LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

10 ml carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alfaxan 10 mg/ml solution for injection for dogs, cats and pet rabbits
alfaxalone

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

alfaxalone 10 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

[10 ml]

5. TARGET SPECIES

Pictogram of dog, cat, rabbit

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous use.

8. WITHDRAWAL PERIOD

Do not use in rabbits intended for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

User warnings:
This product is a sedative.
In case of accidental self-injection seek immediate medical attention and show the product literature.
Rinse any splashes from skin or eyes immediately with water.

10. EXPIRY DATE

EXP. (month/year)

11. SPECIAL STORAGE CONDITIONS

This product does not contain an antimicrobial preservative. Any solution remaining in the vial following withdrawal of the required dose should be discarded.
Keep the vial in the outer carton.

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

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

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

For animal treatment only.

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

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

16. MARKETING AUTHORISATION NUMBER

Vm 42058/4217

17. MANUFACTURER'S BATCH NUMBER

Batch:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alfaxan 10 mg/ml solution for injection for dogs, cats and pet rabbits
alfaxalone

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

10 mg/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

[10 ml]

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous use.

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Batch

7. EXPIRY DATE

EXP. (month/year)

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Alfaxan 10 mg/ml solution for injection for dogs, cats and pet rabbits
For animal treatment only

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

Marketing Authorisation Holder:
Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

Manufacturers responsible for batch release:
Zoetis Belgium SA
Rue Laid Burniat 1
1348 Lovain-La-Neuve
Belgium

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alfaxan 10 mg/ml solution for injection for dogs, cats and pet rabbits
alfaxalone

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

alfaxalone 10 mg/ml
Clear colourless solution for injection.

4. INDICATION(S)

As an induction agent prior to inhalation anaesthesia in cats, dogs and non-food rabbits.

As a sole anaesthetic agent for the induction and maintenance of anaesthesia for the performance of examination or surgical procedures in cats and dogs.

5. CONTRAINDICATIONS

Do not use in combination with other intravenous anaesthetic agents.

6. ADVERSE REACTIONS

In clinical studies using Alfaxan, 44% of dogs, 19% of cats and 7% of rabbits experienced post induction apnoea, which was defined as the cessation of breathing for 30 seconds or more. The mean duration of apnoea in these animals was 100 seconds in dogs, 60 seconds in cats and 53 seconds in rabbits. Endotracheal intubation and oxygen supplementation should therefore be employed. In rabbits, oxygenation prior to administration of the product for induction of anaesthesia is essential in order to reduce the risk of life-threatening hypoxaemia post-induction occurring secondary to respiratory

depression or apnoea.

In rabbits, behavioural reactions such as head-shaking may be observed during intravenous (marginal ear vein) administration, therefore a pre-placed IV catheter is recommended.

Based on post marketing safety experience, neurological signs (convulsions, myoclonus, tremor, prolonged anaesthesia), cardio-respiratory signs (cardiac arrests, bradycardia, bradypnea) and behavioural signs (hyperactivity, vocalisation) have been reported very rarely (less than 1 animal in 10,000 animals treated).

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs, cats and non-food rabbits.

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

For intravenous use.

Induction of anaesthesia in dogs, cats, and non-food rabbits:
The induction dose of Alfaxan 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		RABBITS	
	Un-premedicated	Premedicated	Un-premedicated	Premedicated	Un-premedicated	Premedicated
mg/kg	3	2	5	5	5	4
ml/kg	0.3	0.2	0.5	0.5	0.5	0.4

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 in non-food rabbits:
Following induction of anaesthesia with Alfaxan, the rabbit may be intubated and anaesthesia maintained with an inhalation anaesthetic agent.

Maintenance of anaesthesia in dogs and cats:
Following induction of anaesthesia with Alfaxan, the animal may be intubated and maintained on Alfaxan or an inhalation anaesthetic agent. Maintenance doses of Alfaxan

may be given as supplemental boluses or as constant rate infusion. Alfaxan has been used safely and effectively in dogs, cats and rabbits 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 each target species. However the actual dose will be based on the response of the individual patient.

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

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

Do not use in rabbits intended for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the vial in the outer carton.
This product does not contain an antimicrobial preservative. Any solution remaining in the vial following withdrawal of the required dose should be discarded.

12. SPECIAL WARNING(S)

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

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

The safety of Alfaxan in animals less than 12 weeks of age (dogs and cats) and16 weeks of age (rabbits) has not been demonstrated.

