FREEDOM OF INFORMATION SUMMARY

ORIGINAL REQUEST FOR ADDITION TO THE INDEX OF LEGALLY MARKETED UNAPPROVED NEW ANIMAL DRUGS FOR MINOR SPECIES

MIF 900-031

Alfaxan® Multidose IDX
(alfaxalone)
Injectable Solution

For sedation and anesthesia in captive reptiles, excluding any food-producing species

For sedation and anesthesia in captive amphibians, excluding any food-producing species

For sedation and anesthesia in ornamental fish, including species used in research such as the zebra fish

For sedation and anesthesia in captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, excluding any food-producing species

For sedation and anesthesia in non-human primates

For sedation and anesthesia in captive rodents

For sedation and anesthesia in captive mustelids

For sedation and anesthesia in captive marsupials

For induction of anesthesia and immobilization in captive minor species ungulates, excluding any food-producing species

Requested by:
Jurox PTY LTD
# TABLE OF CONTENTS

I. **GENERAL INFORMATION:** ................................................................. 1

II. **EFFECTIVENESS AND TARGET ANIMAL SAFETY:** .............................................. 2
    A. Findings of the Qualified Expert Panel: ...................................................... 2
    B. Literature Considered by the Qualified Expert Panel: .............................. 4

III. **USER SAFETY:** .................................................................................. 8

IV. **AGENCY CONCLUSIONS:** ................................................................. 9
    A. Determination of Eligibility for Indexing: .................................................. 10
    B. Qualified Expert Panel: .......................................................................... 10
    C. Marketing Status: .................................................................................. 11
    D. Exclusivity: .......................................................................................... 11
I. GENERAL INFORMATION:

File Number:
MIF 900-031

Requestor:
Jurox PTY LTD
85 Gardiner Street
Rutherford, New South Wales, 2320
Australia

U.S. Agent:
James H. Schafer, DVM
Schafer Veterinary Consultants, LLC
800 Helena Court
Fort Collins, CO 80524

Proprietary Name:
Alfaxalone

Established Name:
Alfaxan® Multidose IDX

Pharmacological Category:
Anesthetic; Drug Enforcement Agency (DEA) Schedule IV (CIV) controlled substance

Dosage Form:
Injectable solution

Amount of Active Ingredient:
10 mg alfaxalone/mL

How Supplied:
10 and 20 mL vials

How Dispensed:
by Prescription (Rx)

Dosage:
Dependent on species

Routes of Administration:
Intravascular (IV) injection, Intramuscular (IM) injection, Subcutaneous (SC) injection, Intraperitoneal (IP) injection, or Immersion

Species/Class:
Captive reptiles, captive amphibians, ornamental fish, captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, non-human
Indications:

- For sedation and anesthesia in captive reptiles, excluding any food-producing species
- For sedation and anesthesia in captive amphibians, excluding any food-producing species
- For sedation and anesthesia in ornamental fish, including species used in research such as the zebra fish
- For sedation and anesthesia in captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, excluding any food-producing species
- For sedation and anesthesia in non-human primates
- For sedation and anesthesia in captive rodents
- For sedation and anesthesia in captive mustelids
- For sedation and anesthesia in captive marsupials
- For induction of anesthesia and immobilization in captive minor species ungulates, excluding any food-producing species

II. EFFECTIVENESS AND TARGET ANIMAL SAFETY:

In accordance with 21 CFR part 516, a qualified expert panel evaluated the target animal safety and effectiveness of Alfaxan® Multidose IDX, for sedation and anesthesia in multiple minor species, to determine whether the benefits of using Alfaxan® Multidose IDX for the proposed uses outweigh its risks to the target animals. The members of the qualified expert panel were:

Angela Lennox, DVM, DABVP (Avian), DECZM (Small Mammal) - Panel Leader
Nigel Caulkett, DVM, MVetSc, DACVAA
Cora Lau, PhD
Gregory Lewbart, MS, VMD, DACZM, DECZM (Zoo Health Management)

