SevoFlo®
(sevoflurane)

Inhalation Anesthetic For Use in Dogs

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

DESCRIPTION:
SevoFlo® (sevoflurane), a volatile liquid, is a halogenated general inhalation anesthetic drug. Its chemical name is fluoromethyl 2,2,2-trifluoro-l-( trifluoromethyl) ethyl ether, and its structural formula is: 

\[
F_3\text{C} \quad H \quad C \quad - \quad O \quad H
\]

SevoFlo is nonflammable and nonexplosive as defined by the requirements of the National Electrical Safety Code Commission 601-2-13.

SevoFlo is a clear, colorless, stable liquid containing no additives or chemical stabilizers. SevoFlo contains no stabilizer. Nothing in the drug product alters calibration of the administering equipment.

SevoFlo is nonpungent. It is miscible with ethanol, ether, chloroform and petroleum benzene, and it is slightly soluble in water. SevoFlo is stable when stored under normal room temperature and petroleum benzene, and it is slightly soluble in water. SevoFlo is nonpungent. It is miscible with ethanol, ether, chloroform and petroleum benzene, and it is slightly soluble in water. SevoFlo is stable when stored under normal room temperature.

SevoFlo Physical Constants are:

- Molecular weight: 202.05
- Boiling point at 760 mm Hg: 58.6°C
- Specific gravity at 20°C: 1.500-1.525 g/mL
- Vapor pressure in mm Hg at 20°C: 167
- at 25°C: 197
- at 36°C: 317

Distribution Partition Coefficients at 37°C:

- Blood/Gas: 0.63-0.69
- Water/Gas: 0.36
- Olive Oil/Gas: 47-54
- Brain/Gas: 1.15

Mean Component/Gas Partition Coefficients at 25°C for Polymers Used Commonly in Medical Applications:

- Conductive rubber: 14.0
- Butyl rubber: 7.7
- Polyvinyl chloride: 17.4
- Polyethylene: 1.3

Sevoflurane is stable when stored under normal room lighting condition according to instructions.

INDICATIONS:
SevoFlo is indicated for induction and maintenance of general anesthesia in dogs.

DOSEAGE AND ADMINISTRATION:
Inhaled Concentration: The delivered concentration of sevoflurane should be known. Since the depth of anesthesia may be altered easily and rapidly, only vaporizers producing predictable percentage concentrations of sevoflurane should be used. Sevoflurane should be vaporized using a precision vaporizer specifically calibrated for sevoflurane. Sevoflurane contains no stabilizer. Nothing in the drug product alters calibration or operation of these vaporizers. The administration of general anesthesia must be individualized based on the patient’s response. WHEN USING SEVOFLURANE, PATIENTS SHOULD BE CONTINUOUSLY MONITORED AND FACILITIES FOR MAINTENANCE OF PATIENT AIRWAY, ARTIFICIAL VENTILATION, AND OXYGEN SUPPLEMENTATION MUST BE IMMEDIATELY AVAILABLE.

Replacement of Desiccated CO2 Absorbents: When a clinician suspects that the CO2 absorbent may be desiccated, it should be replaced. An exothermic reaction occurs when sevoflurane is exposed to CO2 absorbents. This reaction is increased when the CO2 absorbent becomes desiccated (see PRECAUTIONS).

Premedication: No specific premedication is either indicated or contraindicated with sevoflurane. The necessity for and choice of premedication is left to the discretion of the veterinarian. Preanesthetic doses for premedicants may be lower than the label directions for discretion of the veterinarian. Preanesthetic doses for the healthy dog. These concentrations can be expected to produce surgical anesthesia in 3 to 14 minutes. Due to the rapid and dose dependent changes in anesthetic depth, care should be taken to prevent overdosing. Respiration must be monitored closely in the dog and supported when necessary with supplemental oxygen and/or assisted ventilation.

Maintenance: SevoFlo® may be used for maintenance anesthesia following mask induction using sevoflurane or following injectable induction agents. The concentration of sevoflurane to maintain anesthesia is much less than that required to induce it. Surgical levels of anesthesia in the healthy dog may be maintained with inflated concentrations of 3.7-4.0% sevoflurane in oxygen in the absence of premedication and 3.3-3.6% in the presence of premedication. The use of injectable induction agents without premedication has little effect on the concentrations of sevoflurane required for maintenance. Anesthetic regimens that include opioid, alpha2-agonist, benzodiazepine or phenothiazine premedication will allow the use of lower sevoflurane maintenance concentrations.

CONTRAINdications:
SevoFlo is contraindicated in dogs with a known sensitivity to sevoflurane or other halogenated agents.

