Adverse Effects
Labeled adverse effects include transient tachycardia and decreased borborygmal sounds that last for approximately 30 minutes after IV dosing. Transient pupil dilation can be noted. Other effects include decreased secretions and dry mucous membranes.

Because this drug can cause increases in heart rate, heart rate cannot be used as a valid pain indicator for 30 minutes after injection.

When used for labeled indications, a lack of response may indicate a more serious problem that may require surgery or more aggressive care (White 2005b).

Reproductive/Nursing Safety
As no data is available to document safety, the manufacturer does not recommend use in nursing foals or pregnant or lactating mares.

Overdosage/Acute Toxicity
Dosages up to 10X (3 mg/kg) were administered to horses as part of pre-approval studies. Clinical effects noted included dilated pupils (returned to normal in 4–24 hours), tachycardia (returned to normal within 4 hours) and dry mucous membranes (returned to normal in 1–2 hours). Gut motility was inhibited, but returned to baseline within 4 hours and normal feces were seen within 6 hours. Two of the four horses treated at 10X dosage developed mild signs of colic which resolved without further treatment.

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

- **ATROPINE or other anticholinergic agents**: May cause additive effects if used with N-butylscopolammonium
- **METOCLOPRAMIDE and other drugs that have cholinergic-like actions on the GI tract**: These drugs and N-butylscopolammonium may counteract one another's actions on GI smooth muscle

Laboratory Considerations
No specific concerns noted.

Doses
- **HORSES:**

For labeled indications:

a) 0.3 mg/kg (30 mg or 1.5 mL per 100 kg of body weight) via slow IV, one time (Label Dosage; *Buscopan*®—BI)

Monitoring
- Heart rate (**Note:** heart rate cannot be used as indicator for pain for the first 30 minutes after administration)
- GI motility via gut sounds and feces output

Client Information
- Because an accurate patient assessment must be performed prior to the use of this medication and intravenous administration and subsequent monitoring are required, this drug should only be administered by veterinarians

Chemistry/Synonyms
N-butylscopolammonium bromide, a derivative of scopolamine, is a synthetic, quaternary ammonium antispasmodic-anticholinergic agent. It occurs as a white crystalline substance that is soluble in water.

N-butylscopolammonium bromide may also be known as: butylscopolamine bromide, hysocine butylbromide, hysocine N-butylbromide, scopolamini butylbromidum, hyoscini butylbromidum, *Buscopan*® or *Buscapina*®.

Storage/Stability
The commercially available injection should be stored at room temperature (15–30°C).

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

N-butylscopolammonium bromide Injection: 20 mg/mL in 50 mL multi-dose vials, *Buscopan*® (Boehringer Ingelheim); (Rx). Approved for use in horses.

In the UK, *Buscopan Compositum*® (BI) is commercially available. This product contains metamizole (a form of dipyrone) 500 mg/mL and hyoscine butylbromide (synonym for N-butylscopolammonium Br) 4 mg/mL. It is labeled for use in horses, cattle and dogs.

HUMAN-LABELED PRODUCTS:

None in the USA. There are several products with the trade name *Buscopan*® or *Buscapina*® available in many countries. Refer to actual product labels as ingredients and concentrations may vary.

NEOMYCIN SULFATE

(nee-o-*mye*-sin) Biosol®, Neomix®

AMINOGLYCOSIDE ANTIBIOTIC

Prescriber Highlights
- **Aminoglycoside antibiotic usually used orally (gut "sterilization") or in topical formulations**
- **Contraindications: Oral: Hypersensitive to aminoglycosides, intestinal blockage; rabbits**
- **Adverse Effects: Parenteral use can be very toxic (nephrotoxic) & is not recommended. Chronic use can lead to GI superinfections. Rarely, oral neomycin may cause ototoxicity, nephrotoxicity, severe diarrhea, & intestinal malabsorption**
- **Minimal amounts absorbed via GI (if intact)**

Uses/Indications
Because neomycin is more nephrotoxic and less effective against several bacterial species than either gentamicin or amikacin, its use is generally limited to topical formulations for skin, eyes, and ears, oral treatment of enteric infections, to reduce microbe numbers in the colon prior to colon surgery, and oral or enema administration to reduce ammonia-producing bacteria in the treatment of hepatic encephalopathy. Doses for parenteral administration are listed below, but should be used only with extreme caution due to the drug's toxic potential.

