### Contraindications/Precautions/Warnings
Because there is a risk of anaphylaxis occurring secondary to the horse serum, many recommend performing sensitivity testing before administration.

### Adverse Effects
The most significant adverse effect associated with the use of the equine origin product is anaphylaxis secondary to its equine serum source; an incidence rate of less than 2% has been reported. A 1:10 dilution of the antivenin given intracutaneously at a dose of 0.02–0.03 mL has been suggested as a test for hypersensitivity. Wheal formation and erythema indicate a positive reaction and are generally seen within 30 minutes of administration. However, a negative response does not insure that anaphylaxis will be avoided and slow intravenous administration is usually sufficient to identify animals that will react to the product. A pre-treatment dose of diphenhydramine is often recommended before administering antivenin primarily to sedate the patient and, theoretically, to reduce any possible allergic reactions to the antivenin. Should an anaphylactoid reaction be detected (nausea, pruritus, hyperemia of the inner pinna), stopping the infusion, giving an additional dose of diphenhydramine and restarting the infusion 5 minutes later at a slower rate may allow the dose to be administered without further problems.

### 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*).

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

**BETA-BLOCKERS:** May mask the early signs associated with anaphylaxis

### Doses
- **DOGS/CATS:**
  a) After reconstituting the antivenin, add to 100 mL of normal saline and administer via slow IV over 30 minutes. Pretreatment with 2–4 mg/kg of diphenhydramine SC may help calm the patient and may possibly protect against allergic reactions from the antivenin. Monitor inner pinna during infusion for signs of anaphylaxis (hyperemia). If hyperemia occurs, discontinue infusion and give a second dose of diphenhydramine. If allergic reactions abate, may restart infusion at a slower rate; if they recur, stop infusion and seek consultation. Use care with administration of IV fluids as envenomation can cause significant hypertension. Benzodiazepines may alleviate muscle cramping. (Peterson and McNalley 2006)
  b) Dissolve contents of one vial and add to 100–200 mL of warm 0.9% NaCl and infuse over 2–6 hours. Administer diphenhydramine at 0.5–1 mg/kg prior to infusion. (Atkins 2006a)

### Client Information
- Clients must be made aware of the potential for anaphylaxis as well as the expenses associated with treatment, monitoring and hospitalization.

### Monitoring
- Signs associated with an allergic response to the antivenin (anaphylaxis, anaphylactoid-reactions, serum sickness)
- Respiratory/cardiac rate
- Blood pressure
- Serum chemistry (blood glucose mandatory)
- CBC
- Urine output; urinalysis

### Chemistry
This product is concentrated serum globulins obtained from horses immunized with the venom of the black widow spider. It is provided as refined, lyophilized product with a suitable diluent.

### Storage/Stability/Compatibility
Product should be stored in the refrigerator (2–8°C). It is reconstituted by adding 2.5 mL of the diluent provided; shake the vial to completely dissolve the contents. Do not freeze the reconstituted solution. For IV use, further dilute the solution in 10–100 mL of normal saline injection.

### Dosage Forms/Regulatory Status
**VETERINARY-LABELED PRODUCTS:** None

**HUMAN-LABELED PRODUCTS:**

Antivenin (*Latrodectus mactans*) Powder for Injection: 6000 antivenin units/vial in vials with 1 vial diluent (2.5 mL vial of sterile water for injection) and 1 mL vial of normal horse serum (1:10 dilution) for sensitivity testing; *Antivenin (Lactrodectus mactans)*; (Merck) (Rx)

**Note:** It has been reported that veterinarians may have difficulty in obtaining this product directly from the manufacturer. Alternative sources include obtaining from a local hospital pharmacy or having a physician colleague obtain directly from the manufacturer for your practice.

