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

- **ACETAMINOPHEN:** Use within 72 hours prior to busulfan can reduce busulfan clearance by reducing glutathione concentrations in tissues and blood
- **CYCLOPHOSPHAMIDE:** Can potentially reduce clearance of busulfan, probably by competing for available glutathione
- **ITRACONAZOLE:** Potential decreased busulfan clearance
- **MYELOSUPPRESSANT AGENTS:** Concurrent use with other bone marrow depressant medications may result in additive myelosuppression
- **PHENYTOIN:** Possible increased clearance of busulfan
- **THIOGUANINE:** Used concomitantly with busulfan may result in hepatotoxicity

Laboratory Considerations
- Busulfan may raise serum **uric acid** levels. Drugs such as allopurinol may be required to control hyperuricemia.

Doses
For more information on cancer chemotherapy, refer to the protocols found in the appendix or other dosages/protocols found in numerous references, including: *Withrow and MacEwen's Small Animal Clinical Oncology, 4th Ed.* (Withrow and Vail 2007); *Canine and Feline Geriatric Oncology* (Villalobos 2007); *Small Animal Internal Medicine, 3rd Edition* (Nelson and Couto 2003); *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat 6th Edition* (Ettinger and Feldman 2005); and *The 5-Minute Veterinary Consult Canine & Feline, 3rd Ed.* (Tilley and Smith 2004).

- **SMALL ANIMALS:**
  a) For chronic granulocytic leukemias (not during "blastic" phase—of no benefit): 3–4 mg/m2 PO once daily. Discontinue when total white blood cell count reaches approximately 15,000. Repeat as necessary. May require up to two weeks to observe a positive response. If there is too rapid a decline in total WBC's, discontinue drug. (Jacobs, Lumsden et al. 1992)
  b) For chronic myelogenous leukemia or polycythemia vera: 2 mg/m2 PO once daily; rarely used (Kitchell 2005)

Monitoring
- CBC
- Serum uric acid
- Efficacy

Client Information
- Clients must understand the importance of both administering busulfan as directed and reporting immediately any signs associated with toxicity (*e.g.*, abnormal bleeding, bruising, urination, depression, infection, shortness of breath, etc.).

Chemistry/Synonyms
An alkylsulfonate antineoplastic agent, busulfan occurs as white, crystalline powder. It is slightly soluble in alcohol and very slightly soluble in water.

Busulfan may also be known as: bussulfam, busulfanum, busulphan, CB-2041, GT-41, myelosan, NSC-750, WR-19508, *Bussulfam®, Busulfanum®, Busulivex®, Mielucin®, Misulban®,* or *Myleran®.*

Storage/Stability
Busulfan tablets should be stored in well-closed containers at room temperature.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Busulfan Tablets: 2 mg; *Myleran®* (GlaxoSmithWellcome); (Rx)

Busulfan Injection: 6 mg/mL in 10 mL amps with syringe filters; *Busulfex®* (Orphan Medical); (Rx)

BUTORPHANOL TARTRATE

(byoo-*tor*-fa-nol) Stadol®, Torbutrol®, Torbugesic®

OPIATE PARTIAL AGONIST

Prescriber Highlights
- **Partial opiate agonist/antagonist used in a variety of species as an analgesic, premed, antitussive, or antiemetic**
- **Not a good choice as an analgesic for moderate to severe pain in small animals**
- **Contraindicated or caution in patients with liver disease, hypothyroidism, or renal insufficiency, Addison's, head trauma, increased CSF pressure or other CNS dysfunction (*e.g.*, coma) & in geriatric or severely debilitated patients**
- **Potential adverse effects in DOGS/CATS: Sedation, ataxia, anorexia or diarrhea (rarely)**
- **HORSES (at usual doses) may include a transient ataxia & sedation, but CNS excitement possible**
- **Controlled substance (C-IV)**

Uses/Indications
Approved indication for dogs is ". . . for the relief of chronic nonproductive cough associated with tracheobronchitis, tracheitis, tonsillitis, laryngitis and pharyngitis originating from inflammatory conditions of the upper respiratory tract" (Package Insert; *Torbutrol®*—Fort Dodge). It is also used in practice in both dogs and cats as a preanesthetic medication, analgesic, and as an antiemetic prior to cisplatin treatment (although not very effective in cats for this indication). Compared with other opiate analgesics, butorphanol is not very useful in small animals (particularly dogs) for treating pain and has to be dosed frequently.

