Monitoring
- Analgesic efficacy
- Heart rate and respiratory rate

Client Information
- Fentanyl injection should be used only by professionals familiar with its use in a setting where adequate monitoring can occur.
- Fentanyl Patches: Explain carefully to clients how to apply (if applicable), remove and dispose of patches. Consider making application, removal, and disposal an outpatient procedure, thereby bypassing concerns with clients.
- Should accidental human skin contact occur with the patch, wash with water only (no soap, etc.). Use cautiously in households where young children or animals could remove and ingest or be exposed to patches.

Chemistry/Synonyms
Fentanyl citrate, a very potent opiate agonist, occurs as a white, crystalline powder. It is sparingly soluble in water and soluble in alcohol. It is odorless and tasteless (not recommended for taste test because of extreme potency) with a pK_a of 8.3 and a melting point between 147°–152°C.

Fentanyl and fentanyl citrate may also be known as: fentanylum, fentanyli citras, McN-JR-4263-49, phentanyl citrate, R-4263, *Actiq®*, *Fenodid®*, *Fenta-Hameln®*, *Fentabbott®*, *Fentanest®*, *Fentax®*, *Fentora®*, *Haldid®*, *Ionsys®*, *Leptanal®*, *Nafluvent®*, *Sintenyl®*, *Sublimaze®*, *Tanyl®*, and *Trofentyl®*.

Storage/Stability/Compatibility
Fentanyl transdermal patches should be stored at temperatures less than 25°C and applied immediately after removing from the individually sealed package. Do not cut patches.

The transmucosal (buccal) tablets should be stored at room temperature; do not refrigerate or freeze.

Fentanyl injection should be stored protected from light. It is hydrolyzed in an acidic solution. The injection is **compatible** with normal saline and D5W.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 1 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Fentanyl Buccal Tablets: 100 mcg, 200 mcg, 400 mcg, 600 mcg, & 800 mcg with mannitol in color-coded blister packs; *Fentora®* (Cephalon); (Rx, C-II)

Fentanyl Injectable: 0.05 mg/mL (50 mcg/mL) in 2, 5, 10, and 20 mL amps; 30 mL and 50 mL vials; preservative free in 2, 5, 10 mL, & 20 mL amps; *Sublimaze®* (Akorn); generic; (Rx, C-II)

Fentanyl Transdermal System:

1.25 (5 cm^2; **12.5 mcg/hr**);

2.5 to 2.75 (6.25–10 cm^2; **25 mcg/hr**);

2.5 to 5.5 (12.5–20 cm^2; **50 mcg/hr**);

7.5 to 8.25 (18.75–30 cm^2; **75 mcg/hr**);

10 to 11 (25–40 cm^2; **100 mcg/hr**);

Duragesic®-12, -25, -50, -75 and -100 (Janssen); generic; (Rx, C-II)

Fentanyl Iontophoretic Transdermal System: 40 mcg/dose fentanyl hydrochloride (equivalent to 44.4 mcg of fentanyl) delivered over a 10-minute period upon each activation of the dose button; Each system contains fentanyl hydrochloride 10.8 mg; *Ionsys®* (Ortho-McNeil); (Rx; C-II)

Fentanyl Transmucosal System: Lozenges on a stick: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg and 1600 mcg (as base); *Actiq®* (Cephalon); generic; (Rx, C-II)

All fentanyl products are Class-II controlled substances.

FERROUS SULFATE

(*fer*-us sul-*fayte*) **Fer-In-Sol®, Feosol®**

NUTRITIONAL/HEMATINIC

Prescriber Highlights
- **Oral iron supplement for the treatment of iron-deficiency anemias**
- **Contraindications: Patients with hemosiderosis, hemochromatosis, hemolytic anemias, or known hypersensitivity; some consider it contraindicated with GI ulcers**
- **Adverse Effects: With non-toxic doses, mild gastrointestinal upset**
- **May be very toxic (life threatening) if OD'd**

Uses/Indications
While iron is a necessary trace element in all hemoglobin-utilizing animals, the use of therapeutic dosages of ferrous sulfate (or other oral iron) preparations in veterinary medicine is limited primarily to the treatment of iron-deficiency anemias in dogs (usually due to chronic blood loss), and as adjunctive therapy in cats when receiving epoetin (erythropoietin) therapy. Injectable iron products are usually used in the treatment of iron deficiency anemias associated with newborn animals.

