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PRESCRIPTION COMPOUNDING FOR VETERINARY MEDICINE

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FELINE ANALGESIC AGENT

The pharmacokinetics of tramadol were examined after intravenous and oral administration of tramadol to cats - “Pharmacokinetics of tramadol, and its metabolite O-desmethyl-tramadol, in cats” (J Vet Pharmacol Ther. 2008 Feb;31(1):52-9).

**ABSTRACT:** “Tramadol is an analgesic agent and is used in dogs and cats. Tramadol exerts its action through interactions with opioid, serotonin and adrenergic receptors. The opioid effect of tramadol is believed to be, at least in part, related to its metabolite, O-desmethyl-tramadol. The pharmacokinetics of tramadol and O-desmethyl-tramadol were examined after intravenous (i.v.) and oral administration of tramadol to six cats. A two-compartment model (with first-order absorption in the central compartment for the oral administration) with elimination from the central compartment best described the disposition of tramadol in cats. After i.v. administration, the apparent volume of distribution of the central compartment, the apparent volume of distribution at steady-state, the clearance, and the terminal half-life (mean +/- SEM) were 1553 +/- 118 mL/kg, 3103 +/- 132 mL/kg, 20.8 +/- 3.2 mL/min/kg, and 134 +/- 18 min, respectively. Systemic availability and terminal half-life after oral administration were 93 +/- 7% and 204 +/- 8 min, respectively. O-desmethyl-tramadol rapidly appeared in plasma following tramadol administration and had terminal half-lives of 261 +/- 28 and 289 +/- 19 min after i.v. and oral tramadol administration, respectively. The rate of formation of O-desmethyl-tramadol estimated from a model including both tramadol and O-desmethyl-tramadol was 0.014 +/- 0.003/min and 0.004 +/- 0.0008/min after i.v. and oral tramadol administration, respectively.” PMID: 18177319

The following study found tramadol to be a safe and effective analgesic in cats - “Pharmacokinetics, intraoperative effect and postoperative analgesia of tramadol in cats” (Res Vet Sci. 2011 Jun;90(3):503-9).

**ABSTRACT:** “Tramadol is a synthetic codeine analogue used as an analgesic in human and veterinary medicine, but not approved for use in cats. Tramadol (2mg/kg) was administered intravenously (IV) as preoperative analgesic in 12 cats (6 males) undergoing surgical gonadectomy. The pharmacokinetic profile of the drug and its O-desmethyl metabolite were determined in 8 animals (4 males), while intraoperative effects and postoperative analgesia, estimated by subjective pain score (0-24), were evaluated in all. Mean intraoperative isoflurane consumption was reduced, but hypoventilation was not observed. Sex-related differences were not observed, particularly in terms of postoperative analgesia: rescue analgesic was never administered. Concentrations of the active O-desmethyl metabolite were persistently high in all the animals. Considering the results obtained in this study, tramadol, at the dose of 2mg/kg IV, did not produce any evident intraoperative cardiorespiratory side effects and with additional investigation may prove to be an appropriate intraoperative analgesic in cats undergoing gonadectomy.” PMID: 20708759

We have the ability to compound tramadol into a transdermal cream or flavored oral suspension, in a variety of strengths to meet the unique needs of each of your cats.

**COMPOUNDED MEDICATION**

<table>
<thead>
<tr>
<th>Tramadol 10% Transdermal Cream</th>
<th>30gm</th>
<th>Apply as directed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol 50mg/ml Flavored Oral Suspension</td>
<td>30ml</td>
<td>Give as directed</td>
</tr>
</tbody>
</table>
FELINE HYPERTENSION & RENAL FAILURE

The following clinical study found that benazepril is effective in correcting renal hypertension and may provide renal benefits to cats with CRF - “Effects of benazepril hydrochloride in cats with experimentally induced or spontaneously occurring chronic renal failure” (J Vet Med Sci. 2007 Oct;69(10):1015-23).

**ABSTRACT:** “We examined effects of an angiotensin converting-enzyme inhibitor, benazepril hydrochloride (BH), on renal hypertension and chronic renal failure (CRF) in cats. For experimental CRF, healthy cats (n=5) underwent 7/8 renal ablation. After renal insufficiency and hypertension were confirmed by blood urea nitrogen (BUN), serum creatinine, creatinine clearance and telemetric recording of systemic blood pressure, BH was administered orally once daily at 0.9 to 2.0 mg/kg/day for 2 to 3 weeks. Within 2 months after renal ablation, renal failure and hypertension developed as evidenced by significant increases in BUN, serum creatinine and systemic blood pressure (p<0.01 or 0.05) and significantly decreased creatinine clearance accompanied by elevated plasma renin activity, angiotensin I and II, and aldosterone (p<0.01 or 0.05). BH administration corrected systemic hypertension (p<0.05) and significantly reduced angiotensin II and aldosterone (p<0.05). Upon discontinuation of BH, these values returned to the pre-administration levels. Studies on spontaneous CRF enrolled 11 cats with spontaneously occurring CRF. BH was administered orally to 6 cats once daily for 24 weeks at a final dose of 1.0 mg/kg/day, while 5 cats served as control. BH administration reduced serum creatinine and urinary protein concentration in every cat. Results demonstrate that in cats, loss of renal mass leads to activation of the renin-angiotensin-aldosterone system and associated renal hypertension, and indicate that BH is effective in correcting renal hypertension and may provide renal benefits to cats with CRF.” PMID: 17984588

We have the ability to compound benazepril into a flavored oral suspension.

