Overdosage/Acute Toxicity
Limited information is available. One human subject taking 12 grams over 12 hours only developed mild gastric distress and a slightly increased heart rate.

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

- **PHENOBARBITAL**: When felbamate is added to patients taking phenobarbital it may cause increases in phenobarbital levels. When phenobarbital is added to patients taking felbamate, felbamate levels may decrease. The same effect can occur with **phenytoin**.
- **VALPROATE**: Felbamate can cause increases in valproic acid levels

Doses
- **DOGS:**

For seizures:

a) As a third choice antiepileptic agent: 15–65 mg/kg PO q8h. Steady state reached after 4th oral dose. Monitor CBC and liver function tests as you would for phenobarbital. Therapeutic serum concentration reported to be 15–100 mcg/mL. (Quesnel 2000)

b) For patients on phenobarb and bromides (both in therapeutic range) and seizure activity unchanged or having intolerable side effects with this combination: If intolerable side effects, do levels and decrease the dose of the one that is in the high end of the range. Then add felbamate at 5–20 mg/kg PO three times daily. (Neer 2000)

c) In dogs refractory to phenobarbital and bromides: Felbamate initial dose of 15 mg/kg PO q8h. May increase the dose in 15 mg/kg increments every 2 weeks until seizures are controlled. Dosages as high as 70 mg/kg, q8h may be necessary and be tolerated by some dogs. (Thomas 2000)

Monitoring
- There is some controversy about monitoring felbamate use in dogs, probably since there is such limited experience with its use. Some clinicians state that liver function tests and CBC's should be regularly assessed (q2–3 months). Others state that the drug is very safe in dogs and that monitoring does not appear to be necessary. Clearly, if the dog is receiving other drugs (especially phenobarbital), monitoring is essential.
- Therapeutic drug levels for felbamate in dogs are not truly known, but appear to be in the 25–100 mcg/mL range. The usefulness of monitoring serum levels is questionable at this point.

Client Information
- Clients must understand the importance of giving doses as prescribed. Because of its short half-life, three times daily administration is routinely administered to adequately judge the efficacy of this drug.
- Because felbamate use in dogs has been limited, the adverse effect profile and possible incidence of serious effects (liver, blood) is not truly known.

Chemistry/Synonyms
Felbamate is a unique dicarbamate anticonvulsant agent, that is slightly soluble in water.

Felbamate may also be known by as: AD-03055, W-554, *Felbamyl®*, *Felbatol®*, *Taloxa®*, and *Taloxa®*.

Storage/Stability/Compatibility
Felbamate preparations should be stored at room temperature. The suspension should be shaken well before use.

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:

Felbamate Tablets: 400 mg, & 600 mg; *Felbatol®* (Wallace Labs); (Rx)

Felbamate Suspension: 120 mg/mL in 240 and 960 mL: *Felbatol®* (Wallace Labs); (Rx)

FENBENDAZOLE

(fen-***ben***-da-zole) **Panacur®, Safe-Guard®**

ANTIPARASITIC AGENT

Prescriber Highlights
- **Anthelmintic useful for a variety of parasites in dogs, cats, cattle, horses, swine, etc**
- **Adverse Effects: Antigen release by dying parasites may occur; particularly at high dosages; vomiting may occur infrequently in dogs or cats**

Uses/Indications
Fenbendazole is indicated (labeled) for the removal of the following parasites in dogs: ascarids (*Toxocara canis, T. leonina*), Hookworms (*Ancylostoma caninum, Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), and tapeworms (*Taenia pisiformis*). It is not effective against *Dipylidium caninum*. Fenbendazole has also been used clinically to treat *Capillaria aerophilia*, *Filaroides hirthi*, and *Paragonimus kellicotti* infections in dogs.

