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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid

15 february 2016

MODULE 1

PRODUCT SUMMARY

Marketing Authorisation number (Dutch)	REG NL 117045
EU Procedure number	NL/V/0196/001/DC
Name, strength and pharmaceutical form	ISOFLURIN 1000 mg/g Inhalation Vapour, Liquid [BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, LT, LU, LV, NL, PL, PT, SI, SK, UK] FUXIEN vet 1000 mg/g Inhalation Vapour, Liquid [DK, FI, NO, SE]
Marketing Authorisation Holder (MAH)	Vetpharma Animal Health, S.L.
Active substance(s)	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 website:
http://mri.medagencies.org/veterinary/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised Procedure	18 November 2015
Concerned Member States for original procedure	BG, CZ, ES, FR, HR, IE, LT, LV, PL, PT, SI, SK.

I. SCIENTIFIC OVERVIEW

Isoflurin 1000 mg/g Inhalation Vapour, Liquid, 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; the slight reactions observed are indicated in the SPC.
Isoflurin 1000 mg/g Inhalation Vapour, Liquid, is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

The safety and efficacy aspects of Isoflurin 1000 mg/g Inhalation Vapour, Liquid are based on bioequivalence with the *ISOFLO 100% w/w vloeistof voor inhalatiedamp* (REG NL 9132).
Warnings statements and precautions are adopted from the reference product.
Adverse events, warnings and contraindications are indicated in the SPC.

QUALITY ASPECTS

A. COMPOSITION

The product contains 1000 mg/g isoflurane.
The container system is an amber type III glass container with a polypropylene screw cap.

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

B. METHOD OF PREPARATION OF THE PRODUCT

The applicant is utilising an active substance which complies with the European Pharmacopoeial monograph, and therefore is of appropriate quality.

Comparative impurity profile data for the product and reference product were also not required.

The preparation of the product consists of the filling of 100 ml and 250 ml bottles. Batch size is considered to be the volume held within the holding tank used to fill the bottles. The liquid is poured into the bottles and the bottles are then sealed

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. CONTROL OF STARTING MATERIALS

The active substance isoflurane is 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.
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.

A certificate of suitability is granted for isoflurane by the EDQM:
R0-CEP 2010-078-Rev 01 to Shandong New Time Phar. Co., Ltd., China.

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

D. CONTROL ON INTERMEDIATE PRODUCTS

Not applicable.

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.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. The finished product tests mirror those for the active substance

specification, (see Control of Starting Materials), because the product is 100% isoflurane. This was considered satisfactory.

Acceptable batch analysis data were submitted for three pilot scaled batches per pack volume of the product, adhering to the methods specified in the European Pharmacopoeia.

F. STABILITY

A re-test period of 36 months if stored in a polyethylene/steel complex drum with a polyethylene cap for isoflurane is granted by the EDQM.

Sufficient stability data in accordance with applicable European guidelines on the finished product have been provided, therefore, the shelf-life and storage conditions are acceptable.

G. OTHER INFORMATION

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and clinical tests tests are not required.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers. Adverse events, warnings and contraindications are indicated in the SPC.

III.A Safety Testing

User Safety

The applicant has provided a brief summary regarding user safety. Being a generic procedure the applicant refers to the reference product for information on this section.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

As the product is an anaesthetic and used to treat a small number of animals the ERA ends in Phase I and a Phase II assessment is not deemed necessary.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, no residue depletion studies were conducted.

MRLs

Isoflurane has been evaluated by the EMA according to the Council Regulation (EEC) No. 2377/90 and it has been considered that there is no need to establish an MRL for isoflurane.

Withdrawal Periods

The applicant proposes the same withdrawal time as approved for the reference product. As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, a withdrawal period of 2 days for meat in horses is justified and is adequate to ensure consumer safety.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

This section 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.

18 November 2020	Renewal