The approved indication for horses is ". . . for the relief of pain associated with colic in adult horses and yearlings" (Package Insert; *Torbugesic®*—Fort Dodge). It has also been used clinically as an analgesic in cattle.

Pharmacology/Actions
Butorphanol is considered to be, on a weight basis, 4–7 times as potent an analgesic as morphine, 15–30 times as pentazocine, and 30–50 times as meperidine; however a ceiling effect is reached at higher dosages, where analgesia is no longer enhanced and may be reduced. Its agonist activity is thought to occur primarily at the kappa and sigma receptors and the analgesic actions at sites in the limbic system (sub-cortical level and spinal levels). Its use as an analgesic in small animals has been disappointing, primarily because of its very short duration of action and ability to alleviate only mild to moderate pain.

The antagonist potency of butorphanol is considered to be approximately 30 times that of pentazocine and 140th that of naloxone and will antagonize the effect of true agonists (*e.g.*, morphine, meperidine, oxymorphone).

Besides the analgesic qualities of butorphanol, it possesses significant antitussive activity. In dogs, butorphanol has been shown to elevate CNS respiratory center threshold to CO_2 but, unlike opiate agonists, not depress respiratory center sensitivity. Butorphanol, unlike morphine, apparently does not cause histamine release in dogs. CNS depression may occur in dogs, while CNS excitation has been noted (usually at high doses) in horses and dogs.

Although possessing less cardiovascular effects than the classical opiate agonists, butorphanol can cause a decrease in cardiac rate secondary to increased parasympathetic tone and mild decreases in arterial blood pressures.

The risk of causing physical dependence seems to be minimal when butorphanol is used in veterinary patients.

Pharmacokinetics

Butorphanol is absorbed completely in the gut when administered orally but, because of a high first-pass effect, only about 1/6th of the administered dose reaches the systemic circulation. The drug has also been shown to be completely absorbed following IM administration.

Butorphanol is well distributed, with highest levels (of the parent compound and metabolites) found in the liver, kidneys, and intestine. Concentrations in the lungs, endocrine tissues, spleen, heart, fat tissue and blood cells are also higher than those found in plasma. Approximately 80% of the drug is bound to plasma proteins (human data). Butorphanol will cross the placenta and neonatal plasma levels have been roughly equivalent to maternal levels. The drug is also distributed into maternal milk.

Butorphanol is metabolized in the liver, primarily by hydroxylation. Other methods of metabolism include N-dealkylation and conjugation. The metabolites of butorphanol do not exhibit any analgesic activity. These metabolites and the parent compound are mainly excreted into the urine (only 5% is excreted unchanged), but 11–14% of a dose is excreted into the bile and eliminated with the feces.

Following IV doses in horses, the onset of action is approximately 3 minutes with a peak analgesic effect at 15–30 minutes. The duration of action in horses may be up to 4 hours after a single dose.

Contraindications/Precautions/Warnings

The drug is contraindicated in patients having known hypersensitivity to it. All opiates should be used with caution in patients with hypothyroidism, severe renal insufficiency, adrenocortical insufficiency (Addison's), and in geriatric or severely debilitated patients. Like other opiates, butorphanol must be used with extreme caution in patients with head trauma, increased CSF pressure or other CNS dysfunction (*e.g.*, coma).

Dogs with MDR1 mutations (many Collies, Australian shepherds, etc.) may develop a more pronounced sedation that persists longer than normal. It may be prudent to reduce initial doses by 25% to determine the reaction of a patient identified or suspected of having this mutation.