Fenbendazole is indicated (labeled) for the removal of the following parasites in cattle: Adult forms of: *Haemonchus contortus, Ostertagia ostertagi, Trichostrongylus axei, Bunostomum phlebotomum, Nematodirus helvetianus, Cooperia* spp., *Trichostrongylus colubriformis, Oesophagostomum radiatum,* and *Dictyocaulus vivaparus*. It is also effective against most immature stages of the above listed parasites. Although not approved, it has good activity against *Moniezia* spp., and arrested 4th stage forms of *Ostertagia ostertagi.*

Fenbendazole is indicated (labeled) for the removal of the following parasites in horses: large strongyles (*S. edentatus, S. equinus, S. vulgaris*), small strongyles (*Cyathostomum* spp., *Cylicocylus* spp., *Cylicostephanus* spp., *Triodontophorus spp.),* and pinworms (*Oxyuris equi*).

Fenbendazole is indicated (labeled) for the removal of the following parasites in swine: large roundworms (*Ascaris suum*), lungworms (*Metastrongylus pair*), nodular worms (*Oesphagostomum dentatum, O. quadrispinolatum*), small stomach worms (*Hyostrongylus rubidus*), whipworms (*Trichuris suis*), and kidney worms (*Stephanurus dentatus*; both mature and immature).

Although not approved, fenbendazole has been used in cats, sheep, goats, pet birds, and llamas. See Dosage section for more information.

Pharmacology/Actions

Benzimidazole antiparasitic agents have a broad spectrum of activity against a variety of pathogenic internal parasites. In susceptible parasites, their mechanism of action is believed due to disrupting intracellular microtubular transport systems by binding selectively and damaging tubulin, preventing tubulin polymerization, and inhibiting microtubule formation. Benzimidazoles also act at higher concentrations to disrupt metabolic pathways within the helminth, and inhibit metabolic enzymes, including malate dehydrogenase and fumarate reductase.

Pharmacokinetics

Fenbendazole is only marginally absorbed after oral administration. After oral dosing in calves and horses, peak blood levels of 0.11 micrograms/mL and 0.07 micrograms/mL, respectively, were measured. Absorbed fenbendazole is metabolized (and vice-versa) to the active compound, oxfendazole (sulfoxide) and the sulfone. In sheep, cattle, and pigs, 44–50% of a dose of fenbendazole is excreted unchanged in the feces, and <1% in the urine.

Contraindications/Precautions/Warnings

Fenbendazole is not approved for use in horses intended for food purposes.

Adverse Effects

At usual doses, fenbendazole generally does not cause any adverse effects. Hypersensitivity reactions secondary to antigen release by dying parasites may occur, particularly at high dosages. Vomiting may infrequently occur in dogs or cats receiving fenbendazole. Pancytopenia has been reported in one dog.

Single doses (even at exaggerated doses) are not effective in dogs and cats; must treat for 3 days.

Reproductive/Nursing Safety

Fenbendazole is considered safe to use in pregnant bitches and is generally considered safe to use in pregnancy for all species. In a system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***A*** (*Probably safe. Although specific studies may not have proved the safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Overdosage/Toxicity

Fenbendazole is apparently well tolerated at doses up to 100X recommended. The LD_{50} in laboratory animals exceeds 10 grams/kg when administered PO. It is unlikely an acute overdosage would lead to clinical signs.

Drug Interactions

- **BROMSALAN FLUKICIDES** (**dibromsalan, tribromsalan**; not available in the USA): Oxfendazole or fenbendazole should not be given concurrently with the bromsalan flukicides; abortions in cattle and death in sheep have been reported after using these compounds together

Doses

- **DOGS:**

For susceptible ascarids, hookworms, whipworms, and tapeworms (*Taenia* spp. only):

a) 50 mg/kg, PO for 3 consecutive days (Package insert; *Panacur*®—Hoechst), (Cornelius and Roberson 1986)

b) 55 mg/kg, PO for 3 days (5 days for Taenia) (Chiapella 1988), (Reinemeyer 1985)

To prevent transplacental and transmammary transmission of somatic *T. canis* and *A. caninum*:

a) 50 mg/kg PO once daily from the 40th day of gestation to the 14th day of lactation. (Kazacos 2002)

