

Inhalation anesthetic for use in horses and dogs

Isoflurane

Isoflurane inhalation anesthetic is used for induction and maintenance of general anesthesia in horses and dogs.

- Rapid induction and recovery from anesthesia
- Nonflammable and nonexplosive
- Available in 250 mL bottles



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WARNING:

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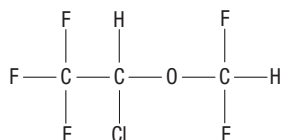
Isoflurane

Inhalation Anesthetic**For Use in Horses and Dogs****CAUTION:**

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

Isoflurane is a nonflammable, nonexplosive general inhalation anesthetic agent. Its chemical name is 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether, and its structural formula is:



Each mL contains 99.9% isoflurane.

Some physical constants are:

Molecular weight	184.5
Boiling point at 760 mm Hg	48.5°C (uncorr).
Refractive index n_D^{20}	1.2990-1.3005
Specific gravity 25°/25°C	1.496
Vapor pressure in mm Hg**	20°C 238
	25°C 295
	30°C 367
	35°C 450

**Equation for vapor pressure calculation:

$$\log_{10} P_{\text{vap}} = A + \frac{B}{T} \text{ where: } A = 8.056 \\
 \text{and } B = -1664.58 \\
 T = ^\circ\text{C} + 273.16 \text{ (Kelvin)}$$

Partition coefficients at 37°C:

Water/gas	0.61
Blood/gas	1.43
Oil/gas	90.8

Partition coefficients at 25°C – rubber and plastic:

Conductive rubber/gas	62.0
Butyl rubber/gas	75.0
Polyvinyl chloride/gas	110.0
Polyethylene/gas	~ 2.0
Polyurethane/gas	~ 1.4
Polyolefin/gas	~ 1.1
Butyl acetate/gas	~ 2.5
Purity by gas chromatography	>99.9%

Lower limit of flammability in oxygen or nitrous oxide at 9 joules/sec. and 23°C None

Lower limit of flammability in oxygen or nitrous oxide at 900 joules/sec. and 23°C Greater than useful concentration in anesthesia

MAC (Minimum Alveolar Concentration) is 1.31% in horses¹ and 1.28% in dogs.⁶

Isoflurane is a clear, colorless, stable liquid containing no additives or chemical stabilizers. Isoflurane has a mildly pungent, musty, ethereal odor. Samples stored in indirect sunlight in clear, colorless glass for five years, as well as samples directly exposed for 30 hours to a 2 amp, 115 volt, 60 cycle long wave U.V. light were unchanged in composition as determined by gas chromatography. Isoflurane in one normal sodium methoxide-methanol solution, a strong base, for over six months consumed essentially no alkali, indicative of strong base stability. Isoflurane does not decompose in the presence of soda lime (at normal operating temperatures), and does not attack aluminum, tin, brass, iron or copper.

CLINICAL PHARMACOLOGY

Isoflurane is an inhalation anesthetic. Induction and recovery from anesthesia with isoflurane are rapid.^{2,5} The level of anesthesia may be changed rapidly with isoflurane. Isoflurane is a profound respiratory depressant. RESPIRATION MUST BE MONITORED CLOSELY IN THE HORSE AND DOG AND SUPPORTED WHEN NECESSARY. As anesthetic dose is increased, both tidal volume and respiratory rate decrease.^{3,6} This depression is partially reversed by surgical stimulation, even at deeper levels of anesthesia.

Blood pressure decreases with induction of anesthesia but returns toward normal with surgical stimulation. Progressive increases in depth of anesthesia produce corresponding decreases in blood pressure; however, heart rhythm is stable and cardiac output is maintained with controlled ventilation and normal PaCO₂ despite increasing depth of anesthesia. The hypercapnia which attends spontaneous ventilation during isoflurane anesthesia increases heart rate and raises cardiac output above levels observed with controlled ventilation.³ Isoflurane does not sensitize the myocardium to exogenously administered epinephrine in the dog.

Muscle relaxation may be adequate for intra-abdominal operations at normal levels of anesthesia. However, if muscle relaxants are used to achieve greater relaxation, it should be noted that: ALL COMMONLY USED MUSCLE RELAXANTS ARE MARKEDLY POTENTIATED WITH ISOFLURANE, THE EFFECT BEING MOST PROFOUND WITH THE NONDEPOLARIZING TYPE. Neostigmine reverses the effect of nondepolarizing muscle relaxants in the presence of isoflurane but does not reverse the direct neuromuscular depression of isoflurane.

INDICATIONS

Isoflurane is used for induction and maintenance of general anesthesia in horses and dogs.

