Drug Interactions

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

- **AMINOGLYCOSIDES:** Vancomycin may increase the risk of aminoglycoside-related ototoxicity or nephrotoxicity. Because this combination of drugs may be medically required (there is evidence of synergy against staphylococci and enterococci), only enhanced monitoring is suggested.
- **ANESTHETIC AGENTS:** In children, vancomycin used with anesthetic agents has caused erythema and a histamine-like flushing
- **NEPHROTOXIC DRUGS, OTHER** (*e.g.,* **amphotericin B, cisplatin**): Use with caution with other nephrotoxic drugs

Laboratory Considerations

- No specific concerns were noted

Doses

To prepare parenteral solution using vancomycin 500 mg or 1 g powder for injection: Reconstitute the 500 mg for injection vial by adding 10 mL of sterile water for injection. Add 20 mL to the 1 gm vial. Before administering to patient, further dilute reconstituted solutions with (at least 100 mL for 500 mg; 200 mL for 1 gram vial) a compatible diluent (*e.g.*, D_5W, lactated Ringer's, 0.9% NaCl).

- **DOGS:**

  For susceptible infections:

  a) For confirmed bacteremia/septicemia for enterococci or staphylococci resistant to other commonly used antibiotics: 15 mg/kg IV over 30–60 minutes q6–8h. (Ford 2005)

  b) 15 mg/kg IV over 30–60 minutes q6h. For successful therapy of serious infections, an aminoglycoside such as gentamicin or amikacin should also be administered. (Papich 2003b)

  c) For oral use to treat *C. difficile* enterocolitis: 10–20 mg/kg PO q6h for 5–7 days;

  For IV use to treat skin, urinary, soft tissue infections: 10–20 mg/kg IV q12h for 7–10 days;

  For IV use to treat systemic infections, bacteremia: 15 mg/kg IV q6h for 10 days. (Greene, Hartmannn et al. 2006)

- **CATS:**

  For susceptible infections:

  a) For confirmed bacteremia/septicemia for enterococci or staphylococci resistant to other commonly used antibiotics: 15 mg/kg IV over 30–60 minutes q6–8h. (Ford 2005)

  b) 15 mg/kg IV over 30–60 minutes q6h. For successful therapy of serious infections, an aminoglycoside such as gentamicin or amikacin should also be administered. (Papich 2003b)

Monitoring

When used parenterally:

- Renal function, baseline and periodic
- Vancomycin levels, maintain trough level above 5 mcg/mL (some say troughs between 10–15 mcg/mL)
- Periodic CBC if therapy is prolonged

Client Information

- Parenteral vancomycin is used in an inpatient setting
- Oral vancomycin may be used for outpatient therapy; clients should be counseled to give as prescribed
- May give oral dosage forms with a small amount of food

Chemistry/Synonyms

A glycopeptide antibiotic, vancomycin HCl occurs as an odorless, tan to brown free-flowing powder. It is freely soluble in water. A 5% aqueous solution has a pH of 2.5–4.5.

Vancomycin may also be known as: vanco, vancomycini, or *Vancocin*®; there are many registered international trade names available.

Storage/Stability/Compatibility

Vancomycin should be stored at room temperature in tight containers that are protected from light. Once reconstituted (see directions in package insert or in the Doses section), the injectable or oral solutions are stable for 14 days if refrigerated. If diluted further with D_5W or sodium chloride 0.9% for parenteral administration, solutions are stable for 24 hours at room temperature and 2 months if refrigerated.

Vancomycin is **compatible** with D_5W, 0.9% NaCl, and lactated Ringer's injection.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Vancomycin HCl Capsules: 125 mg & 250 mg; *Vancocin*® (ViroPharma); (Rx)

Vancomycin HCl Powder for Oral Solution: 1 gram bottles; generic (ESI Lederle); (Rx)

Vancomycin HCl Powder for Injection: 500 mg, 1, 5, & 10 g; *Vancocin*® (ViroPharma); *Vancoled*® (Lederle); generic (various); (Rx)

VASOPRESSIN

(vay-soe-***press***-in) Pitressin®

HORMONE

Prescriber Highlights

- Hormone used primarily as a diagnostic agent & sometimes for treatment of diabetes insipidus; it may be useful for the adjunctive treatment of shock syndromes
- Contraindications: Chronic nephritis until nitrogen retention is resolved to reasonable levels, or patients hypersensitive to it; Caution: Vascular disease, seizure disorders, heart failure, or asthma
- Adverse Effects: Local irritation at the injection site (including sterile abscesses), skin reactions, abdominal pain, hematuria, &, rarely, a hypersensitivity (urticarial) reaction
- Overdosage can lead to water intoxication

Uses/Indications

Vasopressin is used in veterinary medicine as a diagnostic agent and in the treatment of diabetes insipidus in small animals. In recent years, there has been significant interest in using vasopressin for treating shock syndromes in humans and animals. Ongoing research is being conducted.