For *Capillaria plica*:

a) 50 mg/kg once daily for 3 days; repeat a single 50 mg/kg dose 3 weeks later (Todd, Paul, and DiPietro 1985)

b) 50 mg/kg, PO daily for 3–10 days (Brown and Prestwood 1986)

For *Capillaria aerophilia*:

a) 25–50 mg/kg q12h for 10–14 days (Hawkins, Ettinger, and Suter 1989); (Hawkins 2000)

b) 50 mg/kg PO once daily for 10–14 days (Reinemeyer 1995)

For *Filaroides hirthi*:

a) 50 mg/kg, PO once daily for 14 days. Symptoms may worsen during therapy, presumably due to a reaction when the worm dies. (Hawkins, Ettinger, and Suter 1989)

b) 50 mg/kg PO once daily for 10–14 days (Reinemeyer 1995)

For *Paragonimus kellicotti*:

a) 25–50 mg/kg PO twice daily for 10–14 days (Todd, Paul, and DiPietro 1985); (Hawkins 2000)

b) 50 mg/kg PO once daily for 10–14 days (Reinemeyer 1995)

c) 50 mg/kg, PO once daily for 3 consecutive days; repeat in 2–3 weeks and again in 2 months (DeNovo 1988)

For *Crenosoma vulpis*:

a) 50 mg/kg PO once daily for 3 days (Reinemeyer 1995); (Hawkins 2000)

For Giardia:

a) 50 mg/kg PO once daily for 3 days (Barr and Bowman 1994); (Greene and Watson 1998)

b) 25 mg/kg PO q12h for 3–7 days (Lappin 2000)

For *Eucoleus boehmi*:

a) 50 mg/kg PO once daily for 10–14 days; improvement may only be temporary (Reinemeyer 1995)

- **CATS, DOMESTIC:**

For susceptible ascarids, hookworms, strongyloides, and tapeworms (*Taenia* spp. only):

a) 50 mg/kg, PO for 5 days (Dimski 1989)

For lungworms (*Aelurostrongylus abstrusus*):

a) 25–50 mg/kg q12h for 10–14 days (Hawkins, Ettinger, and Suter 1989); (Hawkins 2000)

b) 50 mg/kg, PO for 10 days (Pechman 1989)

c) 20 mg/kg PO once daily for 5 days; repeat in 5 days (Reinemeyer 1995)

For lungworms (*Capillaria aerophilia*):

a) 50 mg/kg, PO for 10 days (Pechman 1989)

b) 50 mg/kg PO once daily for 10–14 days (Reinemeyer 1995)

For *Capillaria feliscati*:

a) 25 mg/kg, twice daily PO for 3–10 days (Brown and Prestwood 1986)

b) 25 mg/kg, PO q12h for 10 days (Brown and Barsanti 1989)

For *Paragonimus kellicotti*:

a) 25–50 mg/kg PO twice daily for 10–14 days (Hawkins 2000)

b) 50 mg/kg PO once daily for 10–14 days (Reinemeyer 1995)

For *Eurytrema procyonis* (pancreatic fluke):

a) 30 mg/kg, PO daily for 6 days (Steiner and Williams 2000)

For Giardia:

a) In young kittens: 50 mg/kg PO (using the suspension) once a day for 3–5 days (Tams 1999)

b) 50 mg/kg PO q24h for 3–5 days (Vasilopulos 2006)

■ **CATS, LARGE (EXOTIC):**

For labeled parasites:

a) 10 mg/kg PO once daily for 3 consecutive days. (Label information; *Panacur® 22.25 Granules*—Intervet)

■ **BEARS (*URSIDAE*):**

For labeled parasites:

a) 10 mg/kg PO once daily for 3 consecutive days. (Label information; *Panacur® 22.25 Granules*—Intervet)

