

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
Carton box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sevohale 100% v/v Inhalation vapour, liquid for dogs and cats.
sevoflurane

2. STATEMENT OF ACTIVE SUBSTANCES

Sevoflurane 100% v/v

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid

4. PACKAGE SIZE

250 ml
6 x 250 ml

5. TARGET SPECIES

Dogs and cats

6. INDICATION(S)

For induction and maintenance of anaesthesia.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Administer by inhalation using a vaporiser calibrated for sevoflurane.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Do not use in animals with known hypersensitivity to sevoflurane or other halogenated anaesthetic agents.

Do not use in animals with a known or suspected genetic susceptibility to malignant hyperthermia.

For operator warnings - read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Do not refrigerate.
Keep the bottle tightly closed.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.,
Loughrea,
Co. Galway,
IRELAND

16. MARKETING AUTHORISATION NUMBER(S)

Vm 08749/5026

17. MANUFACTURER'S BATCH NUMBER

BN{number}

PARTICULARS TO APPEAR ON THE INNER PACKAGE

Bottle label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sevohale 100% v/v Inhalation vapour, liquid for dogs and cats.
sevoflurane

2. STATEMENT OF ACTIVE SUBSTANCES

100% v/v sevoflurane

3. PHARMACEUTICAL FORM

Inhalation vapour, liquid

4. PACKAGE SIZE

250 ml

5. TARGET SPECIES

Dogs and cats

6. INDICATION(S)

For induction and maintenance of anaesthesia.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

For operator warnings. Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Do not refrigerate.
Keep the bottle tightly closed.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Read the package leaflet before use.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.,
Loughrea,
Co. Galway,
IRELAND

16. MARKETING AUTHORISATION NUMBER(S)

Vm 08749/5026

17. MANUFACTURER'S BATCH NUMBER

BN{number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Sevohale
Inhalation vapour, liquid for dogs and cats, 100% v/v sevoflurane

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

Chanelle Pharmaceuticals Manufacturing Ltd.,
Loughrea,
Co. Galway,
IRELAND

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sevohale 100% v/v Inhalation vapour, liquid for dogs and cats.
sevoflurane

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

100% v/v sevoflurane.

4. INDICATION(S)

For the induction and maintenance of anaesthesia.

5. CONTRAINDICATIONS

Do not use in animals with known hypersensitivity to sevoflurane or other halogenated anaesthetic agents.

Do not use in animals with a known or suspected genetic susceptibility to malignant hyperthermia.

6. ADVERSE REACTIONS

Hypotension, tachypnoea, muscle tenseness, excitation, apnoea, muscle fasciculations and emesis have been reported very commonly, based on post-authorisation spontaneous reporting experience.

Dose-dependent respiratory depression is commonly observed while using sevoflurane, therefore respiration should be closely monitored during sevoflurane anaesthesia and the inspired concentration of sevoflurane adjusted accordingly.

Anaesthetic-induced bradycardia is commonly observed during sevoflurane anaesthesia. It may be reversed by administration of anticholinergics.

Paddling, retching, salivation, cyanosis, premature ventricular contractions and excessive cardiopulmonary depression have been reported very rarely, based on post-authorisation spontaneous reporting experience.

In dogs, transient elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), bilirubin and white blood cell counts may occur with sevoflurane, as with the use of other halogenated anaesthetic agents. In cats, transient increases in AST and ALT may occur with sevoflurane, however, hepatic enzymes tend to remain within the normal range.

Hypotension during sevoflurane anaesthesia may result in decreased renal blood flow.

The possibility of sevoflurane triggering episodes of malignant hyperthermia in susceptible dogs and cats cannot be ruled out.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs and cats.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Inspired concentration:

Sevohale should be administered via a vaporiser specifically calibrated for use with sevoflurane so that the concentration delivered can be accurately controlled.

Sevohale contains no stabiliser and does not affect the calibration or operation of these vaporisers in any way. The administration of sevoflurane must be individualised based on the dog's or cat's response.