In human medicine, vasopressin has been used to treat acute GI hemorrhage and to stimulate GI peristalsis. Vasopressin CRI is also being used for treatment of hypotensive septic patients unresponsive to conventional vasopressor. Prior to radiographic procedures, it has been used to dispel interfering gas shadows or help concentrate contrast media.

Pharmacology

Vasopressin or antidiuretic hormone (ADH) promotes the renal reabsorption of solute-free water in the distal convoluted tubules and collecting duct. ADH increases cyclic adenosine monophosphate (cAMP) at the tubule which increases water permeability at the luminal surface resulting in increased urine osmolality and decreased urine flow. Without vasopressin, urine flow can be increased up to 90% greater than normal.

At doses above those necessary for antidiuretic activity, vasopressin can cause smooth muscle contraction. Capillaries and small arterioles are most affected, with resultant decreased blood flow to several systems. Hepatic flow may actually be increased, however.

Vasopressin can cause contraction of smooth muscle of the bladder and gall bladder and increase intestinal peristalsis, particularly of the colon. Vasopressin may decrease gastric secretions and increase GI sphincter pressure; gastric acid concentration remains unchanged.

Vasopressin possesses minimal oxytocic effects, but at large doses may stimulate uterine contraction. Vasopressin also causes the release of corticotropin, growth hormone, and follicle-stimulating hormone (FSH).

Pharmacokinetics

Vasopressin is destroyed in the GI prior to being absorbed and therefore must be administered either intranasally or parenterally. After IM or SC administration in dogs, aqueous vasopressin has antidiuretic activity for 2–8 hours.

Vasopressin is distributed throughout the extracellular fluid. The hormone apparently is not bound to plasma proteins.

Vasopressin is rapidly destroyed in the liver and kidneys. The plasma half-life has been reported to be only 10–20 minutes in humans.

Contraindications/Precautions/Warnings

In humans, vasopressin is contraindicated in patients hypersensitive to it or with chronic nephritis until nitrogen retention is resolved to reasonable levels.

Because of its effects on other systems, particularly at high doses, vasopressin should be used with caution in patients with vascular disease, seizure disorders, heart failure, or asthma.

Adverse Effects

Adverse effects that can be seen include local irritation at the injection site (including sterile abscesses), skin reactions, abdominal pain, hematuria, and, rarely, a hypersensitivity (urticarial) reaction. Overdosage can lead to water intoxication (see below).

Reproductive/Nursing Safety

Although the drug has minimal effects on uterine contractions at usual doses, it should be used with caution in pregnant animals. 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.*)

Overdosage/Acute Toxicity

Early clinical signs of overdose-induced water intoxication can include listlessness or depression. More severe intoxication clinical signs can include coma, seizures, and eventually death. Treatment for mild intoxication is stopping vasopressin therapy and restricting water access until resolved. Severe intoxication may require the use of osmotic diuretics (mannitol, urea, or dextrose) with or without furosemide.

Drug Interactions

The following drugs may **inhibit** the antidiuretic activity of vasopressin:

- **ALCOHOL**
- **DEMECLOCYCLINE**
- **EPINEPHRINE** (**large doses**)
- **HEPARIN**
- **NOREPINEPHRINE** (**large doses**)

The following drugs may **potentiate** the antidiuretic effects of vasopressin:

- **ANTIDEPRESSANTS, TRICYCLIC**
- **CARBAMAZEPINE**
- **CHLORPROPAMIDE**
- **CLOFIBRATE**
- **FLUDROCORTISONE**
- **PHENFORMIN**
- **UREA**

Doses

- **DOGS:**

  As a diagnostic agent after the water deprivation test (WDT); monitor carefully. The WDT is considered contraindicated in animals that are dehydrated or have known renal disease and is used to characterize whether DI is central or nephrogenic in origin. Refer to a current small animal internal medicine text for further information.

  a) Exogenous vasopressin test: After WDT, empty bladder and start IV catheter and slowly reintroduce water. Give aqueous vasopressin in D_5W IV at a dose of 2.5 mU/kg over one hour. To make one liter of a 5 mU/mL solution add 5 Units of vasopressin to one liter of D_5W. Empty bladder and collect urine at 30 minutes, 60 minutes, and 90 minutes. If urine specific gravity >1.1015 = ADH-responsive DI; if <1.015 = either nephrogenic DI or medullary washout effect. (Nichols and Miller 1988)

  For adjunctive treatment of shock:

  a) Dogs with persistent hypotension after optimal fluid therapy; Vasopressin (1–4 microUnits/kg/minute) and/or norepinephrine (0.1–2 mcg/kg/minute). Goal of pressor therapy is to maintain mean arterial blood pressure between 70–90 mmHg. (Hansen 2007a)

  For treatment of central diabetes insipidus: **Note**: Because vasopressin tannate in oil is no longer commercially available; most clinicians are using desmopressin (DDAVP) for treating central DI. Refer to that monograph for more information.

