ZYCORTAL® Suspension
Monitoring and Dose Adjustments
As with all drugs, side effects may occur. In field studies, the most common side effects reported were polyuria, polydipsia, depression/lethargy, inappropriate urination, alopecia, decreased appetite/anorexia, panting, vomiting, diarrhea, shaking/trembling, polyphagia, urinary tract infection, urinary tract incontinence and restlessness. ZYCORTAL Suspension should be used with caution in dogs with congestive heart disease, edema, severe renal disease or primary hepatic failure. Dogs presenting in Addisonian crisis must be rehydrated with appropriate intravenous therapy before starting treatment with ZYCORTAL Suspension. Refer to the prescribing information for complete details or visit www.dechra-us.com.

**Initial dose of ZYCORTAL Suspension is 2.2 mg/kg (1 mg/lb) body weight, administered by subcutaneous injection (SQ).**

Start glucocorticoid therapy with prednisone or prednisolone 0.2-0.4 mg/kg/day (0.1-0.2 mg/lb/day).

Day 1
- First dose
- Initial dose of ZYCORTAL Suspension
- Administered by subcutaneous injection (SQ)
- Start glucocorticoid therapy

Day 10
- Interim monitoring
- Re-evaluate the dog and serum Na+/K+ ratio
- If the dog’s clinical signs have worsened or not resolved, adjust the dose of prednisone/prednisolone and/or investigate other causes of the clinical signs.

Day 25
- Second dose
- Re-evaluate the dog and serum Na+/K+ ratio

Clinically normal
- Adjust ZYCORTAL Suspension dose according to Day 10 Na+/K+ ratio as described in table below

Clinically abnormal
- Decrease glucocorticoid dose
- Re-evaluate diagnosis or look for concomitant disease

Abnormal Na+/K+ ratio
- Decrease glucocorticoid dose
- Re-evaluate Day 10 electrolytes
- If the Day 10 Na+/K+ ratio is:
  - > 34
    - Decrease dose to 2.0 mg/kg
  - > 32 to 34
    - Decrease dose to 2.1 mg/kg
  - 27 to 32
    - Continue 2.2 mg/kg
  - 24 to < 27
    - Increase dose to 2.3 mg/kg
  - < 24
    - Increase dose to 2.4 mg/kg

PU/PD persists and Na+/K+ > 32
- Increase glucocorticoid dose
- Re-evaluate diagnosis or look for concomitant disease

PU/PD
- Decrease glucocorticoid dose
- Re-evaluate Day 10 electrolytes

Depression, lethargy, vomiting, diarrhea or weakness
- Increase glucocorticoid dose
- Re-evaluate diagnosis or look for concomitant disease

Other clinical signs
- Increase glucocorticoid dose
- Re-evaluate diagnosis or look for concomitant disease

As soon as possible, administer ZYCORTAL Suspension at the dose recommended above. If the dog’s clinical signs have worsened or not resolved, adjust the dose of prednisone/prednisolone and/or investigate other causes of the clinical signs. Re-evaluate the dog and serum Na+/K+ ratio.

**Subsequent doses and long-term management:**

Once the dog is optimally controlled, keep the same dosing regimen. In case of abnormal clinical condition or abnormal electrolytes at subsequent visits, continue to titrate the dose in similar increments as described above. Prior to a stressful situation, consider temporarily increasing the dose of prednisone/prednisolone.

Day 25 days after the first dose, administer ZYCORTAL Suspension, as follows*:

- Decrease dose to 2.0 mg/kg
- Decrease dose to 2.1 mg/kg
- Continue 2.2 mg/kg
- Increase dose to 2.3 mg/kg
- Increase dose to 2.4 mg/kg
- Increase dose to 2.5 mg/kg

If the Day 10 Na+/K+ ratio is:

- > 34
  - Decrease dose to 2.0 mg/kg
- > 32 to 34
  - Decrease dose to 2.1 mg/kg
- 27 to 32
  - Continue 2.2 mg/kg
- 24 to < 27
  - Increase dose to 2.3 mg/kg
- < 24
  - Increase dose to 2.4 mg/kg

*Instead of changing the dose, the dose interval can be changed as well. For more information, refer to the full prescribing information or contact Dechra Veterinary Technical Support at (866) 933-2472 or support@dechra.com.