The manufacturer states that butorphanol "should not be used in dogs with a history of liver disease" and, because of its effects on suppressing cough, "it should not be used in conditions of the lower respiratory tract associated with copious mucous production." The drug should be used cautiously in dogs with heartworm disease, as safety for butorphanol has not been established in these cases.

Adverse Effects

Adverse effects reported in dogs/cats include sedation, excitement, respiratory depression, ataxia, anorexia or diarrhea (rarely). Adverse effects may be less severe than those seen with pure agonists.

Adverse effects seen in horses (at usual doses) may include a transient ataxia and sedation, but excitement has been noted as well (see below). Although reported to have minimal effects on the GI, butorphanol has the potential to decrease intestinal motility and ileus can occur. Horses may exhibit CNS excitement (tossing and jerking of head, increased ambulation, augmented avoidance response to auditory stimuli) if given high doses (0.2 mg/kg) IV rapidly. Very high doses IV (1–2 mg/kg) may lead to the development of nystagmus, salivation, seizures, hyperthermia and decreased GI motility. These effects are considered transitory in nature.

Reproductive/Nursing Safety

Although no controlled studies have been performed in domestic animals or humans, the drug has exhibited no evidence of teratogenicity or of causing impaired fertility in laboratory animals. The manufacturer, however, does not recommend its use in pregnant bitches, foals, weanlings (equine), and breeding horses. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***B*** (*Safe for use if used cautiously. Studies in laboratory animals may have uncovered some risk, but these drugs appear to be safe in dogs and cats; or these drugs are safe if they are not administered when the animal is near term.*)

Butorphanol can be distributed into milk, but not in amounts that would cause concern in nursing offspring.

Overdosage/Acute Toxicity

Acute life-threatening overdoses with butorphanol should be unlikely. The LD_{50} in dogs is reportedly 50 mg/kg. However, because butorphanol injection is available in two dosage strengths (0.5 mg/mL and 10 mg/mL) for veterinary use, the possibility exists that inadvertent overdoses may occur in small animals. It has been suggested that animals exhibiting clinical signs of overdose (CNS effects, cardiovascular changes, and respiratory depression) be treated immediately with intravenous naloxone. Additional supportive measures (*e.g.*, fluids, O_2, vasopressor agents, and mechanical ventilation) may be required. Should seizures occur and persist, diazepam may be used for control.

Drug Interactions

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

- **OTHER CNS DEPRESSANTS** (*e.g.,* **anesthetic agents, antihistamines, phenothiazines, barbiturates, tranquilizers, alcohol,** etc.): May cause increased CNS or respiratory depression when used with butorphanol; dosage may need to be decreased
- **ERYTHROMYCIN:** Could potentially decrease metabolism of butorphanol
- **FENTANYL** (and other **pure opiate agonists**): Butorphanol may potentially antagonize some analgesic effects (**Note:** this is controversial), but may also reverse some of the sedative and respiratory depressant effects of pure agonists
- **PANCURONIUM** If used with butorphanol may cause increased conjunctival changes
- **THEOPHYLLINE:** Could potentially decrease metabolism of butorphanol

Doses

Note: All doses are expressed in mg/kg of the base activity. If using the human product (*Stadol®*), 1 mg of tartrate salt = 0.68 mg base.