- **CATS:**

  As a diagnostic agent after the water deprivation test (WDT): The WDT is generally considered contraindicated in animals that are dehydrated or have known renal disease and is used to characterize whether DI is central or nephrogenic in origin.

  a) Immediately after the end-point of the WDT, give aqueous vasopressin 0.5 U/kg IM; continue to withhold food and water. At 30, 60, and 120 minutes after vasopressin, empty bladder and determine specific gravity (osmolality). Upon completion, the cat is gradually allowed access to water. Inability to concentrate urine during the water deprivation test followed by a rise in urine specific gravity above 1.025 after vasopressin is indicative of central DI. (Peterson and Randolph 1989)

  For treatment of central diabetes insipidus: **Note**: Because vasopressin tannate in oil is no longer commercially available; most

clinicians are using desmopressin (DDAVP) for treating central DI. Refer to that monograph for more information.

Monitoring
- Urine output/frequency
- Water consumption
- Urine specific gravity &/or osmolality

Chemistry/Synonyms
A hypothalamic hormone stored in the posterior pituitary, vasopressin is a 9-amino acid polypeptide with a disulfide bond. In most mammals (including dogs and humans), the natural hormone is arginine vasopressin, while in swine the arginine is replaced with lysine. Lysine vasopressin has only about 1/2 the antidiuretic activity of arginine vasopressin. The commercially available vasopressin products may be a combination of arginine or lysine vasopressin derived from natural sources or synthetically prepared. The products are standardized by their pressor activity in rats [USP posterior Pituitary (pressor) Units]; their antidiuretic activity can be variable. Commercially available vasopressin has little, if any, oxytocic activity at usual doses.

Vasopressin injection occurs as a clear, colorless or practically colorless liquid with a faint, characteristic odor. Vasopressin is soluble in water.

Vasopressin may also be known as: ADH, antidiuretic hormone, 8-arginine vasopressin, beta-hypophamine, *Neo-Lidocaton®*, *Pitressin®* or *Pressyn®*.

Storage/Stability/Compatibility
Vasopressin (aqueous) injection should be stored at room temperature; avoid freezing.

If the aqueous injection is to be administered as an intravenous or intra-arterial infusion, it may be diluted in either D_5W or normal saline. For infusion use in humans, it is usually diluted to a concentration of 0.1 – 1 Unit/mL.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Vasopressin Injection: 20 pressor Units/mL in 0.5 mL, 1 mL and 10 mL vials; and 1 mL ampules; *Pitressin®* (Monarch); generic; (Rx)

Vasopressin Tannate Sterile Suspension in oil is no longer commercially available.

VECURONIUM BROMIDE

(vek-yew-***roe***-nee-um) Norcuron®

NONDEPOLARIZING NEUROMUSCULAR BLOCKER

Prescriber Highlights
- Nondepolarizing neuromuscular blocking agent
- Contraindications: Hypersensitive to it. Caution: Severe renal dysfunction, hepatic, or biliary disease; extreme caution: myasthenia gravis
- Adverse Effects: None, other than pharmacologic actions
- No analgesia or anesthetic effects

Uses/Indications
Vecuronium is indicated as an adjunct to general anesthesia to produce muscle relaxation during surgical procedures or mechanical ventilation and to facilitate endotracheal intubation. It causes very minimal cardiac effects and generally does not cause the release of histamine.

Pharmacology/Actions
Vecuronium is a nondepolarizing neuromuscular blocking agent and acts by competitively binding at cholinergic receptor sites at the motor endplate, thereby inhibiting the effects of acetylcholine. The potency of vecuronium when compared to pancuronium (on a weight basis) has been described as being equipotent to up to 3 times as potent.

Pharmacokinetics
The onset of neuromuscular blockade after IV injection is dependent upon the dose administered. In dogs administered 0.1 mg/kg IV, full neuromuscular block occurs within 2 minutes and the duration of action at this dose is approximately 25 minutes (also receiving halothane anesthesia). Vecuronium has a shorter duration of action than pancuronium (approx. 1/3 – 1/2 as long), but is very similar to that of atracurium.

Vecuronium is partially metabolized; it and its metabolites are excreted into the bile and urine. Prolonged recovery times may result in patients with significant renal or hepatic disease.

Contraindications/Precautions/Warnings
Vecuronium is contraindicated in patients hypersensitive to it. It should be used with caution in patients with severe renal dysfunction. Lower doses may be necessary in patients with hepatic or biliary disease. Vecuronium has no analgesic or sedative/anesthetic actions. In patients with myasthenia gravis, neuromuscular blocking agents should be used with extreme caution, if at all. One case of successful use in a dog with myasthenia gravis has been reported.

Adverse Effects
In human studies and one limited dog study, adverse effects other than what would be seen pharmacologically (skeletal muscle weakness to profound, prolonged musculoskeletal paralysis) have not been reported.

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.*)

Overdosage/Acute Toxicity
No cases of vecuronium overdosage have yet been reported (human or veterinary). Should an inadvertent overdose occur, treat conservatively (mechanical ventilation, O_2, fluids, etc.). Reversal of blockade might be accomplished by administering an anticholinesterase agent (edrophonium, physostigmine, or neostigmine) with an anticholinergic (atropine or glycopyrrolate). A suggested dose for neostigmine is 0.06 mg/kg IV after atropine 0.02 mg/kg IV.