has not been established in preruminating calves. Do not use in calves to be used for veal.

HUMAN-LABELED PRODUCTS: None

DOXAPRAM HCL

(***docks***-a-pram) Dopram-V®

CNS/RESPIRATORY STIMULANT

Prescriber Highlights

- CNS stimulant usually used to stimulate respirations in newborns or after anesthesia; also used for assessment of laryngeal function in small animals
- Not a substitute for aggressive artificial (mechanical) respiratory support when required
- Possible contraindications: Receiving mechanical ventilation, hypersensitivity, seizure disorders, head trauma/CVA, uncompensated heart failure, severe hypertension, respiratory failure secondary to neuromuscular disorders, airway obstruction, pulmonary embolism, pneumothorax, acute asthma, dyspnea, or whenever hypoxia is not associated with hypercapnia.
- Caution: History of asthma, arrhythmias, or tachycardias. Use extreme caution in patients with cerebral edema or increased CSF pressure, pheochromocytoma, or hyperthyroidism.
- Avoid IV extravasation or using a single injection site for a prolonged period
- Adverse Effects: Hypertension, arrhythmias, seizures, & hyperventilation leading to respiratory alkalosis

Uses/Indications

The manufacturer of *Dopram®-V* lists the following indications: For Dogs, Cats, and Horses: To stimulate respiration during and after general anesthesia and/or to speed awakening and reflexes after anesthesia. For Neonatal Dogs and Cats: stimulate respirations following dystocia or cesarean section.

Doxapram has been used for treatment of CNS depression in food animals (not approved) and has been suggested as a treatment of respiratory depression in small animals caused by reactions to radiopaque contrast media or for barbiturate overdosage (see precautions below).

The use of doxapram to initiate and stimulate respirations in newborns is somewhat controversial as the drug has been shown in experimental animals to increase myocardial oxygen demand and reduce cerebral blood flow.

Doxapram has been shown to be useful to offset suppression of general anesthetic agents when laryngeal function is being assessed.

Pharmacology/Actions

Doxapram is a general CNS stimulant, with all levels of the CNS affected. The effects of respiratory stimulation are a result of direct stimulation of the medullary respiratory centers and, possibly, through the reflex activation of carotid and aortic chemoreceptors. Transient increases in respiratory rate and volume occur, but increases in arterial oxygenation usually do not ensue. This is because doxapram usually increases the work associated with respirations with resultant increased oxygen consumption and carbon dioxide production.

Pharmacokinetics

Little published pharmacokinetic data appears for domestic animals. Onset of effect in humans and animals after IV injection usually occurs within 2 minutes. The drug is well distributed into tissues. In dogs, doxapram is rapidly metabolized and most is excreted as metabolites in the urine within 24–48 hours after administration. Small quantities of metabolites may be excreted up to 120 hours after dosing.

Contraindications/Precautions/Warnings

Doxapram should not be used as a substitute for aggressive artificial (mechanical) respiratory support in instances of severe respiratory depression.

Contraindications from the human literature include: seizure disorders, head trauma, uncompensated heart failure, severe hypertension, cardiovascular accidents, respiratory failure secondary to neuromuscular disorders, airway obstruction, pulmonary embolism, pneumothorax, acute asthma, dyspnea, or whenever hypoxia is not associated with hypercapnia. Doxapram should be used with caution in patients with a history of asthma, arrhythmias, or tachycardias. It should be used with extreme caution in patients with cerebral edema or increased CSF pressure, pheochromocytoma or hyperthyroidism. Patients with a history of hypersensitivity to the drug or are receiving mechanical ventilation should not receive doxapram. The above contraindications/precautions are not listed in the veterinary product literature provided by the manufacturer.

Avoid the use of a single injection site for a prolonged period of time or extravasation when administering intravenously. Subcutaneous injection has been recommended however for use in neonatal feline and canine patients.

Repeated IV doses in neonates should be done with caution as the product contains benzyl alcohol.

Adverse Effects

Hypertension, arrhythmias, seizures, and hyperventilation leading to respiratory alkalosis has been reported. These effects appear most probable with repeated or high doses. The drug reportedly has a narrow margin of safety when used in humans.

Doxapram has been shown in experimental animals to increase myocardial oxygen demand and reduce cerebral blood flow.

Reproductive/Nursing Safety

Safety of doxapram has not been established in pregnant animals. The potential risks versus benefits should be weighed before using. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

It is not known whether this drug is excreted in milk.

Overdosage/Acute Toxicity

Reported LD_{50} for IV administration in neonatal dogs and cats is approximately 75 mg/kg. Clinical signs of overdosage include: respiratory alkalosis, hypertension, skeletal muscle hyperactivity, tachycardia, and generalized CNS excitation including seizures. Treatment is supportive. Drugs such as short acting IV barbiturates may be used to help decrease CNS hyperactivity. Oxygen therapy may be necessary.