Premedication:

The necessity for and choice of premedication is left to the discretion of the veterinarian. Preanaesthetic doses for premedicants may be lower than the label directions for their use as a single medication.

Induction of anaesthesia:

For mask induction using sevoflurane, inspired concentrations of 5 to 7% sevoflurane with oxygen are employed to induce surgical anaesthesia in the healthy dog, and 6 to 8% sevoflurane with oxygen in the cat. These concentrations can be expected to produce surgical anaesthesia in 3 to 14 minutes in dogs and within 2 to 3 minutes in cats. Sevoflurane concentration for induction may be set initially, or may be achieved gradually over the course of 1 to 2 minutes. The use of premedicants does not affect the concentration of sevoflurane required for induction.

Maintenance of anaesthesia:

Sevoflurane may be used for maintenance anaesthesia following mask induction using sevoflurane or following induction with injectable agents. The concentration of sevoflurane necessary to maintain anaesthesia is much less than that required for induction.

Surgical levels of anaesthesia in the healthy dog may be maintained with inhaled concentrations of 3.3 to 3.6% in the presence of premedication. In the absence of premedication, inhaled concentrations of sevoflurane in the range of 3.7 to 3.8% will provide surgical levels of anaesthesia in the healthy dog. In the cat surgical anaesthesia is maintained with sevoflurane concentrations of 3.7-4.5%.

The presence of surgical stimulation may require an increase in the concentration of sevoflurane.

The use of injectable induction agents without premedication has little effect on the concentrations of sevoflurane required for maintenance. Anaesthetic regimens that include opioid, alpha-2-agonist, benzodiazepine or phenothiazine premedication will allow the use of lower sevoflurane maintenance concentrations.

9. ADVICE ON CORRECT ADMINISTRATION

For inhalation use only, using a suitable carrier gas. Sevohale should be administered via a vaporiser specifically calibrated for use with sevoflurane so that the concentration delivered can be accurately controlled. Sevohale contains no stabiliser and does not affect the calibration or operation of these vaporisers.

The administration of general anaesthesia must be individualised based on the dog's or cat's response.

Interaction with other veterinary medicinal products and other forms of interaction

Intravenous anaesthetics:

Sevoflurane administration is compatible with the intravenous barbiturates and propofol and in cats alfaxalone and ketamine. In dogs the concurrent administration of thiopental, however, may slightly increase sensitivity to adrenaline induced cardiac arrhythmias.

Benzodiazepines and opioids:

Sevoflurane administration is compatible with the benzodiazepines and opioids commonly used in veterinary practice. In common with other inhalational

anaesthetics, the minimum alveolar concentration (MAC) of sevoflurane is reduced by the concurrent administration of benzodiazepines and opioids.

Phenothiazines and alpha-2-agonists:

Sevoflurane is compatible with phenothiazines and alpha-2-agonists commonly used in veterinary practice. Alpha-2-agonists have an anaesthetic sparing effect and therefore the dose of sevoflurane should be reduced accordingly. Limited data are available on the effects of the highly potent alpha-2-agonists (medetomidine, romifidine and dexmedetomidine) as premedication. Therefore they should be used with caution. Alpha-2-agonists cause bradycardia which may occur when they are used with sevoflurane. Bradycardia can be reversed by the administration of anticholinergics.

Anticholinergics:

Studies in dogs and cats show that anticholinergic premedication is compatible with sevoflurane anaesthesia in dogs and cats.

In a laboratory study, the use of an acepromazine/oxymorphone/thiopental/sevoflurane anaesthetic regimen resulted in prolonged recoveries in all the dogs treated, compared to recoveries in dogs anaesthetised with sevoflurane alone.

The use of sevoflurane with nondepolarising muscle relaxants has not been evaluated in dogs. In cats sevoflurane has been shown to exert some neuromuscular blocking effect, but this is only apparent at high doses. In humans sevoflurane increases both the intensity and duration of neuromuscular blockade induced by nondepolarising muscle relaxants. Neuromuscular blocking agents have been used in cats anaesthetised with sevoflurane without any unexpected effects

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25 °C.

