CABERGOLINE

(ka-*ber*-go-leen) Dostinex®

PROLACTIN INHIBITOR/DOPAMINE (D2) AGONIST

Prescriber Highlights

- Ergot derivative that may be useful in inducing/synchronizing estrus in dogs & as an abortifacient in dogs or cats
- Limited clinical experience & published references available
- Appears to be well tolerated in dogs & cats; vomiting has been reported
- Potentially very expensive, particularly in large dogs, but generic tablets now available; must usually be compounded

Uses/Indications

For dogs, cabergoline may be useful for inducing estrus, treatment of primary or secondary anestrus, pseudopregnancy, and pregnancy termination in the second half of pregnancy. Cabergoline may be useful in treating some cases of pituitary-dependent hyperadrenocorticism (Cushing's).

In cats, cabergoline, with or without a prostaglandin, may be useful for pregnancy termination, particularly earlier in pregnancy.

Preliminary work has been done in psittacines (primarily Cockatiels) for adjunctive treatment of reproductive-related disorders, particularly persistent egg laying.

In humans, cabergoline is indicated for the treatment of disorders associated with hyperprolactenemia or the treatment of Parkinson's disease.

Pharmacology/Actions

Cabergoline has a high affinity for dopamine$_2$ (D_2) receptors and has a long duration of action. It exerts a direct inhibitory effect on the secretion of prolactin from the pituitary. When compared to bromocriptine it has greater D_2 specificity, a longer duration of action, and less tendency to cause vomiting.

Pharmacokinetics

The pharmacokinetics of cabergoline have apparently not been reported for dogs or cats. In humans, the drug is absorbed after oral dosing but its absolute bioavailability is not known. Food does not appear to significantly alter absorption. The drug is only moderately bound to plasma proteins (≈ 50%). Cabergoline is extensively metabolized in the liver via hydrolysis; these metabolites and about 4% of unchanged drug are excreted into the urine. Half-life is estimated to be around 60 hours. Duration of pharmacologic action may persist for 48 hours or more. Renal dysfunction does not appear to significantly alter elimination characteristics of the drug.

Contraindications/Precautions/Warnings

Cabergoline is contraindicated in dogs and cats that are pregnant unless abortion is desired (see indications). Cabergoline should not be used in patients who are hypersensitive to ergot derivatives. Patients that do not tolerate bromocriptine may or may not tolerate cabergoline. In humans, cabergoline is contraindicated in patients who have uncontrolled hypertension.

Patients with significantly impaired liver function should receive the drug with caution, and if required, possibly at a lower dosage.

When using to induce estrus, it is recommended to wait at least 4 months after the prior cycle to allow the uterus to recover.

Adverse Effects

Cabergoline is usually well tolerated by animal patients. Vomiting has been reported, but may be alleviated by administering with food. Dogs receiving cabergoline for more than 14 days may exhibit changes in coat color.

Human patients have reported postural hypotension, dizziness, headache, nausea and vomiting while receiving cabergoline.

Reproductive/Nursing Safety

This drug can cause spontaneous abortion in pregnant dogs or cats. In pregnant humans, cabergoline is designated by the FDA as a category ***B*** drug (*Animal studies have not demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

Because cabergoline suppresses prolactin, it should not be used in nursing mothers.

Overdosage/Acute Toxicity

Overdose information is not available for dogs or cats, and remains very limited for humans. It is postulated that cabergoline overdoses in people could cause hypotension, nasal congestion, syncope or hallucinations. Treatment is basically supportive and primarily focuses on supporting blood pressure.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving cabergoline and may be of significance in veterinary patients:

- **HYPOTENSIVE DRUGS**: Because cabergoline may have hypotensive effects, concomitant use with other hypotensive drugs may cause additive hypotension
- **METOCLOPRAMIDE**: Use with cabergoline may reduce the efficacy of both drugs and should be avoided
- **PHENOTHIAZINES** (*e.g.*, **acepromazine, chlorpromazine**): Use of cabergoline with dopamine (D_2) antagonists may reduce the efficacy of both drugs and should be avoided

Laboratory Considerations

- No particular laboratory interactions or considerations were located for this drug.

Doses

Because of the dosage differences in animals versus human patients and the strength of the commercially available product, a compounding pharmacist must usually reformulate this medication.

- **DOGS:**

  For estrus induction:

  a) 5 mcg/kg PO once daily induces fertile proestrus in 4–25 days. (Davidson 2004c)

  b) 5 mcg/kg PO once daily until an induced proestrus is pronounced for 2 days or until onset of estrus (Concannon 2005)

  c) 0.6 mcg/kg PO once daily. Make a 10 mcg per mL solution by dissolving commercial tablets in warm distilled water (One 0.5 mg tablet (500 mcg) per 50 mL of distilled water.) Give the appropriate dose for the patient within 15 minutes of preparation and discard the remaining solution. Continue until day 2 after the onset of the first signs of proestrus, or until day 42 without signs of proestrus. 81% (22 of 27) of dogs treated at

this low dose showed proestrus between days 4 and 48. (Cirit, Bacinoglu et al. 2006)