A. Findings of the Qualified Expert Panel:

The qualified expert panel thoroughly reviewed all available literature concerning the use of alfaxalone in the relevant minor species. Approximately one hundred and eight (108) articles were available for the review. Expert panel members conducted an in-depth review of each piece of literature and determined if the study design would allow conclusions on safety and effectiveness to be confidently relied upon. Results of the in-depth reviews were summarized, and conclusions were drawn regarding dose rates which could be confidently predicted to be safe and effective in the various minor species. Of the 108 articles reviewed by the expert panel, only information from 68 articles was
found acceptable for use in the construct of the dosage and administration section of the product labeling and package insert. The literature reviewed by the expert panel included the following species:

<table>
<thead>
<tr>
<th>Category</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphibians</td>
<td>oriental fire-bellied toad, Australian frog, axolotl</td>
</tr>
<tr>
<td>Minor Species Birds</td>
<td>flamingo, swan, budgerigar, Bengalese finch</td>
</tr>
<tr>
<td>Ornamental Fish</td>
<td>goldfish, oscar, koi carp, zebrafish</td>
</tr>
<tr>
<td>Marsupials</td>
<td>koala, possum, glider, wombat, wallaby, kangaroo</td>
</tr>
<tr>
<td>Mustelids</td>
<td>ferret</td>
</tr>
<tr>
<td>Non-human primates</td>
<td>macaque, marmoset, lemur</td>
</tr>
<tr>
<td>Reptiles</td>
<td>red-bellied black snake, lowland copperhead snake, eastern tiger snake, coastal carpet python, black-headed python, ball python, garter snake, eastern bluetongue lizard, blotched bluetongue lizard, coastal bearded dragon, inland bearded dragon, Gippsland water dragon, green iguana, veiled chameleon, leopard gecko, perentie monitor, red-eared slider turtle, Hamann’s tortoise, spur-thighed tortoise, margined tortoise, Russian tortoise, Horsfield’s tortoise, red-footed tortoise, pond slider, loggerhead sea turtle</td>
</tr>
<tr>
<td>Rodents</td>
<td>mice, rat, guinea pig, chinchilla</td>
</tr>
<tr>
<td>Minor Species Ungulates</td>
<td>alpaca</td>
</tr>
</tbody>
</table>

In addition, the expert panel members had varying degrees of personal experience with the use of alfaxalone for sedation and anesthesia of the minor species animals. Based on a thorough review of the literature, and their own personal experience, the qualified expert panel concluded that the benefits of using Alfaxan® Multidose IDX for sedation and anesthesia in captive reptiles, captive amphibians, ornamental fish, captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, non-human primates, captive rodents, captive mustelids, captive marsupials; and for induction of anesthesia and immobilization in minor species ungulates outweigh the risks to the target animals.
B. Literature Considered by the Qualified Expert Panel:


18. Escalante GC, Balko JA, Chinnadurai, SK. Intramuscular alfaxalone or butorphanol and midazolam in budgerigars Comparison of the sedative effects of intramuscular alfaxalone with intramuscular butorphanol midazolam in the budgerigar (Melopsittacus undulatus). Accepted into J Av Med Sx, 2018.


52. Radkey DI, Hardie RJ, Smith LJ. Comparison of the effects of alfaxalone and propofol with acepromazine, butorphanol and/or doxapram on laryngeal motion and quality of examination in dogs. Vet Anaesth Analg 2018; May 45(3): 241-249.


### III. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Alfaxan® Multidose IDX:
WARNINGS


Alfaxan® Multidose IDX should be managed to prevent the risk of diversion, through such measures as restriction of access and the use of drug accountability procedures appropriate to the clinical setting.

Exercise caution to avoid accidental self-injection. Overdose is likely to cause cardiorespiratory depression (such as hypotension, bradycardia and/or apnea). Remove the individual from the source of exposure and seek medical attention. Respiratory depression should be treated by artificial ventilation and oxygen. Avoid contact of this product with skin, eyes, and clothes. In case of contact, eyes and skin should be liberally flushed with water for 15 minutes. Consult a physician if irritation persists. In the case of accidental human ingestion, seek medical advice immediately and show the package insert or the label to the physician.

