Laboratory Considerations
No specific laboratory interactions were noted for clonidine.

Doses
■ **DOGS:**

For diagnosing hyposomatotropism:

a) Dosage may be variable depending on the laboratory's protocol. Contact lab prior to test to determine protocol and sample handling instructions. Usual dose is 10 mcg/kg IV. Obtain plasma for growth hormone (GH) levels, prior to clonidine dosing and at 15, 30, 45, 60, and 120 minutes. Larger dosages may cause a more pronounced and prolonged hyperglycemia and a higher incidence of other adverse reactions that may include sedation, aggressive behavior, hypotension, collapse, and bradycardia (responsive to atropine). Adverse effects may persist for 15–60 minutes post dose. Healthy dogs should demonstrate GH levels of 10 ng/mL after clonidine administration. (Feldman and Nelson 1996)

■ **CATS:**

For adjunctive antidiarrheal therapy for refractory cases of inflammatory bowel disease:

a) As fourth line therapy after prostaglandin synthetase inhibitors (*i.e.*, sulfasalazine, bismuth subsalicylate), opioid agonists (*i.e.*, loperamide), and 5-HT3 serotonergic antagonists (*i.e.*, ondansetron) are being used: clonidine 5–10 mcg/kg two to three times a day, SC or PO. (Washabau 2000)

■ **CATTLE:**

For epidural analgesia/analgesia:

a) 2–3 mcg/kg diluted to 8 mL with sterile normal saline epidurally; onset/duration of analgesia = 19 minutes/192 minutes with 2 mcg/kg dose and = 9 minutes/311 minutes with 3 mcg/kg dose; peak effects from 60–180 minutes (De Rossi, Bucker et al. 2003)

Monitoring
- Dependent upon purpose for use. When used for determining GH levels, adverse effects (noted in dosage section) should be evaluated.
- Blood pressure and cardiac rate are most likely to be affected, but effects usually only persist for an hour after dose.
- When used for ongoing diarrhea treatment, evaluation of efficacy and adverse effect profile should be monitored.

Client Information
- When used for chronic therapy, have clients report signs that may indicate adverse effects (weakness, lethargy, behavioral changes, etc.); caution not to alter or discontinue treatment without veterinarian's advice.

Chemistry/Synonyms
An imidazoline derivative centrally acting alpha-adrenergic agonist, clonidine HCl occurs as an odorless, bitter, white or almost white crystalline powder. It is soluble in water and alcohol. It is also considered highly lipid soluble. The commercially available injection for epidural use has its pH adjusted to between 5 to 7.

Clonidine may also be known as: ST-155, clonidini hydrochloridum, *Adesipress-TTS®, Arkamin®, Aruclonin®, Atensina®, Barclyd®, Cantanidin®, Caprysin®, Catanidin®, Catapresan®, Catapresan®, Catapres®, Catapressan®, Clonistada®, Clonnirit®, Dispaclonidin®, Dixarit®, Duraclon®, Epiclodina®, Glausine®, Haemiton®, Menograine®, Mirfat®, Normopresan®, Paracefan®,* or *Tenso-Timelets®*.

Storage/Stability
Clonidine tablets should be stored in tight, light-resistant containers at room temperature; excursions permitted to 15–30°C (59–86°F). The preservative-free injection for epidural use should be stored at controlled room temperature (25°C). Because it contains no preservative, unused portions of the injection should be discarded.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

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

HUMAN-LABELED PRODUCTS:

Clonidine HCl Injection for epidural use: 100 mcg/mL, 500 mcg/mL preservative-free in 10 mL vials; *Duraclon®* (aaiPharma); (Rx)

Clonidine HCl Tablets: 0.1 mg, 0.2 mg & 0.3 mg; *Catapres®* (Boehringer Ingelheim); generic; (Rx)

Clonidine HCl Transdermal: 0.1 mg/24hrs (2.5 mg total clonidine content), 0.2 mg/24hrs (5 mg total clonidine content), & 0.3 mg/24hrs (7.5 mg total clonidine content); *Catapres-TTS-1®, 2®* or *3®* (Boehringer Ingelheim); (Rx)

CLOPIDOGREL BISULFATE

(kloe-*pid*-oh-grel) Plavix®

PLATELET AGGREGATION INHIBITOR

Prescriber Highlights
- **Oral, once-daily platelet aggregation inhibitor that may be useful in preventing thromboembolic disease in cats**
- **Limited clinical experience in feline medicine; but appears well tolerated**
- **Potentially may cause vomiting or bleeding**

Uses/Indications
Clopidogrel, a platelet aggregation inhibitor, may be useful for preventing thrombi in susceptible cats. It may also improve pelvic limb circulation in cats after a cardiogenic embolic event via a vasomodulating effect secondary to inhibition of serotonin release from platelets. Research is ongoing.

Pharmacology/Actions
Clopidogrel is metabolized to an active, highly unstable compound (not yet identified) that is responsible for its inhibitory platelet-aggregation (both primary and secondary aggregation) activity. This compound binds selectively to platelet surface low-affinity ADP-receptors and inhibits ADP binding to the site. This inhibits activation of the platelet glycoprotein Ib/IIIa complex that is necessary for platelet-fibrinogen binding and inhibits the release from platelets other compounds that enhance platelet aggregation (*e.g.,* serotonin, calcium, fibrinogen, thromobospondin, ADP). Clopidogrel's active metabolite irreversibly alters the ADP receptor; the platelet is affected for its lifespan.