## APOMORPHINE HCL

(a-poe-***mor***-feen) Apokyn®

EMETIC

### Prescriber Highlights
- Rapid acting, centrally-mediated emetic used in dogs & sometimes in cats
- Contraindicated in certain species (*e.g.*, rodents, rabbits) & when vomiting may be deleterious (*e.g.*, impending coma, aspiration)
- May cause protracted vomiting; naloxone should reverse CNS effects or cardio-respiratory depression, but not vomiting
- Availability & expense may be an issue

### Uses/Indications
Apomorphine is used primarily as an emetic in dogs, and is considered the emetic of choice for dogs by many clinicians. It is sometimes used in cats, but its use in this species is somewhat controversial.

### Pharmacology/Actions
Apomorphine stimulates dopamine receptors in the chemoreceptor trigger zone, thus inducing vomiting. It can cause both CNS

depression and stimulation, but tends to cause more stimulatory effects. Medullary centers can be depressed with resultant respiratory depression.

## Pharmacokinetics

Apomorphine is slowly absorbed after oral administration and has unpredictable efficacy when given by this route, therefore, it is usually administered parenterally or topically to the eye. When given intravenously in dogs, emesis occurs very rapidly; after IM use, vomiting occurs generally within 5 minutes but may be more prolonged. Topical administration to the conjunctival sac is usually effective but less so than either IV or IM administration.

Apomorphine is primarily conjugated in the liver and then excreted in the urine.

## Contraindications/Precautions/Warnings

Emetics can be an important aspect in the treatment of orally ingested toxins, but must not be used injudiciously. Emetics should not be used in rodents or rabbits, because they are either unable to vomit or do not have stomach walls strong enough to tolerate the act of emesis. Emetics are also contraindicated in patients that are: hypoxic, dyspneic, in shock, lack normal pharyngeal reflexes, seizuring, comatose, severely CNS depressed or where CNS function is deteriorating, or extremely physically weak. Emetics should also be withheld in patients who have previously vomited repeatedly. Because of the risk for additional esophageal or gastric injury with emesis, emetics are contraindicated in patients who have ingested strong acids, alkalis, or other caustic agents. Because of the risks of aspiration, emetics are usually contraindicated after petroleum distillate ingestion, but may be employed when the risks of toxicity of the compound are greater than the risks of aspiration. Use of emetics after ingestion of strychnine or other CNS stimulants may precipitate seizures.

Emetics generally do not remove more than 80% of the material in the stomach (usually 40–60%) and successful induction of emesis does not signal the end of appropriate monitoring or therapy. In addition to the contraindications outlined in the general statement, apomorphine should not be used in cases of oral opiate or other CNS depressant (*e.g.*, barbiturates) toxicity, or in patients hypersensitive to morphine.

The use of apomorphine in cats is controversial, and several clinicians state that it should not be used in this species as it is much less effective than either xylazine or ipecac syrup and possibly, less safe.

If vomiting does not occur within the expected time after apomorphine administration, repeated doses are unlikely to induce emesis and may cause clinical signs of toxicity.

## Adverse Effects

At usual doses, the principal adverse effect that may be seen with apomorphine is protracted vomiting. Protracted vomiting after ophthalmic administration may be averted by washing the conjunctival sac with sterile saline or ophthalmic rinsing solution. Excitement, restlessness, CNS depression or respiratory depression are usually only associated with overdoses of the drug. Anecdotal reports of corneal ulcers have been noted after conjunctival administration.

## Reproductive/Nursing Safety

The reproductive safety of this drug has not been established; weigh the risks of use versus the potential benefits.

## Overdosage/Acute Toxicity

Excessive doses of apomorphine may result in respiratory and/or cardiac depression, CNS stimulation (excitement, seizures) or depression and protracted vomiting. Naloxone may reverse the CNS and respiratory effects of the drug but cannot be expected to halt the vomiting. Atropine has been suggested to treat severe bradycardias.

