DOCP is an insoluble ester of desoxycorticosterone. The crystals are injected intramuscularly as a micro-crystalline depot where they slowly dissolve over time.

INDICATION:
For use as replacement therapy for the mineralocorticoid deficit in dogs with primary adrenocortical insufficiency.

WARNING:
Do not use this drug in pregnant dogs. Do not use in dogs suffering from congestive heart disease, severe renal disease or edema.

Keep this and all drugs out of the reach of children. In case of human consumption, contact a physician or Poison Control Center immediately.

PRECAUTIONS:
Some patients are more sensitive to the actions of PERCORTEN-V and may exhibit side effects in an exaggerated degree. Some patients may show signs of hypernatremia or hypokalemia. The dosage of PERCORTEN-V should be reduced in these patients.

Concomitant use of PERCORTEN-V with potassium-sparing diuretics, such as spironolactone, may counter the effect of PERCORTEN-V because desoxycorticosterone pivate and potassium-sparing diuretics exhibit opposing mechanisms of action.

Like other adrenocortical hormones, PERCORTEN-V may cause severe side effects if dosage is too high or prolonged. It may cause polyuria, polydipsia, increased blood volume, edema and cardiac enlargement. Excessive weight gain may indicate fluid retention secondary to sodium retention. PERCORTEN-V should be used with caution in patients with congestive heart disease, edema or renal disease.

ADVERSE REACTIONS (in controlled clinical field studies):
The following adverse reactions have been reported following the use of PERCORTEN-V: depression, polyuria, polydipsia, anorexia, skin and coat changes, diarrhea, vomiting, weakness, weight loss, incontinence, pain on injection and injection site abscesses.

Some of these effects may resolve with adjustments in dose or interval of PERCORTEN-V or concomitant glucocorticoid medication.

Post-Approval Experience, Rev. 2011:
The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA-CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using this data. The following adverse events are listed in decreasing order of reporting frequency in dogs: depression/lethargy, vomiting, anorexia, polydipsia, polyuria, diarrhea, facial/muzzle edema, weakness, urticaria and anaphylaxis. Anemia has been reported following DOCP administration. For a complete listing of adverse reactions for desoxycorticosterone pivate injectable suspension reported to CVM see:
http://www.fda.gov/AnimalVeterinary

To report adverse effects, access medical information, or obtain additional product information call 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

EFFICACY:
PERCORTEN-V given intramuscularly at the appropriate dose and interval, is effective in replacing the mineralocorticoid deficit in dogs suffering from primary hypoadrenocorticism.

Results of two 75-day clinical studies in dogs with primary hypoadrenocorticism have demonstrated the clinical efficacy of PERCORTEN-V. Each dog received three doses of PERCORTEN-V (on days 0, 25 and 50).

The results are summarized below.

<table>
<thead>
<tr>
<th>Clinical Study 01</th>
<th>Number 02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Dogs</td>
<td>49</td>
</tr>
</tbody>
</table>

Average Diagnostic Values:

- Serum Sodium (mEq/L): 126.4 130.72
- Serum Potassium (mEq/L): 7.28 7.47
- Sodium/Potassium Ratio: 18.09 17.86

ACTH Stimulation Test:

- Cortisol Resting (µg/dl): 0.28 0.68
- Cortisol Post Stimulation (µg/dl): 0.27 1.34

Average PERCORTEN-V Dose (mg/lb):

- Day 0: 0.97 0.99
- Day 25: 0.96 0.99
- Day 50: 0.94 0.97
- Concomitant Glucocorticoid (Pred): 47% 39%
Sodium/Potassium Ratios

<table>
<thead>
<tr>
<th>Day</th>
<th>25.18</th>
<th>26.42</th>
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<tbody>
<tr>
<td>Day 14</td>
<td>36.36</td>
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<tr>
<td>Day 25</td>
<td>29.64</td>
<td></td>
</tr>
<tr>
<td>Day 39</td>
<td>34.94</td>
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<tr>
<td>Day 50</td>
<td>30.33</td>
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<tr>
<td>Day 64</td>
<td>35.30</td>
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<tr>
<td>Day 75</td>
<td>30.32</td>
<td>30.59</td>
</tr>
<tr>
<td>% Efficacy Therapy</td>
<td>96%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Case Management:

An accurate diagnosis of primary canine adrenocortical insufficiency is of paramount importance for treatment success and should be established before initiation of PERCORTEN-V therapy. While hypoglycemia and hyperkalemia are highly suggestive of adrenocortical insufficiency, they are not pathognomonic. A definitive diagnosis can only be made with an ACTH stimulation test. At diagnosis, classic cases of canine adrenocortical insufficiency may include clinical signs. Those signs are anorexia, lethargy, depression, weakness, vomiting and/or regurgitation, weight loss, diarrhea and collapse, serum sodium values less than 135 mEq/L, serum potassium greater than 6 mEq/L, sodium/potassium ratios below 25:1, plasma or serum cortisol concentration less than 4 µg/dL pre-and-post ACTH administration. Once the diagnosis is made, immediate therapy must be given to normalize electrolyte imbalance, correct hypovolemic shock and re-establish normal homeostasis. Such therapy should include large volumes of intravenous physiologic saline, glucocorticoids (i.e., prednisolone, dexamethasone) at shock doses and PERCORTEN-V. Anemia (normocytic, normochromic) may be present at diagnosis, but not identified due to hemococoncentration. Rapid rehydration may reduce the circulating red blood cell count to life-threatening levels in animals with pre-existing anemia. Once the acute crisis has passed, renal and cardiovascular function should return to normal. Patient monitoring and dose adjustments of PERCORTEN-V and glucocorticoids should be instituted at this time (see Dosage).