An example of how you might prescribe follows:

**COMPOUNDED MEDICATION**

<table>
<thead>
<tr>
<th>Benazepril 5mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavored Oral Suspension</td>
</tr>
<tr>
<td>30ml</td>
</tr>
<tr>
<td>Give 1ml QD or as directed</td>
</tr>
</tbody>
</table>
CANINE HYPERADRENOCORTICISM

The following clinical review found that ketoconazole was a safe and effective option for treating dogs with pituitary-dependent hyperadrenocorticism - “Use of ketoconazole to treat dogs with pituitary-dependent hyperadrenocorticism: 48 cases (1994-2007)” (J Am Vet Med Assoc. 2008 Dec 15;233(12):1896-901).

OBJECTIVE: To evaluate the effectiveness of ketoconazole as a treatment for dogs with pituitary-dependent hyperadrenocorticism (PDH).

DESIGN: Retrospective case series.

ANIMALS: 48 client-owned dogs in which PDH was diagnosed.

PROCEDURES: Medical records of dogs with PDH that were treated with ketoconazole were examined. Data collected from each record included signalment, clinical signs, results of ACTH stimulation tests before and after treatment with ketoconazole, serum alkaline phosphatase (ALP) and alanine aminotransferase (ALT) activities, dosage of ketoconazole, clinical response, and survival time.

RESULTS: 43 of 48 (90%) dogs had evidence of clinical improvement during the treatment period. In all dogs, treatment with ketoconazole resulted in significantly lower serum cortisol concentrations as measured before and after ACTH stimulation testing: 69% (33/48) of serum cortisol concentrations measured after ACTH stimulation were within the reference range. Serum ALP and ALT activities significantly decreased after treatment with ketoconazole. Survival time after diagnosis of PDH ranged from 2 to 61 months (mean, 26.9 months; median, 25 months).

CONCLUSIONS AND CLINICAL RELEVANCE: Ketoconazole was a safe and effective option for treating dogs with PDH. Additional research is needed to evaluate the effects of long-term treatment with ketoconazole on adrenal glands. PMID: 19072605

The following study found that ketoconazole was effective in treating hyperadrenocorticism in dogs - “Plasma cortisol response to ketoconazole administration in dogs with hyperadrenocorticism” (J Am Vet Med Assoc. 1990 Jul 1;197(1):71-8).

ABSTRACT: “The effect of orally administered ketoconazole on plasma cortisol concentration in dogs with hyperadrenocorticism was evaluated. Every 30 minutes from 0800 hours through 1600 hours and again at 1800 hours, 2000 hours, and 0800 hours the following morning, 15 clinically normal dogs and 49 dogs with hyperadrenocorticism had plasma samples obtained and analyzed for cortisol concentration. The mean (+/- SD) plasma cortisol concentration for the initial 8-hour testing period was highest in 18 dogs with adrenocortical tumor (5.3 +/- 1.6 micrograms/dl), lowest in 15 control dogs (1.3 +/- 0.5 micrograms/dl), and intermediate in 31 dogs with pituitary-dependent hyperadrenocorticism (PDH; 3.4 +/- 1.2 micrograms/dl). Results in each of the 2 groups of dogs with hyperadrenocorticism were significantly (P less than 0.05) different from results in control dogs, but not from each other. The same cortisol secretory experiment was performed, using 8 dogs with hyperadrenocorticism (5 with PDH; 3 with adrenocortical tumor) before and after administration at 0800 hours of 15 mg of ketoconazole/kg of body weight. Significant (P less than 0.05) decrease in the 8-hour mean plasma cortisol concentration (0.9 +/- 0.2 microgram/dl) was observed, with return to baseline plasma cortisol concentration 24 hours later. Twenty dogs with hyperadrenocorticism (11 with PDH, 9 with adrenocortical tumor) were treated with ketoconazole at a dosage of 15 mg/kg given every 12 hours for a half month to 12 months. The disease in 2 dogs with PDH failed to respond to treatment, but 18 dogs had complete resolution of clinical signs of hyperadrenocorticism and significant (P less than 0.05) reduction in plasma cortisol responsiveness to exogenous adrenocorticotropic (ACTH).” PMID: 2370223

An example of how you might prescribe follows:

**COMPOUNDED MEDICATION**

Ketoconazole 100mg/ml
Flavored Oral Suspension
60ml
Give 1ml po BID or as directed
Directions
_________________________________________________________________________________________________________
_________________________________________________________________________________________________________

Prescriber's Signature____________________________________   Refills:  1    2    3    4    5    6    7    8    9    10   11   12    NR

All topical compound %s are per 1 ml or 1 gm unless otherwise noted

**Feline Analgesic Agent**

- [ ] Tramadol 10%    Transdermal Cream
  Quantity 30gm    Directions: Apply as directed

- [ ] Tramadol 50mg/ml    Flavored Oral Suspension
  Quantity 30ml    Directions: Give as directed

**Feline Hypertension & Renal Failure**

- [ ] Benazepril 5mg/ml    Flavored Oral Suspension
  Quantity 30ml    Directions: Give 1ml QD or as directed

**Canine Hyperadrenocorticism**

- [ ] Ketoconazole 100mg/ml    Flavored Oral Suspension
  Quantity 60ml    Directions: Give 1ml po BID or as directed

**Directions**
_________________________________________________________________________________________________________
_________________________________________________________________________________________________________
_________________________________________________________________________________________________________

Prescriber's Signature______________________________________ Refills:  1  2  3  4  5  6  7  8  9  10  11  12  NR

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