

# Alfaxan<sup>®</sup>

(alfaxalone 10 mg/mL)  
Intravenous Injectable Anesthetic



## What is Alfaxan<sup>®</sup> ?

**INDICATIONS:** Alfaxan<sup>®</sup> is indicated for the induction and maintenance of anesthesia and for induction of anesthesia followed by maintenance with an inhalant anesthetic, in cats and dogs.

**Important Alfaxan<sup>®</sup> Risk Information: Warnings, Precautions and Contraindications:** When using alfaxalone, patients should be continuously monitored, and facilities for the maintenance of a patent airway, artificial ventilation, and oxygen supplementation must be immediately available. Alfaxan<sup>®</sup> does not contain an antimicrobial preservative. Do not use if contamination is suspected. Strict aseptic techniques must be maintained because the vehicle is capable of supporting the rapid growth of microorganisms. Careful monitoring of the patient is necessary due to possibility of rapid arousal. Alfaxan<sup>®</sup> is contraindicated in cats and dogs with a known sensitivity to alfaxalone or its components, or when general anesthesia and/or sedation are contraindicated. **Adverse Reactions:** The most common side effects of alfaxalone include respiratory and cardiovascular derangements, such as apnea, hypotension and hypertension. Appropriate analgesia should be provided for painful procedures.

*Repeatable. Reliable. Relax.*

# Alfaxan®: the essential facts

## Active ingredient and mode of action

**Alfaxan® Intravenous Injectable Anesthetic** is an anesthetic induction agent registered for use in dogs and cats, based on the neurosteroid, alfaxalone. This molecule is similar in structure to progesterone. It works at the same trans-membrane GABA<sub>A</sub> receptor as other (non-dissociative) anesthetic induction drugs.

Alfaxalone binds to a site on the receptor resulting in the opening of the chloride pore, allowing entry of chloride ions.<sup>[1,2]</sup> This causes hyperpolarization of the neurone and inhibition of impulse transmission which gives the molecule its anesthetic properties.

**Alfaxalone is short-acting and is rapidly cleared from the circulation<sup>[3]</sup> and Alfaxan® is suitable for use as an induction, and/or maintenance, anesthetic agent.**

## The development history of Alfaxan®

In the early part of the twentieth century there was a growing recognition of the potential of certain endogenous hormones to act as agents of sedation. Systematic research, beginning in the 1940s, produced a number of candidate compounds among which alfaxalone showed most promise in terms of safety and efficacy.<sup>[4, 5, 6]</sup>

Initial attempts at development and marketing of an anesthetic based on the alfaxalone molecule were not successful as the active ingredient is not soluble in aqueous solution and was consequently formulated in suspension with a castor oil derivative, Cremophor. This compound produced undesirable side effects which manifested as allergic-type reactions.<sup>[7]</sup> The two products containing alfaxalone which were then available, Althesin in human anesthesia and Saffan in veterinary anesthesia, were withdrawn from the market.

However, work continued to develop a formulation that did not cause the above effects.<sup>[8, 9]</sup> Finally in the late 1990s alfaxalone was formulated in cyclodextrin, a complex sugar that allowed solubilization in aqueous solution without the effects seen with the earlier products.

This formulation is now marketed across the globe as **Alfaxan®**. It is currently registered and marketed in Australia, New Zealand, South Africa, France, the UK,

the Republic of Ireland, Germany, the Netherlands, Spain, Canada, Belgium and Thailand. **Alfaxan®** is now also available in the U.S.

**Alfaxan®** is a 1% (10 mg/mL) clear, colourless, aqueous, pH neutral, iso-osmolar solution of alfaxalone in cyclodextrin and sterile water. It contains no preservative. It is marketed in 10 mL vials. Once **Alfaxan®** has been opened, vial contents should be drawn into sterile syringes; each syringe should be prepared for single patient use only. Unused product should be discarded within 6 hours.<sup>[10]</sup>

**Alfaxan®** is registered for the induction and/or maintenance of anesthesia in dogs and cats. It can be used to maintain anesthesia by intermittent intravenous boluses.

## Use of Alfaxan®: tolerance studies

**Alfaxan®** does not cause tissue irritation after peri-vascular, subcutaneous or intramuscular injection.<sup>[11]</sup>

Acute tolerance to over-dosage with **Alfaxan®** has been demonstrated up to **5 times** the recommended dose of 5 mg/kg in cats and up to **10 times** the recommended dose of 2 mg/kg in dogs.<sup>[12, 13]</sup>

Repeated overdosing of **Alfaxan®** at **5 times** the recommended rate in dogs and **5 times** the recommended rate in cats, at 48 hour intervals on 3 occasions over 7 days, caused no clinical pathology.<sup>[14, 15]</sup>

**Alfaxan®** can be used to supply anesthesia in juvenile patients - puppies from 12 weeks of age<sup>[16]</sup> and kittens from 4 weeks of age.<sup>[17]</sup>