Clopidogrel's mechanism of action on platelet aggregation is different than aspirin's effects. Aspirin acetylates and inactivates COX-1 in platelets, thereby preventing formation of thromboxane A2.

Pharmacokinetics
No specific information was located for the pharmacokinetics of clopidogrel in cats. In a pharmacodynamic study in cats (Hogan, Andrews et al. 2004), doses as low as 18.75 mg were as effective as higher dosages in reducing platelet aggregation; maximal effects were seen after 3 days of therapy and platelet function returned to normal 7 days after stopping treatment. While lower dosages may be effective in cats, they have not been evaluated and are not practical to administer with the presently available 75 mg human-labeled dosage form (tablets).

In humans, clopidogrel is rapidly absorbed with a bioavailability of about 50%. Food does not alter its absorption. Clopidogrel is highly bound to plasma proteins in humans and is rapidly hydrolyzed to a carboxylic acid derivative inactive metabolite that is excreted via the urine and feces. The 2% of drug that is covalently bound to platelets has an approximate elimination half-life of 11 days.

Contraindications/Precautions/Warnings
No specific information is available for cats. In humans, clopidogrel is contraindicated in patients with active pathologic bleeding or known hypersensitivity to the drug.

Adverse Effects
Clopidogrel appears well tolerated by cats, but numbers treated have been relatively few. Some cats may vomit or develop anorexia; giving the drug with food may alleviate these effects.

In humans, the primary adverse effects reported have been bleeding related. In a major pre-clinical study, major bleeding occurred in approximately 2% of patients treated. Use of aspirin with clopidogrel may increase this incidence. Rashes and gastrointestinal effects (diarrhea) have also been reported. Rarely, thrombotic thrombocytopenic purpura (TTP) has been noted; onset can occur after a short period of treatment (<2 weeks).

Reproductive/Nursing Safety
In pregnant rats and rabbits, dosages of approximately 65X and 78X respectively, of the human dose when compared on mg/m2 basis, caused no teratogenic effects. In humans, the FDA categorizes clopidogrel as category ***B*** for use during pregnancy (*Animal studies have not yet 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 in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

In rats, clopidogrel or its metabolites are distributed into milk. Although probably safe to use in nursing veterinary patients, weigh the potential risks to nursing offspring before allowing patients receiving the drug to nurse their young, or use a milk replacer.

Overdosage/Acute Toxicity
Limited information is available. Reported lethal oral doses for mice and rats were 1500 mg/kg and 2000 mg/kg (460X human adult dose on a mg/m2 basis), respectively. Acute toxic signs may include bleeding or vomiting. Platelet transfusions have been suggested if rapid reversal is required.

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

- **ASPIRIN:** Increased risk for bleeding, however many human patients take both medications
- **HEPARIN; LOW MOLECULAR WEIGHT HEPARINS:** Clopidogrel appears safe to use with heparin (both unfractionated and LMW)
- **NSAIDS:** Increased risk for bleeding; clopidogrel may interfere with metabolism
- **PHENYTOIN:** Clopidogrel may interfere with metabolism
- **TORSEMIDE:** Clopidogrel may interfere with metabolism
- **WARFARIN:** Increased risk for bleeding; clopidogrel may interfere with metabolism

Laboratory Considerations
None noted

Doses
- **CATS:**

  To prevent thrombus formation:

  a) 18.75 mg (practically, ¼ of a 75 mg tablet) PO once daily (Hogan 2006)

Monitoring
- Clinical efficacy
- Adverse effects (vomiting, bleeding)

Client Information
- May be given without regard to feeding status
- Potential adverse effects include vomiting, lack of appetite or bleeding
- If vomiting occurs, give with food
- Report any bleeding or black, tarry stools to veterinarian

Chemistry/Synonyms
Clopidogrel bisulfate, a thienopyridine, occurs as a white to off-white powder that is practically insoluble in water at a pH of 7, but freely soluble at a pH of 1.

Clopidogrel may also be known as: SR-259990C, PCR-4099, or clopedogreli. Internationally registered trade names for clopidogrel include: *Antiplaq, Clodian, Cloflow, Clopact, Clopivas, Clopod, Iscover, Iskimil, Nabratin, Noklot, Plavix®, Pleyar,* or *Troken*.

Storage/Stability
Clopidogrel tablets should be stored at 25°C; excursions are permitted to 15–30°C.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Clopidogrel Bisulfate Tablets: 75 mg (as base); *Plavix®* (Bristol-Myers Squibb); (Rx)

CLOPROSTENOL SODIUM

(kloe-***pros***-te-nol) **Estrumate®**

PROSTAGLANDIN (F-CLASS)

Prescriber Highlights
- **Synthetic F-class prostaglandin used in cattle to induce luteolysis, induce abortion, treat pyometra, endometritis, etc.**
- **Contraindications: Pregnancy (when abortion or induced parturition are not desired)**
- **Can cause cholinergic-like adverse effects in dogs**
- **Do not give IV**
- **Pregnant women should not handle; caution handling in humans with asthma & women of childbearing age**