**Use Day 25 electrolytes, if Day 10 electrolytes are normal.

Dechra Veterinary Technical Support: 866-933-2472, www.dechra-us.com, support@dechra.com

NIHCA 161-144. Approved by FDA. CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Dechra Veterinary Products US and the Dechra D logo are registered trademarks of Dechra Pharmaceuticals PLC.
ZYCORTAL® SUSPENSION (desoxycorticosterone pivalate injectable suspension)

For subcutaneous use in dogs only.

Mineralocorticoid

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

**DESCRIPTION:** Desoxycorticosterone pivalate is a mineralocorticoid hormone. Chemically, desoxycorticosterone pivalate is C₂₆H₃₈O₄. The structural formula is:

Chemical Structure:

Molecular Formula: CaH₉O₄

**INDICATION:** For use as replacement therapy for mineralocorticoid deficiency in dogs with primary hyporeninemic hypoaldosteronism (Addison’s disease).

**DOSAGE AND ADMINISTRATION:** Prior to each use, thoroughly shake the vial to resuspend the product.

*ZYCORTAL Suspension* replaces the mineralocorticoid hormones only. Dogs with combined glucocorticoid and mineralocorticoid deficiency should also be treated with prednisone or prednisolone at an initial dosage of 0.2-0.4 mg/kg/day (0.1-0.2 mg/lb/day).

**SUSPENSION (desoxycorticosterone pivalate)**

**FOR SUBSEQUENT DOSES, USE THE FOLLOWING GUIDELINES IF THE DOG IS CLINICALLY NORMAL:**

1. **Day 10 Na+/K+ ratio:** If the Day 10 Na+/K+ ratio is within the range of the respective normal range, adjust the dose to the highest level of the reference range (Day 25 Na+/K+ ratio) according to the guidelines in Table 1, below.

2. **Day 25:**
   - If the Day 25 Na+/K+ ratio is < 32, adjust the dose to the highest level of the reference range (Day 25 Na+/K+ ratio).
   - If the Day 25 Na+/K+ ratio is > 32, adjust the dose to the medium level of the reference range (Day 25 Na+/K+ ratio).

**RE-EVALUATE THE DOG AND MEASURE THE SERUM SODIUM/POTASSIUM RATIO (Na+/K+ RATIO) AT 2 WEEKS:**

**SECOND DOSE OF ZYCORTAL SUSPENSION:** At approximately 25 days after the first dose, re-evaluate the dog and repeat the Na+/K+ ratio.

1. **If the dog is both clinically normal and has a normal Na+/K+ ratio on Day 25, adjust the dose based on the Day 10 Na+/K+ ratio using the guidelines in Table 1, below.**

2. **If the dog is clinically normal and has a Na+/K+ ratio > 32 on Day 25, either adjust the dose based on the Day 10 Na+/K+ ratio according to Table 1 or delay the dose (see Prolonging the Dosing Interval).**

3. **If the dog is neither clinically normal or if the Na+/K+ ratio is abnormal on Day 25, adjust the dose of prednisone/prednisolone or ZYCORTAL Suspension (see Subsequent doses and long-term management).**

**CLINICAL PHARMACOLOGY:**

Desoxycorticosterone is a corticosteroid with primarily mineralocorticoid activity, similar to aldosterone. In the kidney, desoxycorticosterone causes sodium and chloride ion retention, and hydrogen and potassium ion excretion, creating an osmotic gradient. This gradient promotes water absorption from the renal tubules resulting in increased extracellular fluid volume, leading to blood volume expansion, improved venous return to the heart, and increased cardiac output.

