Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

There are oral combination products marketed as "cough" syrups for veterinary use that contain phenylephrine, pyrilamine (antihistamine), guaifenesin, sodium citrate, and sometimes ammonium chloride.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Phenylephrine HCl Tablets: 10 mg (regular, chewable & orally disintegrating); *AH-chew D*® (WE Pharm); *Sudafed PE*® (Pfizer); *Sudogest PE*® (Major); *Nasop*® (Hawthorn); (OTC or Rx)

Phenylephrine HCl Oral Suspension/Liquid/Drops: 2.5 mg/mL, 7.5 mg/5 mL & 2 mg (as phenylephrine HCl)/mL; in 15 mL, 20 mL, 30 mL or 118 mL; *AH-chew D*® (WE Pharm); *Little Colds Decongestant for Infants & Children*® (Vetco); *Lusonal*® (WraSer); (OTC or Rx)

Phenylephrine HCl Strips: 10 mg; *Sudafed*® *PE Quick-dissolve* (Pfizer Consumer Healthcare); (OTC)

Phenylephrine HCl Injection: 1% (10 mg/mL) in 1 mL and 5 mL vials and 1 mL Uni-Nest amps; *Neo-Synephrine*® (Sanofi Winthrop); generic; (Rx)

Phenylephrine is also available in ophthalmic and intranasal dosage forms and in combination with antihistamines, analgesics, decongestants, etc., for oral administration in humans.

PHENYLPROPANOLAMINE HCL

(fen-ill-proe-pa-***nole***-a-meen) **PPA**

SYMPATHOMIMETIC

Prescriber Highlights

- **Sympathomimetic used primarily for urethral sphincter hypotonus**
- **Caution: Glaucoma, prostatic hypertrophy, hyperthyroidism, diabetes mellitus, cardiovascular disorders, or hypertension**
- **Adverse Effects: Restlessness, irritability, hypertension, & anorexia**

Uses/Indications

Phenylpropanolamine is used chiefly for the treatment of urethral sphincter hypotonus and resulting incontinence in dogs and cats. It has also been used in an attempt to treat nasal congestion in small animals.

Pharmacology/Actions

While the exact mechanisms of phenylpropanolamine's actions are undetermined, it is believed that it indirectly stimulates both alpha- and beta-adrenergic receptors by causing the release of norepinephrine. Prolonged use or excessive dosing frequency can deplete norepinephrine from its storage sites, and tachyphylaxis (decreased response) may ensue. Tachyphylaxis has not been documented in dogs or cats when used for urethral sphincter hypotonus, however.

Pharmacologic effects of phenylpropanolamine include increased vasoconstriction, heart rate, coronary blood flow, blood pressure, mild CNS stimulation, and decreased nasal congestion and appetite. Phenylpropanolamine can also increase urethral sphincter tone and produce closure of the bladder neck; its principle veterinary indications are because of these effects.

Pharmacokinetics

No information was located on the pharmacokinetics of this agent in veterinary species. In humans, phenylpropanolamine is readily absorbed after oral administration and has an onset of action (nasal decongestion) of about 15–30 minutes with duration of effect lasting approximately 3 hours (regular capsules or tablets).

Phenylpropanolamine is reportedly distributed into various tissues and fluids, including the CNS. It is unknown if it crosses the placenta or enters milk. The drug is partially metabolized to an active metabolite, but 80–90% is excreted unchanged in the urine within 24 hours of dosing. The serum half-life is approximately 3–4 hours.

Contraindications/Precautions/Warnings

Phenylpropanolamine should be used with caution in patients with glaucoma, prostatic hypertrophy, hyperthyroidism, diabetes mellitus, cardiovascular disorders, or hypertension.

Adverse Effects

Most likely side effects include restlessness, irritability, urine retention, tachycardia, and hypertension. Anorexia may be a problem in some animals. Rare reports of "stroke" have occurred in dogs given therapeutic dosages of phenylpropanolamine.

Reproductive/Nursing Safety

Phenylpropanolamine may cause decreased ovum implantation; uncontrolled clinical experience, however, has not demonstrated any untoward effects during pregnancy.

Overdosage/Acute Toxicity

Clinical signs of overdosage may consist of an exacerbation of the adverse effects listed above or, if a very large over-dose, severe cardiovascular (hypertension to rebound hypotension, bradycardias to tachycardias, and cardiovascular collapse) or CNS effects (stimulation to coma) can be seen.

There were 255 exposures to phenylpropanolamine reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 250 were dogs with 59 showing clinical signs. The remaining 5 cases were cats that showed no clinical signs. Common findings in dogs recorded in decreasing frequency included hypertension, piloerection, vomiting, bradycardia and mydriasis.

A dog ingesting 48 mg/kg of PPA has been reported (Crandell and Ware 2005). Ventricular tachycardia and regions of myocardial necrosis were noted. All abnormalities resolved within 6 months.

If the overdose was recent, empty the stomach using the usual precautions and administer charcoal and a cathartic. Treat clinical signs supportively as they occur. Do not use propranolol to treat hypertension in bradycardic patients and do not use atropine to treat bradycardia. Hypertension may be managed with a phenothiazine (*e.g.*, acepromazine—very low dose such as 0.02 mg/kg IV or IM). If phenothiazines do not normalize blood pressure, consider using a CRI of nitroprusside. Contact an animal poison control center for further guidance.