CONTRAINDICATIONS

Isoflurane is contraindicated in horses and dogs with known sensitivity to isoflurane or to other halogenated agents.

WARNINGS

Increasing depth of anesthesia with Isoflurane may increase hypotension and respiratory depression. The electroencephalographic pattern associated with deep anesthesia is characterized by burst suppression, spiking, and isoelectric periods⁴.

Since levels of anesthesia may be altered easily and rapidly, only vaporizers producing predictable percentage concentrations of isoflurane should be used (see **DOSE AND ADMINISTRATION**).

The action of nondepolarizing relaxants is augmented by isoflurane. Less than the usual amounts of these drugs should be used. If the usual amounts of nondepolarizing relaxants are given, the time for recovery from myoneural blockade will be longer in the presence of isoflurane than in the presence of other commonly used anesthetics.

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PRECAUTIONS

Isoflurane, like some other inhalational anesthetics, can react with desiccated carbon dioxide (CO₂) absorbents to produce carbon monoxide which may result in elevated carboxyhemoglobin levels in some patients. Case reports suggest that barium hydroxide lime and soda lime become desiccated when fresh gases are passed through the CO₂ absorber canister at high flow rates over many hours or days. When a clinician suspects that CO₂ absorbent may be desiccated, it should be replaced before the administration of isoflurane.

Usage in Pregnancy: Reproduction studies have been performed in mice and rats with no evidence of fetal malformation attributable to isoflurane. Adequate data concerning the safe use of isoflurane in pregnant and breeding horses and dogs have not been obtained.

ADVERSE REACTIONS

Hypotension, respiratory depression and arrhythmias have been reported.

OVERDOSAGE

In the event of overdose, or what may appear to be overdose, the following action should be taken:

Stop drug administration, establish that the airway is clear and initiate assisted or controlled ventilation with pure oxygen as circumstances dictate.

DOSE AND ADMINISTRATION

Caution: Operating rooms and animal recovery areas should be provided with adequate ventilation to prevent accumulation of anesthetic vapors.

Premedication: A premedication regimen, which may be employed depending upon the patient status, to avert excitement during induction, might include an anticholinergic, a tranquilizer, a muscle relaxant, and a short-acting barbiturate.

Inspired Concentration: The delivered concentration of Isoflurane should be known. Isoflurane may be vaporized using a flow-through vaporizer specifically calibrated for isoflurane. Vaporizers delivering a saturated vapor which then is diluted (e.g., Vernitrol® vaporizer) also may be used. The delivered concentration from such a vaporizer may

be calculated using the formula:

$$\% \text{ isoflurane} = \frac{100P_v F_v}{F_T(P_A - P_v)}$$

Where: P_A = Pressure of atmosphere
 P_v = Vapor pressure of isoflurane
 F_v = Flow of gas through vaporizer (mL/min)
 F_T = Total gas flow used (mL/min)

Isoflurane contains no stabilizer. Nothing in the drug product alters calibration or operation of these vaporizers.

Induction

Horses: Inspired concentrations of 3.0 to 5.0% isoflurane alone with oxygen following a barbiturate anesthetic induction are usually employed to induce surgical anesthesia in the horse.

Dogs: Inspired concentrations of 2.0 to 2.5% isoflurane alone with oxygen following a barbiturate anesthetic induction are usually employed to induce surgical anesthesia in the dog.

These concentrations can be expected to produce surgical anesthesia in 5 to 10 minutes.

Maintenance: The concentration of vapor necessary to maintain anesthesia is much less than that required to induce it.

Horses: Surgical levels of anesthesia in the horse may be sustained with a 1.5 to 1.8% concentration of isoflurane in oxygen.

Dogs: Surgical levels of anesthesia in the dog may be sustained with a 1.5 to 1.8% concentration of isoflurane in oxygen.

The level of blood pressure during maintenance is an inverse function of isoflurane concentration in the absence of other complicating problems. Excessive decreases, unless related to hypovolemia, may be due to depth of anesthesia and in such instances may be corrected by lightening the level of anesthesia.

Recovery from isoflurane anesthesia is typically uneventful.²

HOW SUPPLIED

Isoflurane is supplied in 250 mL amber-colored bottles.

250 mL bottle package of one

Storage: Store at room temperature 25°C (77° F).

Contact Information:

For inquiries or to report suspected adverse drug experiences, please contact Parnell at 1-800-887-2763 or visit www.parnell.com. For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae

To obtain a Safety Data Sheet(s), contact Parnell at 1-800-887-2763 or www.parnell.com.

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