WARNINGS:
SevoFlo is a profound respiratory depressant. DUE TO THE RAPID AND DOSE DEPENDENT CHANGES IN ANESTHETIC DEPTH, RESPIRATION MUST BE MONITORED CLOSELY IN THE DOG AND SUPPORTED WHEN NECESSARY WITH SUPPLEMENTAL OXYGEN AND/OR ASSISTED VENTILATION. The low solubility of sevoflurane also facilitates rapid elimination by the lungs.

SevoFlo is used in humans increases both the intensity and duration of neuromuscular blockade induced by nondepolarizing muscle relaxants. The use of sevoflurane with nondepolarizing muscle relaxants has not been evaluated in dogs.

Compromised or debilitated dogs: Doses may need adjustment for geriatric or debilitated dogs. Because clinical experience in administering sevoflurane to dogs with renal, hepatic and cardiovascular insufficiency is limited, the drug should be avoided in these conditions. Breeding dogs: The safety of sevoflurane in dogs used for breeding purposes, during pregnancy, or in lactating bitches, has not been evaluated.

Neonates: The safety of sevoflurane in young dogs (less than 12 weeks of age) has not been evaluated.

HUMAN SAFETY:

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

There is no specific work exposure limit established for sevoflurane. However, the National Institute for Occupational Safety and Health has recommended an 8 hour time-weighted average limit of 2 ppm for halogenated anesthetic agents in general.

Direct exposure to eyes may result in mild irritation. If eye exposure occurs, flush with plenty of water for 15 minutes. Seek medical attention if irritation persists.

Symptoms of human overexposure (inhalation) to sevoflurane vapors include respiratory depression, hypoxemia, bradycardia, cyanosis, respiratory arrest, cardiovascular collapse and death (see CLINICAL PHARMACOLOGY).

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Zoetis Inc. at 1-888-963-8471 or www.zoetis.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/AnimalVeterinary/SafetyHealth.

CLINICAL PHARMACOLOGY:
SevoFlo® is an inhalational anesthetic agent for induction and maintenance of general anesthesia. The Minimum Alveolar Concentration (MAC) of sevoflurane as determined in 18 dogs is 2.36%. MAC is defined as that concentration of inhaled anesthetic that facilitates rapid emergence of the healthy patient from the anesthetic when the patient is exposed to a test stimulation without fail to respond to noxious stimuli. Multiples of MAC are used as a guide for surgical levels of anesthesia, which are typically 1.3 to 1.5 times the MAC value.

Because of the low solubility of sevoflurane in blood (blood/gas partition coefficient at 37°C = 0.63-0.69), a minimal amount of sevoflurane is required to be dissolved in the blood before the alveolar partial pressure is in equilibrium with the arterial partial pressure. During sevoflurane induction, there is a rapid increase in alveolar concentration toward the inspired concentration.
Phenothiazines and Alpha₂ Agonists: Sevoflurane is compatible with phenothiazines and alpha₂ agonists as commonly used in surgical practice.

In a laboratory study, the use of the acepromazine/oxycodeone/thiopental/sevoflurane anesthetic regimen resulted in prolonged recoveries in eight (of 8) dogs compared to recoveries from sevoflurane alone.

**CLINICAL EFFECTIVENESS:**

The effectiveness of sevoflurane was investigated in a clinical study involving 196 dogs. Thirty dogs were mask-induced with sevoflurane using anesthetic regimens that included various premedications. Among the various anesthetic regimens, the quality of maintenance anesthesia was considered good or excellent in 169 out of 196 dogs.

The table shows the average vaporizer concentrations and oxygen flow rates during the first 30 minutes for all sevoflurane maintenance anesthesia regimens:

<table>
<thead>
<tr>
<th>Average Vaporizer Concentrations among Anesthetic Regimens</th>
<th>Average Oxygen Flow Rates among Anesthetic Regimens</th>
<th>Average Oxygen Flow Rates among Individual Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 3.0 L/minute</td>
<td>0.97 - 1.31 L/minute</td>
<td>1.6 - 5.1 L/minute</td>
</tr>
</tbody>
</table>

During the clinical trial, when a barbiturate was used for induction, the times to extubation, sternal recumbency and standing recovery were longer for dogs that received anesthetic regimens containing two preanesthetics compared to regimens containing one preanesthetic. Recovery times were shorter when anesthetic regimens used sevoflurane or propofol for induction. The quality of recovery was considered good or excellent in 184 out of 196 dogs.

Anesthetic regimen drug dosages, physical responses, and the quality of induction, maintenance and recovery were comparable between 10 sighthounds and other breeds evaluated in the study. During the clinical study there was no indication of prolonged recovery times in the sighthounds.

**HOW SUPPLIED:**

SevoFlo (sevoflurane) is packaged in amber colored bottles containing 100 mL and 250 mL sevoflurane, List 5A55.

**STORAGE CONDITIONS:**

Store at controlled room temperature 15°-30°C (59°-86°F).

**REFERENCES:**