Do not refrigerate.

Keep the bottle tightly closed.

Do not use this veterinary medicinal product after the expiry date which is stated on the label.

12. SPECIAL WARNING(S)

Special precautions for use in animals:

Halogenated volatile anaesthetics can react with desiccated carbon dioxide (CO₂) absorbents to produce carbon monoxide (CO) that may result in elevated levels of carboxyhaemoglobin in some dogs. In order to minimise this reaction in rebreathing anaesthetic circuits, Sevohale should not be passed through soda lime or barium hydroxide that has been allowed to dry out.

The exothermic reaction that occurs between sevoflurane and CO₂ absorbents is increased when the CO₂ absorbent becomes desiccated (dried out), such as after an extended period of dry gas flow through the CO₂ absorbent canisters. Rare cases of excessive heat production, smoke and/or fire in the anaesthetic machine have been reported during the use of a desiccated CO₂ absorbent and sevoflurane. An unusual decrease in the expected depth of anaesthesia compared to the vaporiser setting may indicate excessive heating of the CO₂ absorbent canister.

If it is suspected that the CO₂ absorbent may be desiccated, it must be replaced. The colour indicator of most CO₂ absorbents does not necessarily change as a result of desiccation. Therefore, the lack of significant colour change should not be taken as an assurance of adequate hydration. CO₂ absorbents should be replaced routinely regardless of the state of the colour indicator.

1,1,3,3,3-pentafluoro-2-(fluoromethoxy)propene (C₄H₂F₆O), also known as Compound A, is produced when sevoflurane interacts with soda lime or barium hydroxide. Reaction with barium hydroxide results in a greater production of Compound A than does the reaction with soda lime. Its concentration in a circle absorber system increases with increasing sevoflurane concentrations and with decreasing fresh gas flow rates. Sevoflurane degradation in soda lime has been shown to increase with temperature. Since the reaction of carbon dioxide with absorbents is exothermic, this temperature increase will be determined by the quantities of CO₂ absorbed, which in turn will depend on fresh gas flow in the anaesthetic circle system, metabolic status of the dog and ventilation. Although Compound A is a dose-dependent nephrotoxin in rats, the mechanism of this renal toxicity is unknown. Long duration, low-flow sevoflurane anaesthesia should be avoided due to the risks of Compound A accumulation.

During the maintenance of anaesthesia, increasing the concentration of sevoflurane produces a dose dependent decrease in blood pressure. Due to sevoflurane's low solubility in blood, these haemodynamic changes may occur more rapidly than with other volatile anaesthetics. Arterial blood pressure should be monitored at frequent intervals during sevoflurane anaesthesia. Facilities for artificial ventilation, oxygen enrichment and circulatory resuscitation should be immediately available. Excessive decreases in blood pressure or respiratory depression may be related to the depth of anaesthesia and may be corrected by decreasing the inspired concentration of sevoflurane. The low solubility of sevoflurane also facilitates rapid elimination by the lungs. The nephrotoxic potential of certain NSAIDs, when used in the perioperative period, may be exacerbated by hypotensive episodes during sevoflurane anaesthesia. In order to preserve renal blood flow, prolonged episodes of hypotension (mean arterial pressure below 60 mmHg) should be avoided in dogs and cats during sevoflurane anaesthesia.

In common with all volatile agents, sevoflurane may cause hypotension in hypovolaemic animals such as those requiring surgery to repair traumatic injury, and lower doses should be administered in combination with appropriate analgesics. Sevoflurane may trigger episodes of malignant hyperthermia in susceptible dogs and cats. If malignant hyperthermia develops, the anaesthetic supply should be interrupted immediately and 100% oxygen administered using fresh anaesthetic hoses and a rebreathing bag. Appropriate treatment should readily be instituted.

