupture and the two dogs with hypoadrenocorticism, an additional four dogs were removed from the study as a result of possible trilostane-related adverse reactions, including collapse, lethargy, inappetence, and trembling.

Complete blood counts conducted pre- and post-treatment revealed a statistically significant (p <0.005) reduction in red cell variables (HCT, HGB, and RBC), but the mean values remained within the normal range. Additionally, approximately 10% of the dogs had elevated BUN values (>40 mg/dL) in the absence of concurrent creatinine elevations. In general, these dogs were clinically normal at the time of the elevated BUN.

In a long-term follow-up study of dogs included in the US effectiveness study, the adverse reactions were similar to the short-term study. Vomiting, diarrhea and general gastrointestinal signs were most commonly observed. Lethargy, inappetence/anorexia, heart murmur or cardiopulmonary signs, inappropriate

urination/incontinence, urinary tract infections or genitourinary disease, and neurological signs were reported. Included in the US follow-up study were 14 deaths, three of which were possibly related to trilostane. Eleven dogs died or were euthanized during the study for a variety of conditions considered to be unrelated to or to have an unknown relationship with administration of trilostane.

In two UK field studies with 75 dogs, the most common adverse reactions seen were vomiting, lethargy, diarrhea/loose stools, and anorexia. Other adverse reactions included: nocturia, corneal ulcer, cough, persistent estrus, vaginal discharge and vulvar swelling in a spayed female, hypoadrenocorticism, electrolyte imbalance (elevated potassium with or without decreased sodium), collapse and seizure, shaking, muscle tremors, constipation, scratching, weight gain, and weight loss. One dog died of congestive heart failure and another died of pulmonary thromboembolism. Three dogs were euthanized during the study. Two dogs had renal failure and another had worsening arthritis and deterioration of appetite.

In a long-term follow-up of dogs included in the UK field studies, the following adverse reactions were seen: hypoadrenocortical episode (including syncope, tremor, weakness, and vomiting) hypoadrenocortical crisis or renal failure (including azotemia, vomiting, dehydration, and collapse), chronic intermittent vaginal discharge, hemorrhagic diarrhea, occasional vomiting, and distal limb edema. Signs of hypoadrenocorticism were usually reversible after withdrawal of the drug, but may be permanent. One dog discontinued VETORYL Capsules and continued to have hypoadrenocorticism when evaluated a year later. Included in the follow-up were reports of deaths, at least 5 of which were possibly related to use of VETORYL Capsules. These included dogs that died or were euthanized because of renal failure, hypoadrenocortical crisis, hemorrhagic diarrhea, and hemorrhagic gastroenteritis.

Foreign Market Experience: The following events were reported voluntarily during post-approval use of VETORYL Capsules in foreign markets. The most serious adverse events were death, adrenal necrosis, hypoadrenocorticism (electrolyte alterations, weakness, collapse, anorexia, lethargy, vomiting, diarrhea, and azotemia), and corticosteroid withdrawal syndrome (weakness, lethargy, anorexia, and weight loss). Additional adverse events included: renal failure, diabetes mellitus, pancreatitis, autoimmune hemolytic anemia, vomiting, diarrhea, anorexia, skin reactions (rash, erythematous skin eruptions), hind limb paresis, seizures, neurological signs from growth of macroadenomas, oral ulceration, and muscle tremors.

For a copy of the Material Safety Data Sheet (MSDS), or to report adverse reactions, call Dechra Veterinary Products at (866) 933-2472.

INFORMATION FOR DOG OWNERS:

Owners should be aware that the most common adverse reactions may include: an unexpected decrease in appetite, vomiting, diarrhea, or lethargy and should receive the Client Information Sheet with the prescription. Owners should be informed that control of hyperadrenocorticism should result in resolution of polyphagia, polyuria and polydipsia. **Serious adverse reactions associated with this drug can occur without warning and in rare situations result in death (see ADVERSE REACTIONS). Owners should be advised to discontinue VETORYL Capsules and contact their veterinarian immediately if signs of intolerance are observed.** Owners should be advised of the importance of periodic follow-up for all dogs during administration of VETORYL Capsules.

CLINICAL PHARMACOLOGY:

Trilostane absorption is enhanced by administration with food. In healthy dogs, maximal plasma levels of trilostane occur within 1.5 hours, returning to baseline levels within twelve hours, although large inter-dog variation occurs. There is no accumulation of trilostane or its metabolites over time.

EFFECTIVENESS:

Eighty-three dogs with hyperadrenocorticism were enrolled in a multi-center US field study. Additionally, 30 dogs with hyperadrenocorticism were enrolled in

two UK field studies. Results from these studies demonstrated that treatment with VETORYL Capsules resulted in an improvement in clinical signs (decreased thirst, decreased frequency of urination, decreased panting, and improvement of appetite and activity). Improvement in post-ACTH cortisol levels occurred in most cases within 14 days of starting VETORYL Capsules therapy.

In these three studies, there were a total of 10 dogs diagnosed with hyperadrenocorticism due to an adrenal tumor or due to concurrent pituitary and adrenal tumors. Evaluation of these cases failed to demonstrate a difference in clinical, endocrine, or biochemical response when compared to cases of pituitary-dependent hyperadrenocorticism.

ANIMAL SAFETY:

In a laboratory study, VETORYL Capsules were administered to 8 healthy 6-month-old Beagles per group at 0X (empty capsules), 1X, 3X, and 5X the maximum starting dose of 6.7 mg/kg twice daily for 90 days. Three animals in the 3X group (receiving 20.1 mg/kg twice daily) and five animals in the 5X group (receiving 33.5 mg/kg twice daily) died between Days 23 and 46. They showed one or more of the following clinical signs: decreased appetite, decreased activity, weight loss, dehydration, soft stool, slight muscle tremors, diarrhea, lateral recumbency, and staggering gait. Bloodwork showed hyponatremia, hyperkalemia, and azotemia, consistent with hypoadrenocortical crisis. Post-mortem findings included epithelial necrosis or cystic dilation of duodenal mucosal crypts, gastric mucosal or thymic hemorrhage, atrial thrombosis, pyelitis and cystitis, and inflammation of the lungs.

ACTH stimulated cortisol release was reduced in all dogs treated with VETORYL Capsules. The dogs in the 3X and 5X groups had decreased activity. The 5X dogs had less weight gain than the other groups. The 3X and 5X dogs had lower sodium, albumin, total protein, and cholesterol compared to the control dogs. The 5X dogs had lower mean corpuscular volume than the controls. There was a dose dependent increase in amylase. Post-mortem findings included dose dependent adrenal cortical hypertrophy.

STORAGE INFORMATION:

Store at controlled room temperature 25°C (77°F) with excursions between 15°-30°C (59°-86°F) permitted.

HOW SUPPLIED:

VETORYL Capsules are available in 10, 30, and 60 mg strengths, packaged in aluminum foil blister cards of 10 capsules, with 3 cards per carton.

VETORYL Capsules 10 mg: NDC 17033-110-30

VETORYL Capsules 30 mg: NDC 17033-130-30

VETORYL Capsules 60 mg: NDC 17033-160-30

NADA 141-291, APPROVED BY FDA.



Distributed by:
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*Greco DS, Behrend EN (1995) Corticosteroid withdrawal syndrome. In: Kirk's Current Veterinary Therapy XII; Bonagura, J. (ed); WB Saunders, Philadelphia PA: pp 413-5.