The Safety Data Sheet (SDS) contains more detailed occupational safety information. To report adverse reactions in users or to obtain a copy of the SDS for this product call 1-844-253-2926.

Note to physician: This product contains an injectable anesthetic.

DRUG ABUSE AND DEPENDENCE

Controlled substance: Alfaxan® Multidose IDX contains alfaxalone a neurosteroid anesthetic and a class IV controlled substance.

Abuse: Alfaxalone is a central nervous system depressant that acts on GABA receptor associated chloride channels, similar to the mechanism of action of Schedule IV sedatives such as benzodiazepines (diazepam and midazolam), barbiturates (phenobarbital and methohexital) and fospropofol. In a drug discrimination behavioral test in rats, the effects of alfaxalone were recognized as similar to those of midazolam. These biochemical and behavioral data suggest that alfaxalone has an abuse potential similar to other Schedule IV sedatives.

Physical dependence: There are no data that assess the ability of alfaxalone to induce physical dependence. However, alfaxalone has a mechanism of action similar to the benzodiazepines and can block the behavioral responses associated with precipitated benzodiazepine withdrawal. Therefore, it is likely that alfaxalone can also produce physical dependence and withdrawal signs similar to that produced by the benzodiazepines.

Psychological dependence: The ability of alfaxalone to produce psychological dependence is unknown because there are no data on the rewarding properties of the drug from animal self-administration studies or from human abuse potential studies.

IV. AGENCY CONCLUSIONS:

The information submitted in support of this request for Alfaxan® Multidose IDX for addition to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (Index) for the following intended uses satisfies the requirements of section 572 of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 516:
For sedation and anesthesia in captive reptiles, excluding any food-producing species

For sedation and anesthesia in captive amphibians, excluding any food-producing species

For sedation and anesthesia in ornamental fish, including species used in research such as the zebra fish

For sedation and anesthesia in captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, excluding any food-producing species

For sedation and anesthesia in non-human primates

For sedation and anesthesia in captive rodents

For sedation and anesthesia in captive mustelids

For sedation and anesthesia in captive marsupials

For induction of anesthesia and immobilization in captive minor species ungulates, excluding any food-producing species

A. Determination of Eligibility for Indexing:

As part of the determination of eligibility for inclusion in the Index, FDA determined that the drug for this intended use was safe to the user, did not individually or cumulatively have a significant effect on the human environment, and that the description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the new animal drug was sufficient to demonstrate that the requestor has established appropriate specifications for the manufacture of the new animal drug. Additionally, the requestor has committed to manufacture the drug in accordance with current good manufacturing practices (cGMP).

The Index is only available for new animal drugs intended for use in minor species for which there is a reasonable certainty that the animal or edible products from the animal will not be consumed by humans or food-producing animals and for new animal drugs intended for use only in a hatchery, tank, pond, or other similar contained man-made structure in an early, non-food life stage of a food-producing minor species, where safety for humans is demonstrated in accordance with the standard of section 512(d) of the act. Because this new animal drug is not intended for use in food-producing animals, FDA did not require data pertaining to drug residues in food (i.e., human food safety) for granting this request for addition to the Index.

B. Qualified Expert Panel:

The qualified expert panel for Alfaxan® Multidose IDX met the selection criteria listed in 21 CFR 516.141(b). The panel satisfactorily completed its responsibilities in accordance with 21 CFR part 516 in determining the target animal safety and effectiveness of Alfaxan® Multidose IDX for sedation and anesthesia in captive
reptiles, captive amphibians, ornamental fish, captive species and pet birds in the orders Psittaciformes, Passeriformes, and Columbiformes, non-human primates, captive rodents, captive mustelids, captive marsupials; and for induction of anesthesia and immobilization in minor species ungulates.

C. Marketing Status:

Alfaxan® Multidose IDX will be marketed by prescription.

D. Exclusivity:

Products listed in the Index do not qualify for exclusive marketing rights.