■ DOGS:

As an antitussive:

a) 0.055–0.11 mg/kg SC q6–12h; treatment should not normally be required for longer than 7 days; or 0.55 mg/kg PO q6–12h; may increase dose to 1.1 mg/kg PO q6–12h (The oral doses correspond to one 5 mg tablet per 20 lbs. and 10 lbs. of body weight, respectively); treatment should not normally be required for longer than 7 days (Package Insert; *Torbutrol®*—Fort Dodge)

b) 0.05–1 mg/kg PO q6–12h; goal is to suppress coughing without causing excessive sedation (Johnson 2000)

c) 0.55–1.1 mg/kg PO as needed (Johnson 2004d)

As an analgesic:

a) 0.1–1 mg/kg IM, IV or SC q1–3h (Hendrix and Hansen 2000)

b) 0.2–0.4 mg/kg SC, IM or IV (use lower dose if given IV); Efficacy is 1–2 hours for moderate pain and 2–4 hours for mild pain. May give orally at 0.4 mg/kg to the nearest quarter tablet 3 times a day (Mathews 1999)

c) 0.5–1 mg/kg PO q6–8h (Hardie 2000)

d) 0.1–0.5 mg/kg IV, IM, SQ; provides only mild to moderate analgesia (good visceral analgesia); duration of sedative action 2–4 hours, but analgesic action may be 1 hour or less (Perkowski 2006b)

e) As a constant rate infusion: 0.1–0.4 mg/kg/hr; occasionally used for abdominal pain (Hellyer 2006)

As a preanesthetic:

a) 0.05 mg/kg IV or 0.4 mg/kg SC, IM (Morgan 1988)

b) 0.2–0.4 mg/kg IM (with acepromazine 0.02–0.04 mg/kg IM) (Reidesel)

As an anti-emetic prior to cisplatin treatment:

a) 0.4 mg/kg IM ½ hour prior to cisplatin infusion (Klausner and Bell 1988)

■ CATS:

As an analgesic:

a) 0.1–1 mg/kg IM, IV or SC q1–3h (Hendrix and Hansen 2000)

b) 0.2–0.4 mg/kg SC, IM or IV (use lower dose if given IV); Efficacy is 1–2 hours for moderate pain and 2–4 hours for mild pain. May give orally at 0.4 mg/kg to the nearest quarter tablet 3 times a day (Mathews 1999)

c) 0.5–1 mg/kg PO q6–8h (Hardie 2000)

d) 0.1–0.5 mg/kg IV, IM, SQ; provides only mild to moderate analgesia (good visceral analgesia); duration of sedative action 2–4 hours, but analgesic action may be 1 hour or less (Perkowski 2006b)

e) As a postoperative CRI (usually in combination with ketamine) for mild to moderate pain: Loading dose of 0.1–0.2 mg/kg IV, then a CRI of 0.1–0.2 mg/kg/hr; Ketamine is used at a loading dose of 0.1 mg/kg IV with a CRI of 0.4 mg/kg/hr. When used with an opioid CRI may allow reduction in dosage of both. (Lichtenberger 2006d)

As a preanesthetic:

a) 0.2–0.4 mg/kg IM (with glycopyrrolate 0.01 mg/kg IM and ketamine 4–10 mg/kg IM) (Reidesel)

■ FERRETS:

a) As a sedative/analgesic:

Butorphanol alone 0.05–0.1 mg/kg IM, SC. Butorphanol/Xylazine: Butorphanol 0.2 mg/kg + Xylazine 2 mg/kg IM

For injectable anesthesia:

Butorphanol 0.1 mg/kg, Ketamine 5 mg/kg, medetomidine 80 mcg/kg. Combine in one syringe and give IM. May need to supplement with isoflurane (0.5–1.5%) for abdominal surgery. (Finkler 1999)

b) Xylazine (2 mg/kg) plus butorphanol (0.2 mg/kg) IM;

Telazol (1.5 mg/kg) plus xylazine (1.5 mg/kg) plus butorphanol (0.2 mg/kg) IM; may reverse xylazine with yohimbine (0.05 mg/kg IM) (Williams 2000)

As an analgesic:

a) 0.05–0.5 mg/kg SC or IM q4h (Williams 2000)

b) For post-op analgesia: 0.1–0.2 mg/kg loading dose, then a constant rate infusion of 0.1–0.2 mg/kg/hr (Lichtenberger 2006a)

■ RABBITS/RODENTS/SMALL MAMMALS:

For chemical restraint in rabbits:

a) 0.1–0.5 mg/kg IV (Burke 1999); (Ivey and Morrisey 2000)

For analgesia:

a) For postsurgical analgesia in rabbits: 0.1–0.5 mg/kg IV or SC q2–4h; lower dosages may be more effective due to "ceiling effect" (Ivey and Morrisey 2000)

b) Rabbits: As an analgesic (post-operative pain): 0.4 mg/kg SC q4–6h; for surgical procedures (in combo with xylazine/ketamine): 0.1 mg/kg once IM or SC (Huerkamp 1995)

c) Rabbits for post-op analgesia: 0.1–0.2 mg/kg loading dose, then a constant rate infusion of 0.1–0.2 mg/kg/hr (Lichtenberger 2006a)

■ BIRDS:

As an analgesic:

a) Psittacines: 2–4 mg/kg IM; frequent re-dosing every 2–4 hours is needed to maintain analgesia. If adverse effects are an issue (*e.g.*, respiratory or cardiovascular depression), may reverse with naloxone (0.05–0.25 mg/kg IM or slow IV) (Clyde and Paul-Murphy 2000)

b) 1–2 mg/kg IM (Lichtenberger 2006a)

c) 1–4 mg/kg q4h IM, IV, PO (Bays 2006)

d) Parrots: 1–3 mg/kg IM (Carpenter 2006)

■ CATTLE:

As an analgesic:

a) For surgery in adult cattle: 20–30 mg IV (jugular) (may wish to pretreat with 10 mg xylazine) (Powers 1985)

b) 0.02–0.25 mg/kg IV, SQ; 20–30 mg (total dose) IV for an adult animal. Duration of effect is 4 hours. An appropriate withdrawal period is 72 hours for milk, and 4 days for meat. (Walz 2006b)

■ HORSES: (**Note:** ARCI UCGFS Class 3 Drug)

As an analgesic:

a) 0.1 mg/kg IV q3–4h; not to exceed 48 hours (Package Insert; *Torbugesic®*—Fort Dodge)

b) For moderate to marked abdominal pain: 0.01–0.02 mg/kg IV alone or in combination with xylazine (0.02–0.1 mg/kg IM) (Moore 1999)

c) For colic pain: 5–10 mg (total dose for a 450–500 kg horse) IV combined with 100–200 mg xylazine (total dose). Compared to IV bolus, a constant rate infusion of butorphanol at 23.7 mcg/kg/hr induces fewer GI side effects while providing analgesia. (Zimmel 2003)

d) Foals: 0.1–0.2 mg/kg IV or IM (Robertson 2003)

e) Two studies have looked at butorphanol CRI in horses for post-op pain. **1**) Loading dose of 0.0178 mg/kg (17.8 mcg/kg), then a constant rate infusion of 23.7 mcg/kg/hr; **2**) Constant rate infusion of 13 mcg/kg/hr (Mogg 2006)

As a preanesthetic, outpatient surgery, or chemical restraint:

a) 0.01–0.04 mg/kg IV (with xylazine 0.1–0.5 mg/kg IV) (Orsini 1988)

b) For field anesthesia: Sedate with xylazine (1 mg/kg IV; 2 mg/kg IM) given 5–10 minutes (longer for IM route) before induction of anesthesia with ketamine (2 mg/kg IV). Horse must be adequately sedated (head to the knees) before giving the ketamine (ketamine can cause muscle rigidity and seizures). If adequate sedation does not occur, either **1**) Redose xylazine: up to half the original dose, **2**) Add butorphanol (0.02–0.04 mg/kg IV). Butorphanol can be given with the original xylazine if you suspect that the horse will be difficult to tranquilize (*e.g.*, high-strung Thoroughbreds) or added before the ketamine. This combination will improve induction, increase analgesia and increase recumbency time by about 5–10 minutes. **3**) Diazepam (0.03 mg/kg IV). Mix the diazepam with the ketamine. This combination will improve induction when sedation is marginal, improve muscle relaxation during anesthesia and prolong anesthesia by about 5–10 minutes. **4**) Guaifenesin (5% solution administered IV to effect) can also be used to increase sedation and muscle relaxation. (Mathews 1999)