Pharmacology/Actions
Iron is necessary for myoglobin and hemoglobin in the transport and utilization of oxygen. While neither stimulating erythropoiesis nor correcting hemoglobin abnormalities not caused by iron deficiency, iron administration does correct both physical signs and decreased hemoglobin levels secondary to iron deficiency.

Ionized iron is a component in the enzymes cytochrome oxidase, succinic dehydrogenase, and xanthine oxidase.

Pharmacokinetics
Oral absorption of iron salts is complex and determined by a variety of factors including diet, iron stores present, degree of erythropoiesis, and dose. Iron is thought to be absorbed throughout the GI tract, but is most absorbed in the duodenum and proximal jejunum. Food in the GI tract may reduce the amount absorbed.

After absorption, the ferrous iron is immediately bound to transferrin, transported to the bone marrow and eventually incorporated into hemoglobin. Iron metabolism occurs in a nearly closed system. Because iron liberated by the destruction of hemoglobin is reused by the body and only small amounts are lost by the body via hair and nail growth, normal skin desquamation and GI tract sloughing, normal dietary intake usually is sufficient to maintain iron homeostasis.

Contraindications/Precautions/Warnings

Ferrous sulfate (or other oral iron products) are considered contraindicated in patients with hemosiderosis, hemochromatosis, hemolytic anemias, or known hypersensitivity to any component of the product. Because of the GI irritating properties of the drugs, oral iron products are considered contraindicated by some clinicians in patients with GI ulcerative diseases.

Adverse Effects

Adverse effects associated with non-toxic doses are usually limited to mild gastrointestinal upset. Division of the daily dosage may reduce this effect, but dosage reduction may also be necessary in some animals.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***A*** for use during pregnancy (*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.*)

Overdosage/Acute Toxicity

Ingestion of iron containing products may result in serious toxicity. While lethal doses are not readily available in domestic species, as little as 400 mg (of elemental iron) is potentially fatal in a child. Initial clinical signs of acute iron poisoning usually present with an acute onset of gastrointestinal irritation and distress (vomiting—possibly hemorrhagic, abdominal pain, diarrhea). The onset of these effects may be seen within 30 minutes of ingestion, but can be delayed for several hours. Peripheral vascular collapse may rapidly follow with clinical signs of depression, weak and/or rapid pulse, hypotension, cyanosis, ataxia, and coma possible. Some patients do not exhibit this phase of toxicity and may be asymptomatic for 12–48 hours after ingestion, when another critical phase may occur. This phase may be exhibited by pulmonary edema, vasomotor collapse, cyanosis, pulmonary edema, fulminant hepatic failure, coma and death. Animals that survive this phase may exhibit long-term sequelae, including gastric scarring and contraction and have persistent digestive disturbances.

Because an acute onset of gastroenteritis may be associated with a multitude of causes, diagnosis of iron intoxication may be difficult unless the animal has been observed ingesting the product or physical evidence suggests ingestion. Ferrous sulfate (and gluconate) tablets are radiopaque and often can be observed on abdominal radiographs. Serum iron levels and total iron binding capacity (TIBC) may also be helpful in determining the diagnosis, but must be done on an emergency basis to have any clinical benefit.

Treatment of iron intoxication must be handled as an emergency. In humans who have ingested 10 mg/kg or more of elemental iron within 4 hours of presentation, the stomach is emptied, preferably using gastric lavage with a large bore tube to remove tablet fragments. It is generally recommended to avoid using emetics in patients who already have had episodes of hemorrhagic vomiting. These patients are lavaged using tepid water or 1–5% sodium bicarbonate solution.

In dogs, one author (Mount 1989), has recommended using oral milk of magnesia to help bind the drug, administering apomorphine if appropriate to help dislodge tablets, and to instill a gastric lavage slurry of 50% sodium bicarbonate with a portion left in the stomach. Deferoxamine is useful in chelating iron that has been absorbed. See that monograph for further information.