Drug Interactions

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

- **HALOTHANE**: An increased risk of arrhythmias developing can occur if phenylpropanolamine is administered to patients who have received cyclopropane or a halogenated hydrocarbon anesthetic agent. Propranolol may be administered should these occur.
- **MONAMINE OXIDASE (MAO) INHIBITORS** (*e.g.*, **amitraz**, possibly **selegiline**): Phenylpropanolamine should not be given within two weeks of a patient receiving monoamine oxidase inhibitors
- **NSAIDS**: An increased chance of hypertension if given concomitantly with NSAIDs, including aspirin
- **RESERPINE**: An increased chance of hypertension if given concomitantly
- **SYMPATHOMIMETIC AGENTS, OTHER**: Phenylpropanolamine should not be administered with other sympathomimetic agents (*e.g.*, ephedrine) as increased toxicity may result
- **TRICYCLIC ANTIDEPRESSANTS** (**clomipramine, amitriptyline,** etc.): An increased chance of hypertension if given concomitantly

Doses

- **DOGS:**

  For urethral sphincter hypotonus:
  a) 12.5–50 mg PO q8h (Labato 1988), (Polzin and Osborne 1985), (Bartges 2003a)
  b) Using the time-release 75 mg capsules: Dogs weighing less than 40 lbs: 1/2 capsule PO daily. Dogs 40–100 lbs: 1 capsule PO daily. Dogs weighing >100 lbs: 1.5 capsules PO per day. (Label information; *Cystolamine*® —VPL)
  c) 1–1.5 mg/kg PO two to three times a day controls 74–92% of dogs with primary sphincter mechanism incontinence. Over half of dogs not responding to regular PPA will respond to sustained-release PPA. Incontinence control becomes less over time in some dogs. (Chew 2007)
  d) 5–50 mg per dog PO q8h or 1.5 mg/kg PO q8h–12h (Vernau 2006)

  For retrograde ejaculation:
  a) 3–4 mg/kg PO twice daily may be tried. (Fontbonne 2007)

- **CATS:**

  For urethral sphincter hypotonus:
  a) 12.5 mg PO q8h (Labato 1988), (Polzin and Osborne 1985)
  b) 1.5 mg/kg PO q8h (Bartges 2003a)
  c) 1.1 –2.2 mg/kg PO two to three times daily (Lane 2003)

Monitoring

- Clinical effectiveness
- Adverse effects (see above)
- Blood pressure

Client Information

- In order for this drug to be effective, it must be administered as directed by the veterinarian; missed doses will negate its effect. It may take several days for the full benefit of the drug to take place.
- Contact veterinarian if the animal demonstrates ongoing changes in behavior (restlessness, irritability) or if incontinence persists or increases.

Chemistry/Synonyms

A sympathomimetic amine, phenylpropanolamine HCl occurs as a white crystalline powder with a slightly aromatic odor, a melting range between 191°–194°C, and a pK_a of 9.4. One gram is soluble in approximately 1.1 mL of water or 7 mL of alcohol.

Phenylpropanolamine may also be known as: (+/-)-norephedrine, dl-norephedrine or PPA, *Cystolamine*®, *Proin*®, *Propalin*®, *Uricon*®, and *Uriflex-PT*®.

Storage/Stability/Compatibility

Store phenylpropanolamine products at room temperature in light-resistant, tight containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Phenylpropanolamine Chewable Tablets: 25 mg, 50 mg, & 75 mg; *Proin*® (PRN Pharmacal), *Propalin*® (Vetoquinol), *Uriflex-PT*® (Butler), *Uricon*® (Neogen); (Rx). Labeled for use in dogs.

Phenylpropanolamine Timed-Release Capsules: 75 mg; *Cystolamine*® (VPL); (Rx). Labeled for use in dogs.

Phenylpropanolamine oral solution: 25 mg/mL in 60 mL bottles; *Proin*® *Drops* (PRN Pharmacal) (Rx); 50 mg/mL in 30 mL and 100 mL bottles; (Rx). Labeled for use in dogs.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

In the USA, phenylpropanolamine is classified as a list 1 chemical (drugs that can be used as precursors to manufacture methamphetamine) and in some states it may be a controlled substance or have other restrictions placed upon its sale. Be alert to persons desiring to purchase this medication.

HUMAN-LABELED PRODUCTS:

Note: Because of potential adverse effects in humans, phenylpropanolamine has been removed from the US market for human use.

PHENYTOIN SODIUM

(***fen***-i-toe-in) **Dilantin®**

ANTICONVULSANT, ANTIDYSRHYTHMIC

Prescriber Highlights

- **Rarely used (in USA) for seizures in small animals; sustained release formulations may be useful (not available in USA)**
- **Potentially useful as a treatment for ventricular dysrhythmias in horses or digoxin-induced arrhythmias in dogs or horses; may be useful in cats with myokemia and neuromyotonia**
- **Contraindications: Hypersensitivity; IV use contraindicated for 2nd or 3rd degree heart block, sinoatrial block, Adams-Stokes syndrome, or sinus bradycardia.**
- **Adverse Effects: DOGS: Anorexia & vomiting, ataxia, sedation, gingival hyperplasia, hepatotoxicity. CATS: Ataxia, sedation, anorexia, dermal atrophy syndrome, thrombocytopenia**
- **Potentially teratogenic; many drug interactions possible**