SAFETY:

In a laboratory study the safety of PERCORTEN-V was established in five month old Beagle dogs. PERCORTEN-V was administered IM to 24 Beagles at 0.2, 2.2, 6.6 or 11 mg/kg of body weight daily over a consecutive 3-day period every 28 days (equivalent to a cumulative monthly dosage of 0.6, 18.6 or 33 mg/kg) for 6 months. This resulted in no mortality or any significant effects on body weight, food consumption, and ophthalmic observations at any dose level. However, polyuria and polydipsia were noted and creatinine concentration decreased (14-49 mg/dL) in the 1X, 3X and 5X groups. Histopathological changes were only observed in the kidneys when PERCORTEN-V was administered at ≥ 6.6 mg/kg. The primary renal lesion consisted of glomerulonephropathy seen in all males at ≥ 6.6 mg/kg, in one female at 6.6 mg/kg, and in all females at 11 mg/kg. Other possible treatment related lesions in the kidney, observed sporadically in the 6.6 and 11.0 mg/kg groups, were tubular hyperplasia, inflammation and tubular dilatation. Glomerulonephropathy may possibly be attributed to the pharmacological effects of the drug although there were no clinical measurements assessed in this study. In conclusion, PERCORTEN-V was well tolerated, when administered at 2.2 mg/kg on three consecutive days every 28-day period for six months.

DOSE:1,2

In treating canine hypoadrenocorticism, PERCORTEN-V replaces the mineralocorticoid hormones only. Glucocorticoid replacement must be supplied by small daily doses of glucocorticoid hormones (e.g., prednisone or prednisolone) (0.2 – 0.4 mg/kg/day).

Dosage requirements are variable and must be individualized on the basis of the response of the patient to therapy. Begin treatment with PERCORTEN-V at a dose of 1.0 mg per pound of body weight every 25 days. In some patients the dose may be reduced. Serum sodium and potassium levels should be monitored to assure the animal is properly compensated. Most patients are well controlled with a dose range of 0.75 to 1.0 mg per pound of body weight, given every 21 to 30 days.

The well-controlled patient will have normal electrolytes at 14 days after administration or may exhibit slight hyponatremia and hyperkalemia. This needs no additional therapy as long as the patient is active and eating normally. Watch closely for depression, lethargy, vomiting or diarrhea which indicate a probable glucocorticoid deficiency.

At the end of the 25-day dosing interval, the patient should be clinically normal and have normal serum electrolytes. Alternatively, they may have slight hyponatremia and slight hyperkalemia. This constellation of signs indicate that the dosage and dosing interval should not be altered.

Occasionally, dogs on PERCORTEN-V therapy may develop polyuria and polydipsia (PU/PD). This usually indicates excess glucocorticoid, but may also indicate a PERCORTEN-V excess. It is prudent to begin by decreasing the glucocorticoid dose first. If the PU/PD persists, then decrease the dose of PERCORTEN-V without changing the interval between doses.

Please note: Failure to administer glucocorticoids is the most common reason for treatment failure. Signs of glucocorticoid deficiency include depression, lethargy, vomiting and diarrhea. Such signs should be treated with high doses of injectable glucocorticoids (prednisolone or dexamethasone), followed by controlled oral therapy 0.2 – 0.4 mg/kg/day. Oral supplementation with salt (NaCl) is not necessary with animals receiving PERCORTEN-V.

Guide to Maintenance Therapy

Starting Dose:

DOPC 1 mg/fb every 25 days
Prednisone 0.2 - 0.4 mg/kg/day

Guides for Adjustment:

Clinical Problem/Solution
Polyuria/Polydipsia
→ decrease prednisone dose first,
→ then decrease DOPC dose,
→ do not change DOPC interval
Depression, lethargy, vomiting or diarrhea
→ increase prednisone dose
Hyperkalemia, Hyponatremia
→ decrease DOPC interval 2-3 days

ADMINISTRATION:

Before injection, shake the vial thoroughly to mix the microcrystals with the suspension vehicle, PERCORTEN-V suspension is to be injected intramuscularly. Care should be used to prevent inadvertent intravenous injection, which may cause acute collapse and shock. Such animals should receive immediate therapy for shock with intravenous fluids and glucocorticoids.

Once vial is broached, product should be used within 4 months.

HOW SUPPLIED:

Multiple-Dose Vials, 4 ml, each ml containing 25 mg desoxycorticosterone pivalate (DOPC), 10.5 mg methylcellulose, 3 mg sodium carboxymethylcellulose, 1 mg polyoxorbate 80, and 8 mg sodium chloride with 0.002% thimerosal added as preservative in water for injection. Packed one vial per carton.

STORAGE:

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

References:


Manufactured for: Elanco US Inc.
Greenfield, IN 46140, USA

NADA # 141-029, Approved by FDA.

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