In addition to chelation therapy, other supportive measures may be necessary including treatment of acidosis, prophylactic antibiotics, oxygen, treatment for shock, coagulation abnormalities, seizures, and/or hyperthermia. After the acute phases have resolved, dietary evaluation and management may be required.

Drug Interactions

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

- **ANTACIDS**: May bind to iron and decrease oral absorption; administer at least two hours apart
- **CALCIUM** (**ORAL**): May bind to iron and decrease oral absorption; administer at least two hours apart
- **CHLORAMPHENICOL**: Because chloramphenicol may delay the response to iron administration, avoid using chloramphenicol in patients with iron deficiency anemia
- **FLUOROQUINOLONES** (**enrofloxacin,** etc.): Iron may reduce the absorption of oral fluoroquinolones; administer at least two hours apart
- **H2-RECEPTOR ANTAGONISTS** (*e.g.,* **ranitidine, famotidine**, etc.): Increased gastric pH may decrease iron absorption
- **PENICILLAMINE**: Iron can decrease the efficacy of penicillamine, probably by decreasing its absorption; if both drugs are required, space doses of the two drugs as far apart as possible
- **PROTON-PUMP INHIBITORS** (*e.g.,* **omeprazole**): Increased gastric pH may decrease iron absorption
- **TETRACYCLINES**: Oral iron preparations can bind to orally administered tetracyclines, thereby decreasing the absorption of both compounds
- **THYROXINE**: Iron may reduce the absorption of oral thyroxine; administer at least two hours apart
- **VITAMIN C**: May enhance the absorption of iron

Laboratory Considerations

- Large doses of oral iron can color the feces black and cause false-positives with the guaiac test for occult blood in the feces.
- Iron does not usually affect the benzidine test for occult blood.

Doses

CAUTION: Unless otherwise noted, doses are for ferrous sulfate (regular—not dried). Dosing of oral iron products can be confusing; some authors state doses in terms of the iron salt and some state doses in terms of elemental iron. For the doses below, assume that the doses are for ferrous sulfate and not elemental iron, unless specified.

- **DOGS:**

  For iron deficiency anemia:
  a) 60–300 mg PO per day for 2 weeks or more (Adams 1988a)
  b) First correct underlying cause of blood loss, then give ferrous sulfate at 100–300 mg per day (total dose) PO. Absorption is enhanced if administered 1 hour before or several hours after feeding. Reduce dosage if GI side effects occur. (Harvey, French, and Meyer 1982)

  For patients to be treated with epoetin (erythropoietin):
  a) 100–300 mg (total dose) PO per day (Cowgill 2002); (Vaden 2006b)

- **CATS:**

  For iron deficiency anemia:
  a) 50–100 mg PO once daily (Kirk 1986), (Morgan 1988)
  b) 30–200 mg PO per day for 2 weeks or more (Adams 1988a)

  For patients to be treated with epoetin (erythropoietin):
  a) 50–100 mg (total dose) PO per day. Many cats do not tolerate oral iron therapy and are better treated with iron dextran at 50 mg IM q3–4 weeks. (Cowgill 2002)
  b) 5–50 mg per cat PO once daily (DiBartola and Chew 2006a)
  c) 50–100 mg per cat PO once daily (Vaden 2006b)

■ **CATTLE:**

As a hematinic:

a) 8–15 g PO per day for 2 weeks or more (Adams 1988a)

■ **HORSES:**

As a hematinic:

a) 2–8 g PO per day for 2 weeks or more (Adams 1988a)

■ **SWINE:**

As a hematinic:

a) 0.5–2 g PO per day for 2 weeks or more (Adams 1988a)

■ **SHEEP:**

As a hematinic:

a) 0.5–2 g PO per day for 2 weeks or more (Adams 1988a)

Monitoring

■ Efficacy; adverse effects:

a) Hemograms

b) Serum iron and total iron binding capacity, if necessary. Normal serum iron values for dogs and cats are reported as 80–180 micrograms/dl and 70–140 micrograms/dl, respectively. Total iron binding for dogs and cats are reported as 280–340 micrograms/dl and 270–400 micrograms/dl, respectively. (Morgan 1988). Serum transferrin saturation can estimated by dividing serum iron by total iron binding capacity.