■ **SMALL MAMMALS/RODENTS:**

a) For pinworms in mice, rats, hamsters, gerbils and rabbits: 50 mg/kg PO once (Burke 1999)

b) For Giardia in Chinchillas: 25 mg/kg PO once a day for 3 days (Hayes 2000)

c) Mice, Rats, Gerbils, Hamsters, Guinea pigs, Chinchillas: 20–50 mg/kg PO once daily for 5 days (Higher dose is for Giardia) (Adamcak and Otten 2000)

■ **CATTLE:**

For removal/control of *Haemonchus contortus, Ostertagia ostertagi, Trichostrongylus axei, Bunostomum phlebotomum, Nematodirus helvetianus, Cooperia* spp., *Trichostrongylus colubriformis, Oesophagostomum radiatum*, and *Dictyocaulus vivaparus*:

a) 5 mg/kg, PO (Paul 1986)

b) 7.5 mg/kg, PO (Roberson 1988b)

c) 4 mg/kg PO; under conditions of continuous exposure to parasites, animals may need to be retreated after 4–6 weeks, (Label information *Panacur® Paste*—Intervet)

For *Moniezia* spp., and arrested 4th stage forms of *Ostertagia ostertagi*:

a) 10 mg/kg, PO (Paul 1986), (Roberson 1988b)

For giardiasis in calves:

a) 15 mg/kg PO for 3 successive days and then moved to a pen that was thoroughly cleaned and disinfected with 10% ammonia. (Claerebout 2006)

■ **HORSES:**

For susceptible parasites:

a) For control of large and small strongyles, and pinworms in adult horses: 5 mg/kg PO;

For foals and weanlings (less than 18 months of age) where ascarids are a common problem: 10 mg/kg PO;

For control of encysted early 3rd stage, late 3rd stage and 4th stage cyathostome larvae and 4th stage *Strongylus vulgaris* larvae) 10 mg/kg PO for 5 consecutive days. (Label information *Panacur® Paste*—Intervet)

For treatment of migrating large strongyles:

a) 50 mg/kg PO for 3 consecutive days, or 10 mg/kg for 5 consecutive days (Herd 1987)

For mucosal stage of small strongyles:

a) 7.5–10 mg/kg PO once daily for 5 days; a single dose of 30 mg/kg is effective against older encysted stages (Lyons and Drudge 2000)

■ **SWINE:**

For susceptible parasites:

a) 5 mg/kg PO; 3 mg/kg in feed for 3 days; 10 mg/kg for ascarids (Roberson 1988b)

b) For whipworms in potbellied pigs: 9 mg/kg PO for days (Braun 1995)

■ **SHEEP & GOATS:**

For susceptible parasites:

a) 5 mg/kg in feed for 3 days (Roberson 1988b)

■ **LLAMAS:**

For susceptible parasites:

a) 10–15 mg/kg PO (as paste or suspension) (Fowler 1989)

b) 5–10 mg/kg PO for 1–3 days. Fenbendazole and ivermectin are the most effective and safest anthelmintics for use in llamas. (Cheney and Allen 1989)

■ **BIRDS:**

a) For Ascarids: 10–50 mg/kg PO once; repeat in 10 days. Do not use during molt (may cause stunted feathers) or while nesting.

For flukes or microfilaria: 10–50 mg/kg PO once daily for 3 days

For *Capillaria*: 10–50 mg/kg PO once daily for 5 days. Is not effective against gizzard worms in finches. (Clubb 1986)

b) For nematodes, some trematodes: 10–50 mg/kg PO once daily for 3–5 days; 20–100 mg/kg oral single dose range; 125 mg/L of drinking water for 5 days (50 mg/L for 5 days in finches); or 100 mg/kg of feed for 5 days. Not recommended to be used in breeding season during molting. (Marshall 1993)

c) Ratites: 15 mg/kg PO once daily for 3 days. Has efficacy against ostrich tapeworm. (*Houttuynia struthionus*) (Jenson 1998)

■ **REPTILES:**

For susceptible infections:

a) For most species: 50–100 mg/kg PO once; repeat in 2–3 weeks; very effective against Strongyloides. (Gauvin 1993)

Chemistry/Synonyms

A benzimidazole anthelmintic, fenbendazole occurs as a white, crystalline powder. It is only slightly soluble in water.

