

ISOFLURANE - isoflurane liquid
ASPEN VETERINARY RESOURCES LTD

Isoflurane, USP INHALATION ANESTHETIC , Vet [Piveta]

SPL UNCLASSIFIED SECTION

ISOFLURANE, USP
INHALATION ANESTHETIC

Nonflammable, nonexplosive.

For Veterinary Use in Horses and Dogs.

WARNING

Not for use in horses intended for food.

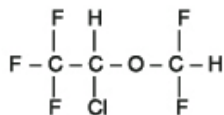
Caution

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

Operating rooms should be provided with adequate ventilation to prevent the accumulation of anesthetic vapors.

DESCRIPTION

Isoflurane, USP 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 to 1.3005D
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:

$\log_{10} P_{\text{vap}} = A + B/T$ where: $A = 8.056$

$$B = -1664.58$$

$$T = ^\circ\text{C} + 273.16 \text{ (Kelvin)}$$

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, USP 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 intraabdominal 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 & USAGE

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

CONTRAINDICATIONS

Isoflurane, USP 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 periods.⁴

Since levels of anesthesia may be altered easily and rapidly, only vaporizers producing predictable percentage concentrations of isoflurane should be used. (See DOSAGE 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.

Not for use in horses intended for food.

Keep out of reach of children.

PRECAUTIONS

Isoflurane, USP, like 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, USP.

PREGNANCY

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 overdosage, or what may appear to be overdosage, 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.

DOSAGE & ADMINISTRATION

Caution: Operating rooms should be provided with adequate ventilation to prevent the 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 is then diluted (e.g. Vernitrol® vaporizer) also may be used. The delivered concentration from such a vaporizer may be calculated using the formula:

$$\% \text{ Isoflurane} = \frac{100 P_V F_V}{F_T (P_A - P_V)}$$

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 (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, USP, is packaged in 100 ml (NDC 46066-115-03) amber-colored bottle.

Isoflurane, USP, is packaged in 250 ml (NDC 46066-115-04) amber-colored bottle.

Storage: Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

REFERENCES

1. Steffey, E.P., Howland, D. Jr., Giri, S. and Eger, E.I. II.: Enflurane, Halothane and Isoflurane Potency in Horses. **Am. J.Vet. Res.** **38**(7): 1037- 1039, 1977.
2. Auer, J.A., Garner, H.E., Amend, J.F., Hutcheson, D.P. and Salem, C.A.: Recovery from Anesthesia in Ponies: A Comparative Study of the Effects of Isoflurane, Enflurane, Methoxyflurane and Halothane. **Equine Vet. J.** **10**(1): 18-23 1978.
3. Steffey, E.P. and Howland, D. Jr.: Comparison of Circulatory and Respiratory Effects of Isoflurane and Halothane Anesthesia in Horses. **Am. J.Vet. Res.** **41**(5): 821-825, 1980.
4. Auer, J.A., Amend, J.F., Garner, H.E., Hutcheson, D.P. and Salem, C.A.: Electroencephalographic Responses During Volatile Anesthesia in Domestic Ponies: A Comparative Study of Isoflurane, Enflurane, Methoxyflurane and Halothane. **Equine Practice** **3**: 130-134, 1979.
5. Kilde, A.M.: Cardiopulmonary Effects of Enflurane and Isoflurane in the Dog. **Am. J.Vet. Res.:****Vol. 37, No 2:** 127-131, 1976.
6. Steffey, E.P., Howland, D.: Isoflurane Potency in the Dog and Cat. **Am. J.Vet. Res.,Vol. 38, No 11:** 1833-1836, 1977.

100 ml - Text revised: August 2023

250 ml - Text revised: July 2023

Manufactured for:

Aspen Veterinary Resources®, LTD.
Liberty, MO 64068 **pivetaivet.com**
P0107.PHC
Rev. 02/24
Product of India

To report adverse drug events, for technical assistance or to obtain a copy of the SDS, contact Aspen Veterinary Resources at info@aspenveterinaryresources.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/reportanimalae>.

Approved by FDA under ANADA # 200-237

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

LABEL-100 ml

NDC 46066-115-03

ISOFLURANE, USP
INHALATION ANESTHETIC

100mL

Nonflammable, nonexplosive

For Veterinary Use in Horses and Dogs

84 mm


Fold

NDC 46066-115-03

ISOFLURANE, USP
INHALATION ANESTHETIC


Nonflammable, nonexplosive
For Veterinary Use
in Horses and Dogs

WARNING: Not for use in horses intended for food.
For Animal Use Only
Approved by FDA under ANADA # 200-237

Net Contents: 100 mL 

IMPORTANT: See accompanying product information for dosage and direction for use.
WARNING: Keep out of reach of children.
CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
CAUTION: Operating rooms should be provided with adequate ventilation to prevent the accumulation of anesthetic vapors. Each mL contains 99.9% isoflurane.
Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].
Manufactured for:
Aspen Veterinary Resources®, LTD.
Liberty, MO 64068 pivotalvet.com

P0107.PHC
Rev. 08/23
Product of India
Code: AP/DRUGS/220/96


0 99355 03618 5

IN/EL/0023/23/00

LABEL-250 ml

NDC 46066-115-04

ISOFLURANE, USP
INHALATION ANESTHETIC

250mL

Nonflammable, nonexplosive.

For Veterinary Use in Horses and Dogs.

88.5 mm

Fold

NDC 46066-115-04

ISOFLURANE, USP

INHALATION ANESTHETIC

Nonflammable, nonexplosive
For Veterinary Use
in Horses and Dogs

WARNING: Not for use in horses intended for food.

For Animal Use Only

Approved by FDA under ANADA # 200-237

Net Contents: 250 mL



IMPORTANT: See accompanying product information for dosage and direction for use.

WARNING: Keep out of reach of children.

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

CAUTION: Operating rooms should be provided with adequate ventilation to prevent the accumulation of anesthetic vapors. Each mL contains 99.9% isoflurane.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

Manufactured for:

Aspen Veterinary Resources®, LTD.
Liberty, MO 64068 pivotalvet.com

P0108.PHC

Rev. 08/23

Product of India

Code: AP/DRUGS/220/96

INELJ0024/23/00



ISOFLURANE

isoflurane liquid

Product Information

Product Type	PREScription ANIMAL DRUG	Item Code (Source)	NDC:46066-115
Route of Administration	RESPIRATORY (INHALATION)		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ISOFLURANE (UNII: CYS9AKD70P) (ISOFLURANE - UNII:CYS9AKD70P)	ISOFLURANE	1 mL in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:46066-115-03	100 mL in 1 BOTTLE, GLASS		
2	NDC:46066-115-04	250 mL in 1 BOTTLE, GLASS		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200237	03/01/2024	

Labeler - ASPEN VETERINARY RESOURCES LTD (627265361)

Registrant - ASPEN VETERINARY RESOURCES LTD (627265361)

Establishment

Name	Address	ID/FEI	Business Operations
Piramal Pharma Limited		919067108	ANALYSIS, API MANUFACTURE, LABEL, MANUFACTURE, PACK

Revised: 2/2024

ASPEN VETERINARY RESOURCES LTD