Pharmacology/Actions
Neomycin has a mechanism of action and spectrum of activity (primarily gram-negative aerobes) similar to the other aminoglycosides, but in comparison to either gentamicin or amikacin, it is significantly less effective against several species of gram-negative organisms, including strains of Klebsiella, *E. coli*, and Pseudomonas. However, most strains of neomycin-resistant bacteria of these species remain susceptible to amikacin. More detailed information on the aminoglycosides mechanism of action and spectrum of activity is outlined in the amikacin monograph.

Pharmacokinetics

Approximately 3% of a dose of neomycin is absorbed after oral or rectal (retention enema) administration, but this can be increased if gut motility is slowed or if the bowel wall is damaged. Therapeutic levels are not attained in the systemic circulation after oral administration.

After IM administration, therapeutic levels can be attained with peak levels occurring within 1 hour of dosing. The drug apparently distributes to tissues and is eliminated like the other aminoglycosides (refer to Amikacin monograph for more details). Orally administered neomycin is nearly all excreted unchanged in the feces.

Contraindications/Precautions/Warnings

Oral neomycin is contraindicated in the presence of intestinal obstruction or if the patient is hypersensitive to aminoglycosides.

Chronic usage of oral aminoglycosides may result in bacterial or fungal superinfections.

Because aminoglycosides can cause irreversible ototoxicity, they should be used with caution in "working" dogs.

Aminoglycosides should be used with caution in patients with neuromuscular disorders (*e.g.*, myasthenia gravis) due to their neuromuscular blocking activity.

Because aminoglycosides are eliminated primarily through renal mechanisms, they should be used cautiously, preferably with serum monitoring and dosage adjustment in neonatal or geriatric animals.

Aminoglycosides are generally considered contraindicated in rabbits/hares, as they adversely affect the GI flora balance in these animals.

Adverse Effects

Refer to the amikacin monograph for more information regarding these topics with parenteral neomycin; however, parenterally administered neomycin is much more nephrotoxic than is amikacin.

Rarely, oral neomycin may cause ototoxicity, nephrotoxicity, severe diarrhea, and intestinal malabsorption.

Reproductive/Nursing Safety

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 class: ***A*** (*Probably safe. Although specific studies may not have proved he safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Neomycin is excreted in cow's milk following a single IM injection. If used orally, it is unlikely neomycin poses significant systemic risk to nursing offspring, but may negatively alter gut flora and cause diarrhea.

Drug Interactions

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

- **DIGOXIN:** Oral neomycin with orally administered digoxin may result in decreased absorption. Separating the doses of the two medications may not alleviate this effect. Some human patients (<10%) metabolize digoxin in the GI tract and neomycin may increase serum digoxin levels in these patients. It is recommended that enhanced monitoring be performed if oral neomycin is added or withdrawn from the drug regimen of a patient stabilized on a digitalis glycoside.
- **METHOTREXATE:** Absorption may be reduced by oral neomycin but is increased by oral kanamycin (found in *Amforal®*)
- **OTOTOXIC, NEPHROTOXIC DRUGS:** Although only minimal amounts of neomycin are absorbed after oral or rectal administration, the concurrent use of other ototoxic or nephrotoxic drugs with neomycin should be done with caution
- **PENICILLIN VK (oral):** Oral neomycin should not be given concurrently with oral penicillin VK as malabsorption of the penicillin may occur
- **WARFARIN:** Oral neomycin may decrease the amount of vitamin K absorbed from the gut; this may have ramifications for patients receiving oral anticoagulants

Refer to the amikacin monograph for more information regarding drug interactions with parenteral neomycin.

Laboratory Considerations

No specific concerns noted

Doses

- **DOGS:**

  For treatment of hepatic encephalopathy:
  a) 22 mg/kg PO three to four times daily (Hardy 1989)
  b) For emergency treatment of hepatic encephalopathy secondary to portosystemic shunts: Following evacuation enema instill 10–20 mg/kg neomycin sulfate diluted in water. Oral neomycin not recommended. (Cornelius and Bjorling 1988)
  c) 15 mg/kg as an enema every 6 hours after a cleansing enema or 10–20 mg/kg, PO every 6 hours. May be used with lactulose. (Johnson 1986)

  For GI tract infections:
  a) For campylobacteriosis: 20 mg/kg PO q12h (Willard 2003c)

