■ **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.

Contraindications/Precautions/Warnings
Filgrastim is contraindicated in patients hypersensitive to it. Dogs or cats that have developed antibodies to filgrastim with resultant neutropenia should probably not receive it in the future.

Adverse Effects
Because the human DNA origin product can be immunogenic to dogs and cats, some patients may develop severe neutropenia by mounting an immune response against both endogenously produced and exogenously administered G-CSF. Studies in cats have demonstrated that short pulse doses of 3–5 days at the time of neutropenia may be safe and minimize the development of neutrophil neutralizing antibodies. Preliminary studies using canine origin G-CSF have not demonstrated autoantibody formation in either dogs or cats.

Additionally, there are concerns that exogenously administered filgrastim can elicit undesirable responses in other tissues, including causing myelofibrosis and medullary histiocytosis.

Occasionally irritation at the injection site may occur. Bone pain, splenomegaly, and hypotension have been reported in humans.

Reproductive/Nursing Safety
Adverse effects in females and offspring have been demonstrated after filgrastim was administered to pregnant laboratory animals at high dosages. To interpret this data for use in a clinical setting is difficult, but filgrastim should be used in pregnant females only when the benefits of treating outweigh the potential risks. 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.*)

It is not known whether filgrastim is excreted in milk, but it is unlikely to pose significant risk to nursing offspring.

Overdosage/Acute Toxicity
Limited information is available. Because of the expense of the drug and its apparent limited acute toxic potential, clinically significant overdoses are unlikely.

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

- **ANTINEOPLASTICS:** While filgrastim was developed primarily to prevent the neutropenias associated with some chemotherapeutic agents, some controversy exists about using filgrastim within 24 hours of a dose of antineoplastic agents that target rapidly proliferating cells; generally, in human medicine, use is avoided within 24 hours of such antineoplastics

Doses
Note: To avoid the development of autoantibody formation, most clinicians using this agent recommend using filgrastim in dogs or cats using a "pulse" therapy of no more than 5 days in duration.

- **DOGS:**
  a) For adjunctive therapy of neutropenia (secondary to drug induced aplastic pancytopenia): 5 mcg/kg SC daily (Ruiz de Gopegui and Feldman 2000)
  b) For neutropenia: 1–5 mcg/kg SC daily (Ritt and Modiano 1999)
- **CATS:**
  a) For neutropenia secondary to drug toxicity, infectious diseases, FeLV-associated cyclic neutropenia or idiopathic causes: 5 mcg/kg SC twice daily. Cost and/or development of antibodies usually limit usefulness to a few weeks, but often it is effective for acute or life-threatening neutropenia. (Levy 2000)
  b) For neutropenia: 1–5 mcg/kg SC daily (Ritt and Modiano 1999)
  c) For adjunctive therapy of neutropenia: 5 mcg/kg SC daily until neutrophil count exceeds 3,000/mcl for 2 days (Levy 2002)

Monitoring
- CBC with platelets, routinely

Client Information
- Clients should be briefed on the cost of this agent as well as the possibility that it may cause antibodies to form against endogenously produced G-CSF, thereby causing a potentially life threatening neutropenia.

Chemistry/Synonyms
Prepared via recombinant DNA technology from human DNA, filgrastim is a single chain polypeptide containing 175 amino acids with a molecular weight of about 18,800 daltons. The commercially available injection occurs as a clear solution; buffered to a pH of 4.

Filgrastim may also be known as: granulocyte colony-stimulating factor, G-CSF, recombinant methionyl human GCS-F, r-metHuG-CSF, *Filgen®*, *Gran®*, *Granulen®*, *Granulokine®*, *Neulasta®*, *Neupogen®*, and *Neutromax®*.

Storage/Stability/Compatibility
Injection should be stored in the refrigerator (2–8°C). Do not freeze or shake contents of vial. The drug should never be diluted with saline as a precipitate may form. If necessary it may be diluted into 5% dextrose for injection, but if diluted to concentrations between 5 and 15 mcg/mL, it is recommended that albumin be added to the solution to a concentration of 2 mg/mL to reduce adsorption to plastic IV tubing. It is not recommended to dilute to a concentration of less than 5 mcg/mL.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Filgrastim Injection: 300 mcg/mL preservative free in 1 mL and 1.6 mL single dose vials; 300 mcg/0.5 mL preservative free in 0.5 mL and 0.8 mL prefilled syringes; *Neupogen®* (Amgen); (Rx)

FINASTERIDE

(fin-*as*-te-ride) **Proscar®, Propecia®**

5-ALPHA-REDUCTASE INHIBITOR

Prescriber Highlights
- 5-alpha-reductase inhibitor potentially useful for dogs with benign prostatic hypertrophy & ferrets with adrenal disease
- Contraindications: Hypersensitivity to finasteride; sexually developing animals
- Caution: Patients with significant hepatic impairment
- Adverse Effects: Potentially may cause some minor sexual side effects
- Expense may be an issue