1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alfaxan Multidose 10 mg/ml solution for injection for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Alfaxalone 10 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Ethanol	150 mg
Chlorocresol	1 mg
Benzethonium chloride	0.2 mg
Hydroxypropylbetadex	
Sodium Chloride	
Disodium Phosphate Anhydrous	
Potassium Dihydrogen Phosphate	
Sodium Hydroxide (for pH adjustment)	
Hydrochloric Acid, Concentrated (for pH adjustment)	
Water for Injections	

Clear colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each target species

As an induction agent prior to inhalation anaesthesia. As a sole anaesthetic agent for the induction and maintenance of anaesthesia for the performance of examination or surgical procedures.

3.3 Contraindications

Do not use in combination with other intravenous anaesthetic agents.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

The analgesic properties of alfaxalone are limited, therefore appropriate peri-operative analgesia should be provided in cases where procedures are anticipated to be painful.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The safety of the veterinary medicinal product in animals less than 12 weeks of age has not been demonstrated.

Transient post induction apnoea frequently occurs, particularly in dogs - see section 3.6 for details. In such cases, endotracheal intubation and oxygen supplementation should be employed. Facilities for intermittent positive pressure ventilation should be available. In order to minimise the possibility of apnoea, administer the veterinary medicinal product by slow intravenous injection and not as a rapid dose. The use of a preplaced catheter in dogs and cats is recommended as best practice for anaesthetic procedures.

Especially when using higher doses of the veterinary medicinal product, a dose-dependent respiratory depression may occur. Oxygen and/or intermittent positive pressure ventilation should be administered to counteract the threatening hypoxaemia/hypercapnia. This should be particularly important in risky anaesthetic cases and whenever the anaesthesia is to be carried out for a longer period of time.

In both dogs and cats, the dose interval for maintenance of anaesthesia by intermittent bolus administration may require lengthening by more than 20%, or the maintenance dose by intravenous infusion may require reduction by more than 20%, when hepatic blood flow is severely diminished or hepatocellular injury is severe. In cats or dogs with renal insufficiency, doses for induction and maintenance may require reduction.

As with all general anaesthetic agents:
- It is advisable to ensure that the patient has been fasted before receiving the anaesthetic.
- As with other intravenous anaesthetic agents, caution should be exercised in animals with cardiac or respiratory impairment, or in hypovolaemic or debilitated animals.
- Additional monitoring is advised and particular attention should be paid to respiratory parameters in aged animals, or in cases where there may be additional physiological stress imposed by pre-existing pathology, shock or caesarean section.
- Following induction of anaesthesia, the use of an endotracheal tube is recommended to maintain airway patency.
- It is advisable to administer supplemental oxygen during maintenance of anaesthesia.
- Respiratory embarrassment may occur – ventilation of the lungs with oxygen should be considered if haemoglobin saturation with oxygen (SpO_2%) falls below 90% or if apnoea persists for longer than 60 seconds.
- If cardiac arrhythmias are detected, attention to respiratory ventilation with oxygen is the first priority followed by appropriate cardiac therapy or intervention.

During recovery, it is preferable that animals are not handled or disturbed. This may lead to paddling, minor muscle twitching or movements that are more violent. While better avoided, such reactions are clinically insignificant. Post-anaesthetic recovery should thus take place in appropriate facilities and under sufficient supervision. Use of a benzodiazepine as the sole premedicant may increase the probability of psychomotor excitement.

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

This veterinary medicinal product is a sedative, exercise caution to avoid accidental self-injection. Preferably use a guarded needle until the moment of injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. The veterinary medicinal product may cause irritation if it comes into contact with the skin or eyes.
Rinse any splashes from skin or eyes immediately with water.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs and cats:

Very common (>1 animal / 10 animals treated)	Apnoea[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports)	Hyperactivity, vocalisation; Bradycardia, cardiac arrest; Convulsion, myoclonus, prolonged anaesthesia, tremor; Bradypnoea.