## Drug Interactions

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

- **ANTIDOPAMINERGIC DRUGS** (*e.g.*, **phenothiazines**) may negate the emetic effects of apomorphine
- **OPIATES or OTHER CNS or RESPIRATORY DEPRESSANTS** (*e.g.*, **barbiturates**): Additive CNS, or respiratory depression may occur when apomorphine is used with these agents

## Doses

- **DOGS:**

  For induction of emesis:

  a) 0.03 mg/kg IV or 0.04 mg/kg IM (IV route preferred); alternatively a portion of tablet may be crushed in a syringe, dissolved with few drops of water and administered into the conjunctival sac. After sufficient vomiting occurs, rinse conjunctival sac free of unabsorbed apomorphine. (Beasley and Dorman 1990)

  b) 0.04 mg/kg IV or 0.08 mg/kg IM or SC (Bailey 1989), (Riviere 1985), (Mount 1989)

  c) 0.04 mg/kg IV, 0.07 mg/kg IM, or 0.25 mg/kg into the conjunctival sac (Jenkins 1988)

- **CATS:**

  **Note:** Use of apomorphine in cats is controversial and many recommend not using in this species.

  a) For induction of emesis: 0.04 mg/kg IV or 0.08 mg/kg IM or SC (Bailey 1989), (Reid and Oehme 1989)

## Monitoring

- CNS, respiratory, and cardiac systems should be monitored
- Vomitus should be quantified, examined for contents and saved for possible later analysis

## Client Information

- This agent must be used in a professionally supervised setting only

## Chemistry/Synonyms

A centrally-acting emetic, apomorphine occurs as a white powder or minute, white or grayish-white crystals and is sparingly soluble in water or alcohol.

Apomorphine HCl may also be known as: apomorphini hydrochloridum, *APO-go®*, *APO-go Pen®*, *Apofin®*, *Apokinon®*, *Apokyn®*, *Apomine®*, *Britaject®*, *Ixense®*, *Taluvian®*, or *Uprima®*.

## Storage/Stability/Compatibility

Apomorphine soluble tablets should be stored in tight containers at room temperature (15–30°C) and protected from light.

Upon exposure to light and air, apomorphine gradually darkens in color. Discolored tablets or discolored solutions (green to turquoise) should not be used. Apomorphine solutions are more stable in acidic than in alkaline solutions. A 0.3% solution of apomorphine has a pH of about 3–4.

Solutions of apomorphine can be made by solubilizing tablets in at least 1–2 mL of either sterile water for injection or 0.9% sodium chloride for injection. After being sterilized by filtration, the solution is stable for 2 days if protected from light and air and stored in the refrigerator. Do not use solutions that are discolored or form a precipitate after filtering.

### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:**

Pharmaceutical dosage forms of apomorphine have been occasionally difficult to obtain and compounding pharmacies may be required to obtain the drug. One commercially prepared product (6 mg tablets) that may be available is produced by JK Levi Co. Some veterinary distributors (*e.g.*, MWI) reportedly stock this product.

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

**HUMAN-LABELED PRODUCTS:**

Apomorphine HCl for Injection: 10 mg per mL in 2 mL amps and 3 mL cartridges; *Apokyn*® (Mylan Bertek); (Rx)

# APRAMYCIN SULFATE

(a-pra-***mye***-sin) Apralan®

AMINOGLYCOSIDE ANTIBIOTIC

## Prescriber Highlights

- Orally administered aminocyclitol antibiotic for porcine *E. coli* bacillosis in swine (sometimes used in calves—not approved)
- Products no longer available in USA
- May be partially absorbed in neonates; potentially nephro- & ototoxic if absorbed systemically

### Uses/Indications

Apramycin is no longer commercially available in the USA, but it is used in some countries for the treatment of bacterial enteritis, colibacillosis, salmonellosis, etc. in pigs, calves and poultry.