During recovery, it is preferable that animals are not handled or disturbed. In dogs and cats, this may lead to paddling, minor muscle twitching or movements that are more violent. While better avoided, such reactions are clinically insignificant.

Transient post induction apnoea frequently occurs, particularly in dogs – see Adverse Reactions 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 by slow intravenous injection (over a period of approximately 60 seconds) and not as a rapid dose.

Especially when using higher doses of Alfaxan, a dose-dependent respiratory depression may occur. Oxygen and/or intermittent positive pressure ventilation should be administered to counteract the threatening hypoxaemia/hypercapnea. 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 rabbits, oxygenation is essential before induction of anaesthesia and throughout the entire anaesthetic procedure to avoid potentially life-threatening hypoxaemia.
In 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 dogs and cats have been fasted before receiving the anaesthetic. Rabbits should not be fasted, but food should be removed one hour before anaesthesia.
- 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.

Psychomotor excitement may be encountered in a minority of dogs and cats recovering from Alfaxan anaesthesia. Post-anaesthetic recovery should thus take place in appropriate facilities and under sufficient supervision. Use of a benzodiazepine as the

sole premedicant in dogs and cats may increase the probability of psychomotor excitement.
Muscle twitching/tremors may be observed in a small proportion of rabbits anaesthetised with Alfaxan; however, such reactions are not considered to be clinically significant.

Use during pregnancy and lactation
The safety of Alfaxan 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 product should be used in pregnant animals according to the risk-benefit assessment performed by the veterinarian. The 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 Dosage section) and the product was administered as recommended, to effect.

Interaction with other veterinary medicinal products
In dogs and cats, 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

During clinical studies in rabbits, the veterinary medicinal product was used safely with the following premedicant combinations:
i) medetomidine hydrochloride in combination with buprenorphine hydrochloride or butorphanol tartrate,
ii) midazolam hydrochloride in combination with buprenorphine hydrochloride or butorphanol tartrate.

The concomitant use of other CNS depressants should be expected to potentiate the depressant effects of Alfaxan, necessitating cessation of further administration of Alfaxan when the required depth of anaesthesia has been reached. The use of one premedicant or a combination of premedicants often reduces the dose of Alfaxan 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 Alfaxan.

Also refer to Contraindications section.

Overdose
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), up to 5 times the recommended dose of 5 mg/kg in the cat (i.e. up to 25 mg/kg) and up to 3 times the recommended dose in the rabbit (i.e. up to 15 mg/kg). These excessive doses delivered over 60 seconds caused 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.

User warnings
This 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 immediate medical attention and show the product literature.
The product may cause irritation if it comes into contact with the skin or eyes. Rinse any splashes from skin or eyes immediately with water.

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

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

August 2023

15. OTHER INFORMATION

Pharmacodynamic properties: 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 $GABA_A$ cell surface receptors.

Pharmacokinetic particulars: The volume of distribution after a single injection of clinical doses of 2, 5 and 5 mg/kg bw of alfaxalone in dogs, cats and rabbits is 2.4 L/kg, 1.8 L/kg and 3.6 L/kg, respectively. In cats, the mean terminal plasma elimination half-life ($t_{1/2}$) for alfaxalone is approximately 45 minutes for a 5 mg/kg dose. Mean plasma clearance for a 5 mg/kg dose is 25.1 ± 7.6 ml/kg/min. In dogs, the mean terminal plasma elimination half-life ($t_{1/2}$) for alfaxalone is approximately 25 minutes for a 2 mg/kg dose. Mean plasma clearance for a 2 mg/kg dose is 59.4 ± 12.9 ml/kg/min. In rabbits, the harmonic mean terminal plasma elimination half-life ($t_{1/2}$) for alfaxalone is approximately 44 minutes for a 5 mg/kg dose. Mean plasma clearance for a 5 mg/kg dose is 55.7 ± 13.3 ml/kg/min.

In dogs, cats and rabbits the elimination of alfaxalone demonstrates non-linear (dose-dependent) pharmacokinetics. Alfaxalone metabolites are likely to be eliminated from the dog, cat and rabbit by the hepatic/faecal and renal routes, similar to other species.

Details of the immediate packaging:
A glass vial of 10 ml with a bromobutyl rubber stopper and aluminium cap.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder:

Approved 25 August 2023