Fenbendazole may also be known as: Hoe-881V, *Panacur®*, and *Safe-Guard®*.

Storage/Stability

Fenbendazole products should be stored at room temperature.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Fenbendazole Granules: 222 mg/gram (22.2%) in 0.18 oz and 1 g, 2 g, 4 g packets and 1 lb jars; *Panacur® Granules 22.2%* (Intervet); (Rx); *Safeguard® Canine Dewormer* (Intervet), (OTC). Approved for use in dogs, large exotic cats (lions, etc.), and bears (black bears, polar bears, etc.)

Fenbendazole Granules: 222 mg/gram (22.2%); *Panacur® Granules 22.2%* (Intervet). (OTC). Approved for use in horses not intended for food.

Fenbendazole Suspension: 100 mg/mL (10%); available in both equine and bovine labeled products; *Panacur® Suspension* (Intervet); (Rx). Approved for use in horses (not intended for food) and cattle Slaughter withdrawal = 8 days (cattle). *Safe-Guard® Suspension* (Intervet); (OTC). Approved for use in beef and dairy cattle. Slaughter withdrawal at labeled doses = 8 days

Fenbendazole Paste: 100 mg/gram (10%); available in both equine and bovine labeled products and sizes. *Panacur® Paste* (Intervet); (OTC). Approved for use in horses (not intended for food) and cattle. Slaughter withdrawal at labeled doses = 8 days (cattle). *Safe Guard® Paste* (Intervet); (OTC). Approved for use in horses not intended for food and cattle. Slaughter withdrawal at labeled doses = 8 days; no milk withdrawal time at labeled doses.

Fenbendazole Type B Medicated Feed

Safe-Guard® EZ Scoop Swine Dewormer (Intervet) (OTC). 1.8% Fenbendazole No slaughter withdrawal time required at labeled doses

Safe-Guard® 0.96% Scoop Dewormer (Intervet); (OTC). Approved for use in cattle. No milk withdrawal time; slaughter withdrawal time at labeled doses = 13 days

Fenbendazole Type C Medicated Feed

Safe-Guard® Free-choice Cattle Dewormer (Intervet); (OTC); 0.50% Fenbendazole (2.27 g/lb). Approved for use in beef and dairy cattle. No milk withdrawal time.

Safe-Guard® 35% Salt Free-choice Cattle Dewormer (Intervet); (OTC); 1.9 g/lb Fenbendazole. Approved for use in dairy and beef cattle. Slaughter withdrawal time at labeled doses = 13 days; no milk withdrawal time.

Fenbendazole Pellets

Safe-Guard® 0.5% Cattle Top Dress (Intervet); (OTC). At labeled dose, slaughter withdrawal time = 13 days; no milk withdrawal period at labeled doses

Safe-Guard® 1.96% Scoop Dewormer Mini Pellets (Intervet); (OTC). Approved for use in beef and dairy cattle. No milk withdrawal time at labeled doses; slaughter withdrawal time at labeled doses = 13 days

Fenbendazole Premix 20% Type A (200 mg/gram)

Safe-Guard® Premix (Intervet); (OTC). Approved for use in swine, growing turkeys, dairy and beef cattle, zoo and wildlife animals. Slaughter withdrawal for cattle = 13 days; no milk withdrawal time. Slaughter withdrawal for swine at labeled doses = none. Wildlife animal slaughter (hunting) withdrawal = 14 days at labeled doses.