Compromised or debilitated dogs and cats:

Doses of sevoflurane may need adjustment for geriatric or debilitated animals. Doses required for maintenance of anaesthesia may need to be reduced by approximately 0.5% in geriatric dogs (i.e. 2.8 to 3.1% in premedicated geriatric dogs and 3.2 to 3.3% in unpremedicated geriatric dogs). There is no information on the adjustment of the maintenance dose in cats. Adjustment is, therefore, left to the discretion of the veterinarian. Limited clinical experience in administering sevoflurane to animals with renal, hepatic and cardiovascular insufficiency suggests that sevoflurane may be safely used in these conditions. However, it is recommended that such animals be monitored carefully during sevoflurane anaesthesia.

Sevoflurane may cause a small increase in intracranial pressure (ICP) under conditions of normocapnia in dogs. In dogs with head injuries or other conditions placing them at risk from increased ICP, it is recommended that hypocapnia be induced by means of controlled hyperventilation as a means of preventing changes in ICP.

There are limited data to support the safety of sevoflurane in animals less than 12 weeks of age. Therefore, it should only be used in these animals according to a benefit-risk assessment by the responsible veterinary surgeon.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

In order to minimise exposure to sevoflurane vapour, the following recommendations are made:

- Use a cuffed endotracheal tube when possible for the administration of Sevohale during maintenance anaesthesia.
- Avoid using masking procedures for prolonged induction and maintenance of general anaesthesia.
- Ensure that operating rooms and animal recovery areas are provided with adequate ventilation or scavenging systems to prevent the accumulation of anaesthetic vapour.
- All scavenging/extraction systems must be adequately maintained.
- Pregnant and breast-feeding women should not have any contact with the product and should avoid operating rooms and animal recovery areas.
- Care should be taken when dispensing Sevohale, with immediate removal of any spillage.
- Do not inhale the vapour directly.
- Avoid contact by mouth.
- Halogenated anaesthetic agents may induce liver damage. This is an idiosyncratic response very occasionally seen after repeated exposure.

- From an environmental point of view, it is considered good practice to use charcoal filters with scavenging equipment.

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

In case of accidental contact with the skin, wash the affected area with abundant water.

Symptoms of human overexposure (inhalation) to sevoflurane vapours include respiratory depression, hypotension, bradycardia, shivering, nausea and headache. If these symptoms occur, remove the individual from the source of exposure and seek medical attention.

Advice to doctors:

Maintain a patent airway and give symptomatic and supportive treatment.

Pregnancy and lactation:

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. However, there is limited clinical experience of the use of sevoflurane, after propofol induction, in bitches and queens undergoing caesarean section, without any ill effects being detected in either the bitch or queen or the puppies or kittens. Use only according to the risk/benefit assessment of the responsible veterinarian.

Overdose (symptoms, emergency procedures, antidotes):

Sevohale overdose may result in profound respiratory depression. Therefore, respiration must be monitored closely and supported when necessary with supplementary oxygen and/or assisted ventilation.

In cases of severe cardiopulmonary depression, discontinue sevoflurane administration, ensure the existence of a patent airway and initiate assisted or controlled ventilation with pure oxygen. Cardiovascular depression should be treated with plasma expanders, pressor agents, antiarrhythmic agents or other appropriate techniques.

Due to sevoflurane's low solubility in blood, increasing the concentration may result in rapid haemodynamic changes (dose-dependent decreases in blood pressure) compared to other volatile anaesthetics. Excessive decreases in blood pressure or respiratory depression may be corrected by decreasing or discontinuing the inspired concentration of sevoflurane.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

Medicines should not be disposed of via wastewater or household waste.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

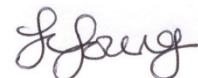
15. OTHER INFORMATION

For animal treatment only.

250 ml amber glass bottle with a yellow collar on the neck, sealed with a poly-seal cap, and secured with PET film.

Cardboard box containing either 1 or 6 bottles.
Not all pack sizes may be marketed.

Approved: 03 March 2021

A handwritten signature in black ink, appearing to read 'J. Berg', is positioned below the approval date.