  For systemic therapy (**Caution**: Very nephrotoxic):
  a) 3.5 mg/kg IV, IM or SC q8h (Kirk 1989)

- **CATS:**

  For treatment of hepatic encephalopathy:
  a) Secondary to portosystemic shunts: 10–20 mg/kg PO two times a day. May be used in combination with lactulose or in cleansing enemas. (Center, Hornbuckle, and Scavelli 1986)
  b) 22 mg/kg q8h PO (Cornelius, Bartges et al. 2000)
  c) Lactulose at 0.5–1 mg/kg PO q8h with or without neomycin at 20 mg/kg PO q8–12h. (Marks 2004a)

  For GI tract infections: For campylobacteriosis:
  a) 20 mg/kg PO q12h (Willard 2003c)

  For systemic therapy (**Caution**: Very nephrotoxic):
  a) 3.5 mg/kg IV, IM or SC q8h (Kirk 1989)

- **FERRETS:**

  For susceptible enteric infections:
  a) 10–20 mg/kg, PO twice to four times daily (Williams 2000)

- **RODENTS, SMALL MAMMALS:**

  Note: Contraindicated in rabbits/hares
  a) Chinchillas: 15 mg/kg, PO once daily. Gerbils**:** 100 mg/kg, PO once daily, Guinea Pigs: 8 mg/kg, PO once daily. Hamsters: 100 mg/kg, PO once daily, or 0.5 mg/mL in drinking water. Mice, Rats: 50 mg/kg, PO once daily (Adamcak and Otten 2000)

- **CATTLE:**

  For oral administration to treat susceptible enteral infections:
  a) 4–7.5 g/day PO divided 2–4 times daily at regular intervals. Calves: 2–3 g/day, PO divided 2–4 times daily at regular intervals. Doses are not standardized; use for general guidance only. (Brander, Pugh, and Bywater 1982)

b) 10–20 mg/kg q12h (general guideline only). (Jenkins 1986)
c) 7–12 mg/kg, PO q12h (Howard 1986)
d) Feed at levels of 70–140 g/ton of feed or mix the appropriate dose in the drinking water which will be consumed by animals in 12 hours to provide 11 mg/kg or mix with reconstituted milk replacers to provide 200–400 mg/gallon. (Label directions; *Neomix Ag® 325*—Upjohn)

■ **HORSES:**

For oral administration to treat susceptible enteral infections:
a) Adults: 4–7.5 g/day PO divided 2–4 times daily at regular intervals. Foals: 2–3 g/day PO divided 2–4 times daily at regular intervals. Doses are not standardized; use for general guidance only. (Brander, Pugh, and Bywater 1982)
b) 5–15 mg/kg PO once daily (Robinson 1987)

For intrauterine infusion:
a) Neomycin alone: 3–4 grams. Combination of neomycin (2 gram) and procaine penicillin G (3,000,000 IU), Combination of Neomycin (1 gram) and Polymyxin B (40,000 IU), Furaltadone (600 mg) and penicillin G (Sodium or potassium, 3,000,000–5,000,000 IU). Little science is available for recommending doses, volume infused, frequency, diluents, etc. Most intrauterine treatments are commonly performed every day or every other day for 3–7 days. (Perkins 1999)

■ **SWINE:**

For oral administration to treat susceptible enteral infections:
a) Young pigs: 0.75–1 g/day, PO divided 2–4 times daily at regular intervals. Doses are not standardized; use for general guidance only. (Brander, Pugh, and Bywater 1982)
b) 7–12 mg/kg, PO q12h (Howard 1986)

■ **SHEEP & GOATS:**

For oral administration to treat susceptible enteral infections:
a) Lambs: 0.75–1 g/day PO divided 2–4 times daily at regular intervals. Doses are not standardized; use for general guidance only. (Brander, Pugh, and Bywater 1982)
b) Feed at levels of 70–140 g/ton of feed or mix the appropriate dose in the drinking water which will be consumed by animals in 12 hours to provide 11 mg/kg or mix with reconstituted milk replacers to provide 200–400 mg/gallon. (Label directions; *Neomix Ag® 325*—Upjohn)

■ **BIRDS:**

For bacterial enteritis:
a) Chickens, turkeys, ducks: Feed at levels of 70–140 g/ton of feed or mix the appropriate dose in the drinking water which will be consumed by animals in 12 hours to provide 11 mg/kg (Label directions; *Neomix Ag® 325*—Upjohn)

■ **SNAKES:**

For susceptible infections:
a) For bacterial gastritis: gentamicin 2.5 mg/kg IM every 72 hours with oral neomycin 15 mg/kg plus oral live lactobacillus (Burke 1986)

Monitoring

For oral use:
■ Clinical efficacy
■ Systemic and GI adverse effects with prolonged use.