HUMAN-LABELED PRODUCTS: None

FENTANYL, TRANSDERMAL FENTANYL CITRATE

(***fen***-ta-nil) Sublimaze®, Duragesic®

OPIATE

Prescriber Highlights

- Class-II opiate analgesic used parenterally & transdermally in small animals
- Contraindications: Use extreme caution when additional respiratory, or CNS depression would be deleterious
- Use caution in geriatric, very ill or debilitated patients & those with a preexisting respiratory problem
- Adverse Effects: Dose related respiratory, CNS & circulatory depression (bradycardia); also, rashes at the patch site, urine retention, constipation, dysphoria, or agitation
- Do NOT cut patches; dispose of properly
- Lab values (amylase, lipase) may be altered

Uses/Indications

In veterinary medicine, fentanyl injection and transdermal patches are used primarily in dogs and cats and have been shown to be useful for the adjunctive control of postoperative pain and in the control of severe pain associated with chronic pain, dull pain, and non-specific, widespread pain (*e.g.*, associated with cancer, pancreatitis, aortic thromboemboli, peritonitis, etc.). Perioperative injectable fentanyl can also reduce the requirements for inhalational anesthetics during surgery, which can be particularly advantageous in patients with compromised cardiac function. Transdermal fentanyl has been clinically effective overall and has not demonstrated substantial adverse effects.

In humans, significant respiratory depression with use of the patches after surgery has precluded post-operative use, but this has not been a significant problem in veterinary medicine.

Pharmacology/Actions

Fentanyl is a *mu* opiate agonist. *Mu* receptors are found primarily in the pain regulating areas of the brain. They are thought to contribute to the analgesia, euphoria, respiratory depression, physical dependence, miosis, and hypothermic actions of opiates. Receptors for opiate analgesics are found in high concentrations in the limbic system, spinal cord, thalamus, hypothalamus, striatum, and midbrain. They are also found in tissues such as the gastrointestinal tract, urinary tract, and in other smooth muscle.

The pharmacology of the opiate agonists is discussed in more detail in the monograph, Narcotic (opiate) Agonist Analgesics.

Pharmacokinetics

When used via a single dose IV injection, fentanyl has a relatively short duration of effect (15–30 minutes.)

When administered to dogs as 10 mcg/kg IV bolus, fentanyl rapidly distributes and exhibits a large volume of distribution (5 L/kg). The terminal elimination half life is about 45 minutes; total clearance is 78 mL/min/kg. After a 10 mcg/kg bolus, dogs administered a constant rate intravenous infusion of 10 mg/kg/hr were able to maintain blood levels around 1 ng/mL (the assumed—but not verified therapeutic analgesic level). (Sano, Nishimura et al. 2006)

Half-life after IV administration in cats is approximately 2.5 hours.

There have been limited pharmacokinetic studies performed with transdermal fentanyl patches in dogs, cats, and horses. While therapeutic levels of fentanyl are attained, there is a significant interpatient variability with both the time to achieve therapeutic levels and the levels themselves. Cats tend to achieve therapeutic levels faster than do dogs; in dogs, the patch should be applied 24 hours in advance of need if possible; minimum of 12 hours pre-need. Most cats attain therapeutic benefit in about 6 hours after application. While applied, duration of action persists for at least 72 hours (usually for at least 104 hours). Duration of action is generally longer in cats than in dogs. For continued use, patches may need to changed every 48 hours in dogs or horses.

In horses, fentanyl patches are rapidly absorbed with therapeutic levels (1 ng/mL?) achieved in about 6 hours after application and persists for 48+ hours.

Contraindications/Precautions/Warnings

Fentanyl is contraindicated in patients with known hypersensitivity to it or any component of the product (including the adhesive for the patch).

Because of its potency, fentanyl injection should be used only by professionals familiar with its use in circumstances where patients can be adequately monitored and supported.

Use cautiously with other CNS depressants. Dosages of other opiates may need to be reduced when given with fentanyl transdermal, particularly several hours after application of the patch. Transdermal fentanyl should be used cautiously in geriatric, very ill or debilitated patients and those with a preexisting respiratory problem. Febrile patients may have increased absorption of fentanyl and will require increased monitoring.