[1] Observed post induction. 44% of dogs and 19% of cats experienced post induction apnoea in clinical studies; mean duration of apnoea was 100 seconds in dogs and 60 seconds in cats. Endotracheal intubation and oxygen supplementation should therefore be employed.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in cases where pregnancy is to be continued or during lactation. Its effects upon fertility have not been evaluated. However, studies using alfaxalone in pregnant mice, rats and rabbits have demonstrated no deleterious effects on gestation of the treated animals, or on the reproductive performance of their offspring. The veterinary medicinal product should be used in pregnant animals according to the benefit-risk assessment performed by the responsible veterinarian. The veterinary medicinal product has been safely used in dogs for the induction of anaesthesia prior to delivery of puppies by caesarean section. In these studies, dogs were not premedicated, a dose of 1-2 mg/kg was drawn up (i.e. slightly lower than the usual 3 mg/kg dose, see section 3.9) and the veterinary medicinal product was administered as recommended, to effect.

3.8 Interaction with other medicinal products and other forms of interaction

The veterinary medicinal product has been demonstrated to be safe when used in combination with the following premedicant classes:

Drug Class	Examples
Phenothiazines	Acepromazine maleate
Anticholinergic agents	Atropine sulfate
Benzodiazepines	Diazepam, midazolam hydrochloride
Alpha-2-adrenoceptor agonists	Xylazine hydrochloride, medetomidine hydrochloride
Opiates	Methadone, morphine sulfate, butorphanol tartrate, buprenorphine hydrochloride
NSAIDs	Carprofen, meloxicam

The concomitant use of other CNS depressants should be expected to potentiate the depressant effects of the veterinary medicinal product, necessitating cessation of further administration of the veterinary medicinal product when the required depth of anaesthesia has been reached.

The use of one premedicant or a combination of premedicants often reduces the dose of the veterinary medicinal product required.

Premedication with alpha-2-adrenoceptor agonists such as xylazine and medetomidine can markedly increase the duration of anaesthesia in a dose dependent fashion. In order to shorten recovery periods it may be desirable to reverse the actions of these premedicants.

Benzodiazepines should not be used as sole premedicants in dogs and cats as the quality of anaesthesia in some patients may be sub-optimal. Benzodiazepines may be used safely and effectively in combination with other premedicants and the veterinary medicinal product.

Refer to section 3.3.

3.9 Administration routes and dosage

Dogs and cats: Intravenous use (IV).

Induction of anaesthesia:
The induction dose of the veterinary medicinal product is based on data taken from controlled laboratory and field studies and is the amount of drug required for 9 of 10 patients (i.e. 90th percentile) to be successfully induced for anaesthesia.

Dosing recommendations for induction of anaesthesia are as follows:

	DOGS		CATS	
	Un-premedicated	**Premedicated**	**Un-premedicated**	**Premedicated**
mg/kg	3	2	5	5
ml/kg	0.3	0.2	0.5	0.5

The dosing syringe should be prepared to contain the above dose. Administration should continue until the clinician is satisfied that the depth of anaesthesia is sufficient for endotracheal intubation, or until the entire dose has been administered. The necessary injection rate can be achieved by administration of one quarter (¼) of the calculated dose every 15 seconds, so that the total dose, if required, would be administered over the first 60 seconds. If, 60 seconds after complete delivery of this first induction dose, intubation is still not possible, one further similar dose may be administered to effect.

Maintenance of anaesthesia:
Following induction of anaesthesia with the veterinary medicinal product, the animal may be intubated and maintained on the veterinary medicinal product or an inhalation anaesthetic agent. Maintenance doses of the veterinary medicinal product may be given as supplemental boluses or as constant rate infusion. The veterinary medicinal product has been used safely and effectively in both dogs and cats for procedures lasting for up to one hour. The following doses suggested for maintenance of anaesthesia are based on data taken from controlled laboratory and field studies and represent the average amount of drug required to provide maintenance anaesthesia for a dog or cat. However, the actual dose will be based on the response of the individual patient.