**Alfaxan®** has been proven to be reliable and effective as an anesthetic induction agent in canine Caesarean section.<sup>[18]</sup>

**Alfaxan®** has been proven to be a reliable and effective anesthetic induction agent in sight hounds.<sup>[19]</sup>

## Pharmacokinetics/pharmacodynamics

The active ingredient of **Alfaxan**<sup>®</sup>, alfaxalone is rapidly eliminated from the body after a single dose, being completely cleared within a few hours.<sup>[3]</sup>

After administration of **Alfaxan**<sup>®</sup> the duration of unconsciousness will vary due to a range of factors. As a general guide, at recommended doses and without premedication, cats will remain anesthetized for approximately 25 minutes and dogs for approximately 10 minutes.<sup>[12, 13]</sup> Concomitant use of sedative and analgesic medications can be expected to decrease the dose

requirements for **Alfaxan**<sup>®</sup> and alter the duration of the resulting anesthesia.

## Cardiorespiratory profile

Patients induced with **Alfaxan**<sup>®</sup> in accordance with the label generally maintain clinically acceptable blood pressure parameters, breathe spontaneously and maintain clinically acceptable respiratory rate.<sup>[21, 22]</sup>

Alfaxan can cause dose dependant alterations in cardio-respiratory functions.

## Features and Benefits of Alfaxan<sup>®</sup>

**Alfaxan**<sup>®</sup> is a clear, aqueous, pH neutral iso-osmolar solution. Therefore it causes no tissue damage if inadvertently given peri-vascularly.<sup>[11]</sup>

**Alfaxan**<sup>®</sup> contains cyclodextrin as the solubilizing agent. Therefore its use is free of allergic-type histaminic reactions. It can be used in both cats and dogs.<sup>[20]</sup>

**Alfaxan**<sup>®</sup> is a neurosteroid molecule similar to endogenous steroids. Therefore there are well developed metabolic processes to eliminate such molecules and the active ingredient is rapidly cleared, giving little or no post-anesthetic hangover, even after its use in maintenance anesthesia.

With **Alfaxan**<sup>®</sup> there is no induction excitement from sub-anesthetic doses.<sup>[21, 22]</sup> Therefore the injection can be given slowly to effect which means the patient chooses the total dose required, reducing the risk of respiratory depression and allowing a smoother, more rapid transition to maintenance with a gaseous agent.

**Alfaxan**<sup>®</sup> has minimal dose-dependant effects on cardiovascular function.<sup>[12, 13]</sup> Therefore blood pressure is generally well maintained and provides acceptable tissue perfusion, important in sustaining normal tissue/organ function.

**Alfaxan**<sup>®</sup> administered as recommended causes minimal dose-dependent respiratory depression.<sup>[21, 22]</sup> Therefore patients often breathe normally, assisting in smooth transition to gaseous maintenance. Apnea and respiratory depression can occur after alfaxalone administration.

**Alfaxan**<sup>®</sup> provides good muscle relaxation.<sup>[12, 13]</sup> Therefore there is no need for adjunctive muscle relaxants.

**Alfaxan**<sup>®</sup> has an extremely wide safety margin, proven in acute tolerance<sup>[12, 13]</sup> as well repeated over-dosage<sup>[14, 15]</sup> trials. Therefore clinic staff can be comfortable in the knowledge that over-dosage can generally be managed with supportive care of respiratory and cardiovascular function.

**Alfaxan**<sup>®</sup> has been proven reliable in young animals.<sup>[16, 17]</sup> Therefore it can be given to kittens as young as 4 weeks and puppies as young as 12 weeks of age.

**Alfaxan**<sup>®</sup> has been evaluated as a safe and effective induction agent in bitches prior to caesarean section.<sup>[18]</sup> Therefore there is no need for a specific drug for such cases, if **Alfaxan**<sup>®</sup> becomes the clinic's routine induction agent.

**Alfaxan**<sup>®</sup> has been proven compatible with the major groups of premedication agents.<sup>[19, 21-34]</sup> Therefore the introduction of **Alfaxan**<sup>®</sup> to the clinic does not alter the premedication protocols which have been used to date.

**Alfaxan**<sup>®</sup> is a rapid, short acting induction agent with a wide safety margin.<sup>[12, 13]</sup> Therefore it is not a stressful experience introducing the drug into the clinic and experience can be quickly gained with confidence, by all members of staff.

Following a single dose of **Alfaxan**<sup>®</sup>, alfaxalone, the active ingredient, is rapidly metabolized in the liver and eliminated in the bile and urine, with the drug being completely cleared from the body within a few hours.<sup>[3]</sup> Therefore the patient returns to normal behavior sooner and can go home with its owners at the shortest practicable time after anesthesia.

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The FOI statement for Alfaxan<sup>®</sup>[NADA#141-342] can be reviewed at:

<http://www.fda.gov/downloads/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/UCM326904.pdf>

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