After subcutaneous administration of 11 mg/kg body weight, the plasma half-life (mean ± standard deviation) is approximately 17 ± 7 days, with a maximum concentration (Cₘₐₓ) of 13.2 ± 5.9 mg/L, and time to maximum concentration (Tₘₐₓ) of 10 ± 3.5 days.

**EFFECTIVENESS:** A double-blind, multi-site, 180-day field study evaluated the effectiveness of ZYCORTAL Suspension. Nineteen (19) dogs were enrolled in a randomized, double-blind study to FDA-approved desoxycorticosterone pivalate active control. One hundred fifty-two (152) dogs of various breeds, 0.5-12.4 years of age and weighing 0.95-61.2 kg were enrolled. One hundred thirteen (113) dogs were treated with ZYCORTAL Suspension and 39 dogs were treated with the active control. Both groups were administered an initial dose of 2.2 mg/kg. Subsequent doses administered and/or frequency of administration were adjusted according to the clinical needs of the dog. A dog was considered a treatment failure if it remained clinically normal or had improved clinical signs compared to baseline and the Na+/K+ concentrations were within the range of the analyzer, or the Na+/K+ ratio was between 27-32. Success rates for ZYCORTAL Suspension were 86.2% and 88.3% on Days 90 and 180, respectively, success rates for the active control were 85.1% and 86.5% on Days 90 and 180, respectively.

The mean final dose for ZYCORTAL Suspension was 1.9 ± 0.27 mg/kg (range 1.2-2.5 mg/kg) and the mean final dose interval was 38.5 ± 12.5 days (range 20-99 days) with the majority of dogs having a dosing interval between 20 and 46 days.

**ANIMAL SAFETY:** In a laboratory study, ZYCORTAL Suspension was administered via subcutaneous injection to 32 Beagle dogs (four groups of 8 dogs each) at doses of 0.1, 3, 5 and 7 times the labeled starting dose (1X = 2.2 mg/kg), once every 21 days for 6 months, for a total of 9 injections. The volume injected in 3X and 5X dogs was equally divided between three and five sites, respectively. Dogs in the 1X group were dosed at a single injection site. Control dogs (0X) received subcutaneous injections of 0.9% sodium chloride at a volume equivalent to the 5X dose.

The most frequently noted abnormal clinical observations in injection site reactions in treated dogs, characterized by erythema and edema. Clinical pathology findings considered related to ZYCORTAL Suspension treatment included: decreased mean corpuscular volume in 3X and 5X groups; increased globulin concentrations in all treated groups; decreased potassium concentrations in all treated groups; increased sodium concentrations in all treated groups; decreased chloride concentrations in the 3X group; decreased blood urea nitrogen concentrations in all treated groups; and decreased urine specific gravity concentrations in all treated groups. Glomerular filtration rate findings considered treatment-related included: increased creatinine and serum osmolality.

**ADVERSE REACTIONS:**

- Respiratory distress
- Diarrhea
- Polydipsia
- Polyuria
- Urinary tract infection
- Acute interstitial nephritis
- Polydipsia
- Polyuria
- Urinary tract infection
- Acute interstitial nephritis

**STORAGE INFORMATION:** Store at controlled room temperature 25°C (77°F) with excursions between 15-30°C (59-86°F) permitted. Do not freeze. Use within 120 days of first puncture.

**HOW SUPPLIED:** ZYCORTAL Suspension is supplied in a clear glass vial with a 1 mL (100 mg) desoxycorticosterone pivalate suspension (25 mg/mL).

NADA 141-444, Approved by FDA

NDC 17033-382-04

Manufactured for: Dechra Veterinary Products

7015 College Boulevard, Suite 525, Overland Park, KS 66211

Manufactured in the United Kingdom.

© 2016 Dechra Ltd.

ZYCORTAL Suspension is a trademark of Dechra Ltd; all rights reserved.

00A-G - ZYC50046-0816