For treatment of pseudocyesis (pseudopregnancy):

a) 5 mcg/kg once a day PO for 5–10 days. (Gobello, Concannon et al. 2001)

b) 5 mcg/kg once a day or every other day SC (likely needs to be compounded). (Davidson 2004c)

For pregnancy termination:

a) Administer after day 40: 5 mcg/kg PO for 5 days; approximately 50% effective (Romagnoli 2006a)

b) Between days 35–45: Cabergoline 5 mcg/kg PO once daily for 7 days in food and cloprostenol at 1 mcg/kg SC (after a tenfold dilution with physiologic saline) on days 1 and 3 given at least 8 hours after food. If pregnancy not terminated by day 8, cabergoline continued (at same dose) until day 12. (Corrada, Rodriguez et al. 2006)

For pituitary-dependent hyperadrenocorticism (Cushing's Disease):

a) 0.1 mg/kg PO every 3 days. Effective in 70% of dogs treated. Dogs with tumor sizes greater than 5 mm did not respond. (Castillo, Lalia et al. 2005)

■ **CATS:**

For pregnancy termination:

a) At 30 days post-coitus, cabergoline at 5 mcg/kg PO q24h and cloprostenol 5 mcg/kg SC q48h in 7–13 days was used to induce abortion. (Davidson 2004c)

■ **BIRDS:**

For persistent egg laying in psittacines combination with removal of males, altered light cycle:

a) Initially 10–20 mcg/kg PO daily; higher dosages were also used. Further work needed to determine the dose rate, etc. (Chitty, Raftery et al. 2006)

Monitoring

■ Efficacy

■ Adverse effects

Client Information

■ Give this medication with food; contact veterinarian if vomiting persists

Chemistry/Synonyms

Cabergoline, a synthetic, ergot-derivative, dopamine agonist similar to bromocriptine, occurs as a white powder that is insoluble in water, and soluble in ethanol or chloroform. The commercially available tablets also contain the inactive ingredients, leucine and lactose.

Cabergoline may also be known as FCE-21336, cabergolina, *Cabasar®*, *Actualene®*, *Sostilar®*, *Dostinex®* or *Galastop®*.

Storage/Stability/Compatibility

The commercially available tablets should be stored at controlled room temperature (20°–25°C; 68°–77°F). It has been reported that the drug is unstable or degrades in aqueous suspensions and if compounded into a liquid that will not be used immediately, should be compounded into a lipid-based product. Preparing a fresh aqueous solution for immediate use should be stable (see Dog dose "c" above).

The veterinary (Europe) product *Galastop®* should be stored below 25°C and protected from light. Do not refrigerate. Once opened, it should be used within 28 days.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None in USA.

Cabergoline is available in Europe as *Galastop®* (Ceva) 50 mcg/mL oral liquid (miglyol base).

HUMAN-LABELED PRODUCTS:

Cabergoline Tablets: 0.5 mg (500 mcg); *Dostinex®* (Pfizer); generic; (Rx)

CALCITONIN SALMON

(kal-si-*toe*-nin *sam*-in) Miacalcin®, Calcimar®

OSTEOCLAST INHIBITING HORMONE

Prescriber Highlights

- Hormone used primarily to control hypercalcemia in small animals (esp. dogs)
- Hypersensitivity possible
- Young animals may be extremely sensitive to effects
- May cause GI effects
- Do not confuse with calcitriol

Uses/Indications

In small animals, calcitonin has been used as adjunctive therapy to control hypercalcemia. Its use has been limited by expense, availability and resistance development to its effects after several days of treatment.

Pharmacology/Actions

Calcitonin has a multitude of physiologic effects. It principally acts on bone inhibiting osteoclastic bone resorption. By reducing tubular reabsorption of calcium, phosphate, sodium, magnesium, potassium and chloride, it promotes their renal excretion. Calcitonin also increases jejunal secretion of water, sodium, potassium and chloride (not calcium).

Pharmacokinetics

Calcitonin is destroyed in the gut after oral administration and therefore must be administered parenterally. In humans, the onset of effect after IV administration of calcitonin salmon is immediate. After IM or SC administration, onset occurs within 15 minutes with maximal effects occurring in about 4 hours. Duration of action is 8–14 hours after IM or SC injection. The drug is thought to be rapidly metabolized by the kidneys, in the blood and peripheral tissues.

Contraindications/Precautions/Warnings

Calcitonin is contraindicated in animals hypersensitive to it. Patients with a history of hypersensitivity to other proteins may be at risk. Young animals are reportedly up to 100 times more sensitive to calcitonin than are older animals (adults).

Adverse Effects

There is not a well-documented adverse effect profile for calcitonin in domestic animals. Anorexia and vomiting have been reported to occur in dogs. Overmedicating can lead to hypocalcemia. The following effects are documented in humans and potentially could be seen in animals: diarrhea, anorexia, vomiting, swelling and pain at injection site, redness and peripheral paresthesias. Rarely, allergic reactions may occur. Tachyphylaxis (resistance to drug therapy with time) may occur in some dogs treated.