Drug Interactions

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

- **ANESTHETICS, GENERAL**: Doxapram may increase epinephrine release; therefore, use should be delayed for approximately 10 minutes after discontinuation of anesthetic agents (*e.g.*, **halothane**, **enflurane**) that have been demonstrated to sensitize the myocardium to catecholamines
- **MUSCLE RELAXANTS**: Doxapram may mask the effects of muscle relaxant drugs
- **SYMPATHOMIMETIC AGENTS**: Additive pressor effects may occur with sympathomimetic agents

Doses

- **DOGS:**
  a) 1.1 mg/kg (for gas anesthesia) or 5.5–11 mg/kg (for barbiturate anesthesia) IV; adjust dosage for depth of anesthesia, respiratory volume and rate. Dosage may be repeated in 15–20 minutes if necessary.

     To initiate or stimulate respirations in neonates after caesarian section or dystocia: May be administered either SC, sublingually, or via the umbilical vein in doses of 1–5 drops (1–5 mg) depending on size of neonate and degree of respiratory crisis. (Package Insert; *Dopram®-V*—Fort Dodge)
  b) To assess laryngeal function: 2.2 mg/kg IV to stimulate respiration and increase intrinsic laryngeal motion. Onset of effect occurs within 15–30 seconds and persists for approximately 2 minutes. Anesthetic depth may lighten substantially. Prepare for immediate intubation should airway obstruction or laryngeal paralysis occur. (McKiernan 2007)
- **CATS:**
  a) 1.1 mg/kg (for gas anesthesia) or 5.5–11 mg/kg (for barbiturate anesthesia) IV; adjust dosage for depth of anesthesia, respiratory volume and rate. Dosage may be repeated in 15–20 minutes if necessary.

     To initiate or stimulate respirations in neonates after caesarian section or dystocia: May be administered either SC, or sublingually in doses of 1–2 drops (1–2 mg) depending on severity of respiratory crisis. (Package Insert; *Dopram®-V*—Fort Dodge)
  b) Cats: 5–10 mg/kg IV (Boothe 1990)
- **RABBITS/RODENTS/SMALL MAMMALS:**

  For respiratory depression:
  a) Rabbits: 2–5 mg/kg SC or IV q15 minute
  b) Rodents: 2–5 mg/kg S C q15 minutes (Huerkamp 1995)
  c) Mice, Rats, Gerbils, Hamsters: 5–10 mg/kg IV; Guinea pigs: 5 mg/kg IV; Chinchillas: 2–5 mg/kg IV (Adamcak and Otten 2000)
- **BIRDS:**
  a) For respiratory depression: 5–10 mg/kg IM or IV (Harris 2003)
- **REPTILES:**
  a) To stimulate respiration after general anesthesia: 5 mg/kg IV (Wilson 2002b)
- **CATTLE & SWINE:**
  a) For primary apnea in newborn calves: 2 mg/kg IV (Constable 2006)
  b) 5–10 mg/kg IV (Howard 1986)
- **HORSES:** (**Note:** ARCI UCGFS Class 2 Drug)
  a) 0.44 mg/kg (for halothane, methoxyflurane anesthesia) or 0.55 mg/kg (for chloral hydrate ± magnesium sulfate anesthesia) IV; adjust dosage for depth of anesthesia, respiratory volume and rate. Dosage may be repeated in 15–20 minutes if necessary. (Package Insert; *Dopram®-V*—Fort Dodge)
  b) 0.5–1 mg/kg IV at 5 minute intervals (do not exceed 2 mg/kg in foals); for foal resuscitation: 0.02–0.05 mg/kg/min IV (Robinson 1987). **Note:** Rarely recommended today.

Monitoring

- Respiratory rate
- Cardiac rate and rhythm
- Blood gases if available and indicated
- CNS level of excitation; reflexes
- Blood pressure if indicated

Client Information

- This agent should be used in an inpatient setting or with direct professional supervision.

Chemistry/Synonyms

Doxapram HCl is a white to off-white, odorless, crystalline powder that is stable in light and air. It is soluble in water, sparingly soluble in alcohol and practically insoluble in ether. Injectable products have a pH from 3.5–5. Benzyl alcohol or chlorobutanol is added as a preservative agent in the commercially available injections.

Doxapram HCl may also be known as: AHR-619, doxaprami hydrochloridum, *Docatone®*, *Dopram ®*, *Doxapril®*, or *Respiram®*.

Storage/Stability/Compatibility

Store at room temperature and avoid freezing solution. Do not mix with alkaline solutions (*e.g.*, thiopental, aminophylline, sodium bicarbonate). Doxapram is physically **compatible** with D_5W or normal saline.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Doxapram HCl for Injection: 20 mg/mL; 20 mL multi-dose vial; *Dopram-V®* (Fort Dodge); *Respiram®* (MVT); (Rx). Approved for use in dogs, cats and horses.

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Doxapram HCl for Injection: 20 mg/mL in 20 mL multi-dose vials; *Dopram®* (Baxter Healthcare Corp); generic; (Bedford); (Rx)