### Pharmacology/Actions

Apramycin is an aminoglycoside that is bactericidal against many gram-negative bacteria (*E. coli*, Pseudomonas, Salmonella, Klebsiella, Proteus, Pasturella, *Treponema hyodysenteriae*, *Bordetella bronchiseptica*), Staphylococcus and Mycoplasma. It prevents protein synthesis by susceptible bacteria, presumably by binding to the 30S ribosomal subunit.

### Pharmacokinetics

After oral administration, apramycin is partially absorbed, particularly in neonates. Absorption is dose related and decreases substantially with the age of the animal. Absorbed drug is eliminated via the kidneys unchanged.

### Contraindications/Precautions/Warnings

Do not use in known cases of apramycin hypersensitivity. The drug apparently has a wide margin of safety when used orally and is safe to use in breeding swine. Apramycin is contraindicated in cats and in patients with myasthenia gravis.

### Adverse Effects

When used as labeled, the manufacturer does not list any adverse reactions. Should substantial amounts of the drug be absorbed, both ototoxicity and nephrotoxicity are a distinct possibility.

### Drug Interactions/Laboratory Considerations

None were noted. May have similar interaction potential as neomycin; refer to that monograph for more information.

### Doses

**SWINE:**

For bacterial enteritis caused by susceptible organisms:

a) Treated pigs should consume enough water to receive 12.5 mg/kg body weight per day for 7 days. Add to drinking water at a rate of 375 mg per gallon. After adding to water, stir and allow to stand for 15 minutes, then stir again. (Label directions; *Apralan® Soluble Powder*—SKB)

b) 20–40 mg/kg PO daily in drinking water (Huber 1988a)

c) Pigs: To be administered via the drinking water. Add 1 small measure (4.4 mL) or 1 sachet of soluble powder per 20 L of drinking water. (Label information; *Apralan Soluble Powder®*—Elanco U.K.)

**CATTLE:**

a) For bacterial enteritis caused by susceptible organisms: 20–40 mg/kg PO daily in drinking water (Huber 1988a)

b) Calves: For the treatment of colibacillosis or salmonellosis: 1–2 sachets to be administered in the drinking water, milk, or milk replacer to provide 20–40 mg of apramycin activity per kg of bodyweight daily according to the severity of the disease. Continue treatment for 5 days. (Label information; *Apralan Soluble Powder®*—Elanco U.K.)

**POULTRY:**

a) For bacterial enteritis caused by susceptible organisms: To be administered via drinking water to provide 250–500 mg of apramycin activity per liter for 5 days. This may be achieved by adding 50 g apramycin per 100–200 liters of water. (Label information; *Apralan Soluble Powder®*—Elanco U.K.)

### Monitoring

- Clinical efficacy

### Chemistry/Synonyms

Apramycin is an aminocyclitol antibiotic produced from *Streptomyces tenebrarius*; it is soluble in water.

Apramycin may also be known as nebramycin factor 2, nebramcyin II, apramycine, apramicina, AIDS166733, *Apralan®* or *Abylan®*.

### Storage/Stability/Compatibility

Apramycin powder should be stored in a cool dry place, in tightly closed containers, protected from moisture. Store at temperatures less than 25°C. If exposed to rust, as in a rusty waterer, the drug can be inactivated. The manufacturer recommends preparing fresh water daily. Shelf life of the powder is 24 months.

### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:**

None at present in the USA. A swine product: Apramycin Sulfate Soluble Powder 37.5 & 48 g (base) bottle; *Apralan®* (Elanco); (OTC), was formerly marketed in the USA and is still available in several countries.

In the UK: Apramycin Soluble Powder: 1 gram sachets and 50 g (apramycin activity) in 220 mL; *Apralan Soluble Powder®* (Elanco); (POM-V). In the UK when used as labeled: Slaughter withdrawal: Pigs = 14 days, Calves = 28 days, Poultry = 7 days. Not for use in laying hens where eggs are for human consumption.

**HUMAN-LABELED PRODUCTS:** None

ASA — see Aspirin