Client Information

■ Because of the potential for serious toxicity when overdoses of oral iron-containing products are ingested by either children or animals, these products should be kept well out of reach of children and pets.

Chemistry/Synonyms

An orally available iron supplement, ferrous sulfate occurs as odorless, pale-bluish-green, crystals or granules having a saline, styptic taste. In dry air the drug is efflorescent. If exposed to moisture or moist air, the drug is rapidly oxidized to a brownish-yellow ferric compound that should not be used medicinally. Exposure to light or an alkaline medium will enhance the conversion from the ferrous to ferric state.

Ferrous sulfate is available commercially in two forms, a "regular" and a "dried" form. Regular ferrous sulfate contains 7 molecules of water of hydration and is freely soluble in water and insoluble in alcohol. Ferrous sulfate contains approximately 200 mg of elemental iron per gram. Dried ferrous sulfate consists primarily of the monohydrate with some tetrahydrate. It is slowly soluble in water and insoluble in water. Dried ferrous sulfate contains 300 mg of elemental iron per gram. Ferrous sulfate, dried may also be known as ferrous sulfate, exsiccated.

Ferrous sulfate may also be known as: eisen(II)-sulfat, ferreux (sulfate), ferrosi sulfas heptahydricus, ferrous sulphate, ferrum sulfuricum oxydulatum, iron (II) sulphate heptahydrate, iron sulphate; many trade names are available.

Storage/Stability

Unless otherwise instructed, store ferrous sulfate preparations in tight, light-resistant containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

No veterinary-approved products containing only ferrous sulfate could be located, but there are many multivitamin with iron containing products available.

HUMAN-LABELED PRODUCTS:

Ferrous Sulfate Tablets: 325 mg (65 mg iron); *Feosol*® (GlaxoSmithKline); *FeroSul*® (Major); generic; (OTC)

Ferrous Sulfate Elixir/Liquid: 220 mg/5mL (44 mg iron/5ml) in 473 mL, 300 mg/5 mL (60 mg iron/5ml) in 5 mL; *Feosol*® (SmithKline Beecham); generic; (OTC)

Ferrous Sulfate Drops: 75 mg/0.6 mL (15 mg iron/0.6 mL) in 50 mL; *Fer-In-Sol*® (Mead Johnson Nutritionals); *Fer-Gen-Sol*® (Goldline); generic; (OTC)

Ferrous Sulfate, Dried (exsiccated) Tablets: 200 mg (65 mg iron) & 300 mg (60 mg iron); *Feosol*® (GlaxoSmithKline); *Feratab*® (Upsher-Smith); generic (Rugby); (OTC)

Ferrous Sulfate, Dried (exsiccated) Tablets, Slow-Release: 160 mg (50 mg iron); *Slow FE*® (Ciba); *Slow Release Iron*® (Cardinal Health);(OTC)

FILGRASTIM (GRANULOCYTE COLONY STIMULATING FACTOR; GCSF)

(fill-*grass*-stim) Neupogen®

CYTOKINE HEMATOPOIETIC AGENT

Prescriber Highlights

- **Cytokine that in the bone marrow primarily increases the proliferation, differentiation, & activation of progenitor cells in the neutrophil-granulocyte line**
- **Human origin product; antibodies may form that can cause prolonged neutropenia**
- **Treatment is very expensive**

Uses/Indications

Filgrastim may be of benefit in treating neutropenias in dogs or cats when the intrinsic response to endogenously produced cytokines is thought to be inadequate and there is evidence that there are precursors in the bone marrow available. Because of the drug's cost and lack of good evidence for its efficacy in reducing mortality versus using antibiotic therapy alone, its use in small animal medicine is somewhat controversial.

Pharmacology/Actions

Filgrastim is a hematopoietic agent that primarily affects the bone marrow to increase the proliferation, differentiation, and activation of progenitor cells in the neutrophil-granulocyte line. While derived from human DNA, the product is not species specific and also affects canine and feline bone marrow.

Pharmacokinetics

After subcutaneous injection, filgrastim is rapidly absorbed and distributed with highest concentrations found in the bone marrow, liver, kidneys and adrenal glands. It is unknown if it crosses the blood-brain barrier, placenta, or enters maternal milk. The elimination pathways of filgrastim are still under investigation.