As an antitussive:

a) 0.02 mg/kg IM two to three times daily (Orsini 1988)

■ REPTILES/AMPHIBIANS:

As an analgesic:

a) 0.05–1 mg/kg q12h IM, IV, PO, SC (up to 20 mg/kg in tortoises) (Bays 2006)

Monitoring

- Analgesic and/or antitussive efficacy
- Respiratory rate/depth
- Appetite and bowel function
- CNS effects

Client Information

- Clients should report any significant changes in behavior, appetite, bowel or urinary function in their animals

Chemistry/Synonyms

A synthetic opiate partial agonist, butorphanol tartrate is related structurally to morphine but exhibits pharmacologic actions similar to other partial agonists such as pentazocine or nalbuphine. The compound occurs as a white, crystalline powder that is sparingly soluble in water and insoluble in alcohol. It has a bitter taste and a pK_a of 8.6. The commercial injection has a pH of 3–5.5. One mg of the tartrate is equivalent to 0.68 mg of butorphanol base.

Butorphanol tartrate may also be known as: levo-BC-2627 (butorphanol), *Dolorex®*, *Equanol®*, *Stadol®*, *Torbutrol®*, *Torbugesic®*, and *Verstadol®*.

Storage/Stability/Compatibility

The injectable product should be stored out of bright light and at room temperature; avoid freezing.

The injectable product is reported to be **compatible** with the following IV fluids and drugs: acepromazine, atropine sulfate, chlorpromazine, diphenhydramine HCl, droperidol, fentanyl citrate, hydroxyzine HCl, meperidine, morphine sulfate, pentazocine lactate, perphenazine, prochlorperazine, promethazine HCl, scopolamine HBr, and xylazine.

The drug is reportedly **incompatible** with the following agents: dimenhydrinate, and pentobarbital sodium.

Dosage Forms/Regulatory Status

Note: Butorphanol is a class IV controlled substance. The veterinary products (*Torbutrol®*, *Torbugesic®*) strengths are listed as base activity. The human product (*Stadol®*) strength is labeled as the tartrate salt.

■ VETERINARY-LABELED PRODUCTS:

Butorphanol Tartrate Injection: 0.5 mg/mL (activity as base) in 10 mL vials; *Torbutrol®* (Fort-Dodge); (Rx, C-IV). Approved for use in dogs.

Butorphanol Tartrate Injection: 2 mg/mL (activity as base) in 10 mL vials. *Torbugesic-SA®* (Fort Dodge); (Rx, C-IV). Approved for use in cats.

Butorphanol Tartrate Injection: 10 mg/mL (activity as base) in 10 mL, 50 mL vials; *Torbugesic®* (Fort-Dodge), *Dolorex®* (Intervet), *Butorject®* (Phoenix), *Torphaject®* (Butler); *Equanol®* (Vedco) generic; (Rx, C-IV). Approved for use in horses not intended for food.

Butorphanol Tartrate Tablets: 1 mg, 5 mg, and 10 mg (activity as base) tablets; bottles of 100; *Torbutrol®* (Fort-Dodge); (Rx, C-IV). Approved for use in dogs.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

■ HUMAN-LABELED PRODUCTS:

Butorphanol Tartrate Injection: 1 mg/mL (as tartrate salt; equivalent to 0.68 mg base) in 1 mL & 2 mL vials; 2 mg/mL (as tartrate salt) in 1 mL, 2 mL, and 10 mL vials; *Stadol®* (Bristol-Myers Squibb); generic; (Rx, C-IV)

Butorphanol Nasal Spray: 10 mg/mL in 2.5 mL metered dose); generic; (Rx, C-IV)

n-Butylscopolammonium Bromide — See the monograph found in the "N's" before neomycin

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