Dosing recommendations for maintenance of anaesthesia are as follows:

	DOGS		**CATS**	
	Un-premedicated	**Premedicated**	**Un-premedicated**	**Premedicated**
Dose for constant rate infusion				
mg/kg/hour	8 - 9	6 - 7	10 - 11	7 - 8
mg/kg/minute	0.13 - 0.15	0.10 - 0.12	0.16 - 0.18	0.11 - 0.13
ml/kg/minute	0.013 - 0.015	0.010 - 0.012	0.016 - 0.018	0.011 - 0.013
Bolus dose for each 10 minutes maintenance				
mg/kg	1.3 - 1.5	1.0 - 1.2	1.6 - 1.8	1.1 - 1.3
ml/kg	0.13 - 0.15	0.10 - 0.12	0.16 - 0.18	0.11 - 0.13

Where maintenance of anaesthesia is with the veterinary medicinal product for procedures lasting more than 5 to 10 minutes, a butterfly needle or catheter can be left in the vein, and small amounts of the veterinary medicinal product injected subsequently to maintain the required level and duration of anaesthesia. In most cases the average duration of recovery when using the veterinary medicinal product for maintenance will be longer than if using an inhalant gas as a maintenance agent.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Acute tolerance to overdose has been demonstrated up to 10 times the recommended dose of 2 mg/kg in the dog (i.e. up to 20 mg/kg) and up to 5 times the recommended dose of 5 mg/kg in the cat (i.e. up to 25 mg/kg). For both dogs and cats, these excessive doses delivered over 60 seconds cause apnoea and a temporary decrease in mean arterial blood pressure. The decrease in blood pressure is not life threatening and is compensated for by changes in heart rate. These animals can be treated solely by intermittent positive pressure ventilation (if required) with either room air or, preferably, oxygen. Recovery is rapid with no residual effects.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

For administration by a veterinarian or under their direct supervision.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN01AX05

4.2 Pharmacodynamics

Alfaxalone (3-α-hydroxy-5-α-pregnane-11,20-dione) is a neuroactive steroid molecule with properties of a general anaesthetic. The primary mechanism for the anaesthetic action of alfaxalone is modulation

of neuronal cell membrane chloride ion transport, induced by binding of alfaxalone to GABAA cell surface receptors.

4.3 Pharmacokinetics

In cats following a single intravenous dose of alfaxalone at 5 mg/kg bw, the mean plasma elimination half-life ($t_{1/2}$) is approximately 45 minutes. Plasma clearance is 25 ml/kg/min. Volume of distribution is 1.8 L/kg.

In dogs following a single intravenous dose of alfaxalone at 2 mg/kg bw, the mean plasma elimination half-life ($t_{1/2}$) is approximately 25 minutes. Plasma clearance is 59 ml/kg/min. Volume of distribution is 2.4 L/kg.

In both dogs and cats the elimination of alfaxalone demonstrates non-linear (dose-dependent) pharmacokinetics. *In vitro* cat and dog hepatocyte studies show that alfaxalone experiences both Phase I (cytochrome P450 dependent) and Phase II (conjugation dependent) metabolism. Both cats and dogs form the same five (5) Phase I alfaxalone metabolites. The Phase II metabolites observed in cats are alfaxalone sulphate and alfaxalone glucuronide, while alfaxalone glucuronide is observed in the dog.

Alfaxalone metabolites are likely to be eliminated from the dog and cat by the hepatic/faecal and renal routes, similar to other species.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 62 days.

5.3 Special precautions for storage

Store below 25°C.
Keep the container in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Glass vial with a bromobutyl rubber stopper and aluminium cap.

Pack sizes:
Cardboard box containing 1 vial of 10 ml.
Cardboard box containing 1 vial of 20 ml.
Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis Belgium S.A.,

7. MARKETING AUTHORISATION NUMBER(S)

VPA10387/105/001

8. DATE OF FIRST AUTHORISATION

07/01/2019

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

19/08/2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).