For parenteral use: Refer to Amikacin monograph

Client Information

■ Clients should understand that the potential exists for severe toxicity (nephrotoxicity, ototoxicity) developing from this medication when used parenterally.

Chemistry/Synonyms

An aminoglycoside antibiotic obtained from *Streptomyces fradiae*, neomycin is actually a complex of three separate compounds, neomycin A (neamine; inactive), neomycin C, and neomycin B (framycetin). The commercially available product almost entirely consists of the sulfate salt of neomycin B. It occurs as an odorless or almost odorless, white to slightly yellow, hygroscopic powder or cryodessicated solid. It is freely soluble in water and very slightly soluble in alcohol. One mg of pure neomycin sulfate is equivalent to not less than 650 Units. Oral or injectable (after reconstitution with normal saline) solutions of neomycin sulfate have a pH from 5–7.5.

Neomycin sulfate may also be known as: fradiomycin sulfate, neomycin sulphate, or neomycini sulfas, *Neo-325®, Neo-fradin®, Neo-Sol 50®*, and *Neovet®*.

Storage/Stability

Neomycin sulfate oral solution should be stored at room temperature (15–30°C) in tight, light-resistant containers. Unless otherwise instructed by the manufacturer, oral tablets/boluses should be stored in tight containers at room temperature. The sterile powder should be stored at room temperature and protected from light.

In the dry state, neomycin is stable for at least 2 years at room temperature.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Neomycin Sulfate Oral Liquid: 200 mg/mL (140 mg neomycin base/mL); generic; (OTC). Depending on labeling approved for use in cattle, swine, sheep, goats, turkeys, laying hens, and broilers. Check labels for slaughter withdrawals; may vary with product. General withdrawal times (when used as labeled): Cattle = 1 day; Sheep = 2 days and swine and goats = 3 days. Withdrawal period has not been established in pre-ruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older.

Neomycin Sulfate Soluble Powder: 325 grams/lb: *Neo-325® Soluble Powder* (Bimeda); *Neovet® 325/100 & NeoVet® 325 AG Grade* (includes turkey label); (AgriPharm) *Neo-Sol 50®* (Alpharma); (OTC). Approved for use in Cattle and goats (not veal calves), swine, sheep, goats and turkeys (some products). Check labels for slaughter withdrawals; may vary with product. General slaughter withdrawal times (when used as labeled): Cattle = 1 day; Turkeys = 0 days; Sheep = 2 days; Swine and Goats = 3 days.

HUMAN-LABELED PRODUCTS:

Neomycin Sulfate Tablets: 500 mg; generic; (Rx)

Neomycin Sulfate Oral Solution: 25 mg/mL in 480 mL; *Neo-fradin®* (Pharma-Tek); (Rx)

NEOSTIGMINE BROMIDE
NEOSTIGMINE METHYLSULFATE

(nee-oh-***stig***-meen) Prostigmin®

PARASYMPATHOMIMETIC (CHOLINERGIC)

Prescriber Highlights

- Parasympathomimetic used to initiate peristalsis, empty the bladder, & stimulate skeletal muscle contractions. Also for diagnosis & treatment of myasthenia gravis & treatment of non-depolarizing neuromuscular blocking agents (curare-type) overdose; has been used for treating massive ivermectin overdoses in cats
- Contraindications: Peritonitis, mechanical intestinal or urinary tract obstructions, late stages of pregnancy, hypersensitivity to this class of compounds, or if treated with other cholinesterase inhibitors
- Adverse Effects: Cholinergic in nature & dose related (nausea, vomiting, diarrhea, excessive salivation & drooling, sweating, miosis, lacrimation, increased bronchial secretions, bradycardia or tachycardia, cardiospasm, bronchospasm, hypotension, muscle cramps & weakness, agitation, restlessness, or paralysis)
- Cholinergic crisis & myasthenic crisis must not be confused

Uses/Indications

Neostigmine is indicated for rumen atony, initiating peristalsis, emptying the bladder, and stimulating skeletal muscle contractions in cattle, horses, sheep, and swine (Package insert; *Stiglyn® 1:500-P/M*—Mallinckrodt). It has been used in the diagnosis and treatment of myasthenia gravis and in treating non-depolarizing neuromuscular blocking agents (curare-type) overdoses in dogs. Neostigmine has also been used to treat massive ivermectin overdoses in cats.

