Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

VetOne Fluriso 1000 mg/g Inhalation Vapour Liquid

Date Created: July 2020

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	VetOne Fluriso 1000 mg/g Inhalation Vapour Liquid,
Applicant	Piramal Critical Care Limited Suite 4 Ground Floor Heathrow Boulevard East Wing 280 Bath Road West Drayton UB7 0DQ United Kingdom
Active substance	Isoflurane
ATC Vetcode	QN01AB06
Target species	Horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets.
Indication for use	Induction and maintenance of general anaesthesia

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	7th May 2020.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, VetOne Fluriso 1000 mg/g Inhalation Vapour Liquid, submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product is IsoFlo 100% w/w Inhalation Vapour, Liquid, authorised in the UK since March 1996 The product is indicated for horses, dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets, for the induction and maintenance of anaesthesia. For administration, refer to the Summary of Product Characteristics (SPC) for the large range of recommendations and interactions for the various species for the product. The product must not be used in cases of known susceptibility to malignant hyperthermia or known cases of hypersensitivity to isoflurane.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC. The product is safe for the user, the consumer of foodstuffs from treated animals, (horses: meat and offal: 2 days. Not authorised for use in mares producing milk for human consumption), and for the environment, when used as recommended.

Suitable warnings and precautions are indicated in the SPC. The efficacy [1] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

[1] Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 1000 mg/g isoflurane. There are no excipients.

The container/closure system consists of Type III amber glass bottles containing 100 ml or 250 ml of isoflurane, fitted with a black polypropylene screw cap with a low-density polyethylene cone insert.
The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the absence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists simply of the filling of isoflurane into bottles.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is isoflurane, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

The container/closure system meets requirements.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control of the final product is the same as the active substance specification.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years.
Do not store above 25°C. Protect from direct sunlight and direct heat.
Store in tightly closed original container.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

As this was an application for a generic product, pharmacological and toxicological data were not required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- Do not breathe the vapour. Users should consult their National Authority for advice on Occupational Exposure Standards for isoflurane.
- Operating rooms and recovery areas should be provided with adequate ventilation or scavenging systems to prevent the accumulation of anaesthetic vapour.
- All scavenging/ extraction systems must be adequately maintained.
- Exposure to anaesthetics can harm the unborn child. Pregnant and/or breast- feeding women should not have any contact with the product and should avoid operating rooms and animal recovery areas.

- Avoid using masking procedures for prolonged induction and maintenance of general anaesthesia.
- Use cuffed endotracheal intubation when possible for the administration of isoflurane during maintenance of general anaesthesia.
- Care should be taken when dispensing isoflurane, with any spillage removed immediately using an inert and absorbent material e.g. sawdust.
- Wash any splashes from skin and eyes and avoid contact with the mouth.
- If severe accidental exposure occurs remove the user from the source of exposure, seek urgent medical assistance and show this label.
- Halogenated anaesthetic agents may induce liver damage. In case of isoflurane this is an idiosyncratic response very rarely seen after repeated exposure.
- *Advice to Doctors:* Ensure a patent airway and give symptomatic and supportive treatment. Note that adrenaline and catecholamines may cause cardiac dysrhythmias.

Other Precautions

Although anaesthetics have a low potential for damage to the atmosphere, it is good practice to use charcoal filters with scavenging equipment, rather than to discharge them into the air.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
A phase I ERA was submitted, written in accordance with appropriate guidance. The assessment ended at question five, as the product will be used for a small number of horses. It ended at question three for the remaining target species, as none of these are food-producing species.

The applicant included the same environmental warning and disposal advice as for the reference product, and this is acceptable.

III.B.2 Residues documentation

Residue Studies

The product has the same pharmaceutical form and contains 1000 mg/g of isoflurane with no excipients, which is the same as the reference product. It is an inhalation vapour anaesthetic intended for food-producing horses, as well as non-food producing dogs, cats, ornamental birds, reptiles, rats, mice, hamsters, chinchillas, gerbils, guinea pigs and ferrets. Isoflurane is in Table 1 of Commission Regulation 37/2010 of pharmacologically active substances.

The application has been submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/82/EC, and has been demonstrated to be essentially similar to an established reference product 'IsoFlo Inhalation vapour, liquid'. Therefore, no studies are required to demonstrate the pharmacokinetics and residue depletion, as these can also be considered equivalent to those of the reference product.

MRLs

A 'No MRL required' entry is given for *Equidae,* and no pharmacokinetic or residues studies have been submitted. However, the applicant proposed the same two-day withdrawal period for meat as for the reference product, which is acceptable given the legal basis of the application. The product is not indicated for mares producing milk for human consumption. This is considered acceptable to ensure consumer safety.

Withdrawal Periods

Based on the data provided, the withdrawal period of for horses is:
Meat and offal: 2 days
Not authorised for use in mares producing milk for human consumption.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Due to the legal basis of the application, not preclinical or clinical data were required, as the proposed product was deemed identical to the reference product. Criteria 7.1 d) and f) of the current EMA veterinary bioequivalence guideline (EMA/CVMP/016/2000-Rev.3) are both applicable, i.e:

d) 'the formulations are identical (identical active substances and excipients as well as physicochemical properties [e.g. identical concentration, dissolution profile, crystalline form, pharmaceutical form and particle size distribution with identical manufacturing process])'

and:

f) 'the product is intended to be a gas for inhalation at the time of administration'.

Therefore, it was not necessary for the applicant to conduct an in vivo bioequivalence study.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics the benefit/risk profile of the product is favourable.

MODULE 4

POST- AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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