Pharmacology/Actions

Neostigmine competes with acetylcholine for acetylcholinesterase. As the neostigmine-acetylcholinesterase complex is hydrolyzed at a slower rate than that of the acetylcholine-enzyme complex, acetylcholine will accumulate with a resultant exaggeration and prolongation of its effects. These effects can include increased tone of intestinal and skeletal musculature, stimulation of salivary and sweat glands, bronchoconstriction, ureter constriction, miosis and bradycardia. Neostigmine also has a direct cholinomimetic effect on skeletal muscle.

In horses, neostigmine may decrease jejunal activity and delay gastric emptying. Its use in treating colon impactions and ileus is controversial.

Pharmacokinetics

Information on the pharmacokinetics of neostigmine in veterinary species was not located. In humans, neostigmine bromide is poorly absorbed after oral administration with only 1–2% of the dose absorbed. Neostigmine effects on peristaltic activity in humans begin within 10–30 minutes after parenteral administration and can persist for up to 4 hours.

Neostigmine is 15–25% bound to plasma proteins. It has not been detected in human milk nor would it be expected to cross the placenta when given at usual doses.

In humans, the half-life of the drug is approximately one hour. It is metabolized in the liver and hydrolyzed by cholinesterases to 3-OH PTM, which is weakly active. When administered parenterally, approximately 80% of the drug is excreted in the urine within 24 hours, with 50% excreted unchanged.

Contraindications/Precautions/Warnings

Neostigmine is contraindicated in patients with peritonitis, mechanical intestinal or urinary tract obstructions, in animals hypersensitive to this class of compounds, or treated with other cholinesterase inhibitors.

Use neostigmine with caution in patients with epilepsy, peptic ulcer disease, bronchial asthma, cardiac arrhythmias, hyperthyroidism, vagotonia, or megacolon.

Adverse Effects

Adverse effects of neostigmine are dose-related and cholinergic in nature. See overdosage section below.

Reproductive/Nursing Safety

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.*)

Because it is ionized at physiologic pH, neostigmine would not be expected to be excreted in maternal milk.

Overdosage/Acute Toxicity

Overdosage of neostigmine can induce a cholinergic crisis. Clinical signs can include: nausea, vomiting, diarrhea, excessive salivation and drooling, sweating (in animals with sweat glands), miosis, lacrimation, increased bronchial secretions, bradycardia or tachycardia, cardiospasm, bronchospasm, hypotension, muscle cramps and weakness, agitation, restlessness, or paralysis. In patients with myasthenia gravis, it may be difficult to distinguish between a cholinergic crisis and myasthenic crisis. A test dose of edrophonium should differentiate between the two.

Treat cholinergic crisis by temporarily ceasing neostigmine therapy and instituting treatment with atropine (doses are listed in the Atropine monograph). Maintain adequate respirations using mechanical assistance if necessary.

Drug Interactions

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

- **ATROPINE**: Atropine will antagonize the muscarinic effects of neostigmine and some clinicians routinely use the two together, but concurrent use should be used cautiously as atropine can mask the early clinical signs of cholinergic crisis
- **CORTICOSTEROIDS**: May decrease the anticholinesterase activity of neostigmine; after stopping corticosteroid therapy, neostigmine may cause increased anticholinesterase activity
- **DEXPANTHENOL**: Theoretically, dexpanthenol may have additive effects when used with neostigmine
- **MAGNESIUM**: Anticholinesterase therapy may be antagonized by administration of parenteral magnesium therapy, as it can have a direct depressant effect on skeletal muscle
- **MUSCLE RELAXANTS**: Neostigmine may prolong the Phase I block of depolarizing muscle relaxants (*e.g.*, **succinylcholine**, **decamethonium**) and edrophonium antagonizes the actions of non-depolarizing neuromuscular blocking agents (*e.g.*, **pancuronium, tubocurarine, gallamine, vecuronium, atracurium,** etc.)