IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Vetofol 10 mg/ml Emulsion for Injection for Cats and Dogs

PRODUCT SUMMARY

EU Procedure Number	IE/V/0533/001 (formerly UK/V/0440/001)
Name, Strength, Pharmaceutical Form	Vetofol 10 mg/ml Emulsion for Injection for Cats and Dogs
Active Substances(s)	Propofol
Applicant	Norbrook Laboratories (Ireland) Limited Rossmore Industrial Estate Monaghan Ireland
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cats, Dogs
Indication For Use	The veterinary medicinal product is a short-acting, intravenous, general anaesthetic for procedures of short duration, lasting up to 5 minutes: For the induction and maintenance of general anaesthesia using incremental doses to effect, For the induction of general anaesthesia where maintenance is provided by inhalation anaesthetics
ATC Code	QN01AX10
Date of completion of the original mutual recognition procedure	27 June 2012 (UK)
Date product first authorised in the Reference Member State (MRP only)	09 January 2009 (UK) 31 August 2012 (IE)
Concerned Member States for original procedure	Denmark, France, Ireland (now RMS), Italy, Norway, Sweden. UK added via RMS change

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive

2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The product is an emulsion for injection containing 1 % w/v propofol. It is indicated for use in dogs and cats as a short-acting, intravenous general anaesthetic for procedures of short duration, lasting up to 5 minutes. Also for the induction and maintenance of general anaesthesia using incremental doses to effect and for the induction of general anaesthesia where maintenance is provided by inhalation anaesthetics. Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs is particularly suitable for cases where a short recovery period is desired. The dose rate is 4.0 - 6.5 mg/kg bodyweight for dogs and 6.0 - 8.0 mg/kg bodyweight for cats.

This Mutual Recognition application is for a generic product in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC. Bioequivalence is claimed with the reference product, Rapinovet 10 mg/ml Emulsion for Injection which has been approved in the UK since 1987.

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, the slight reactions observed are indicated in the SPC. The product is safe for the user, 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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains the active substance propofol and the excipients soya bean oil, egg lecithin, glycerol, sodium hydroxide and water for injection.

The product is packaged in a cardboard box containing one clear glass (Type I) vial of 20 ml or one clear glass (type I) vial of 50 ml. The vials are closed with bromobutyl bungs and aluminium caps.

The choice of the formulation and the absence of a preservative have been 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 product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is propofol an established active substance described in the European Pharmacopoeia (Ph. Eur.). 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 excipients glycerol, soya bean oil, sodium hydroxide and water for injections used in the formulation are supplied against Ph. Eur. monographs and are commonly used in veterinary medicines. Nitrogen meets the requirements of the current Ph. Eur. monographs for Nitrogen and Nitrogen Low Oxygen. Egg lecithin does not appear in the Ph. Eur or the Pharmacopoeia of a member state. It is the subject of a food additive monograph (E322) and a draft monograph for the United States Pharmacopoeia (USP). The supplier's specification is comprehensive, includes the important elements of both of these monographs and is considered to give a very good level of control.

The packaging materials are stated to meet the requirements of the relevant monographs of the Ph. Eur. for containers for parenteral products.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

No material of animal origin is used in the formulation of the product apart from egg lecithin, which is not of ruminant origin.

E. Control on intermediate products

There are no intermediate products.

F. 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.

G. 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.

Stability data on the finished product were provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

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 pharmacological and toxicological 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 and the environment.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment 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:-

- This is a potent drug: particular care should be taken to avoid accidental self-administration. A guarded needle should preferably be used until the moment of injection.
- Wash off splashes from the skin and eyes immediately.
- In the event of accidental self- administration, seek urgent medical attention and show the label to the doctor. **Advice to Doctor:** Do not leave the patient unattended. Maintain airways and give symptomatic and supportive treatment.

Ecotoxicity
The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required.

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

IV. CLINICAL ASSESSMENT

This is an application for a national Marketing Authorisation for a generic product submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/28/EC. Bioequivalence is claimed with the reference product, which has been authorised in the UK since 1987. Bioequivalence has been demonstrated so the results of pre-clinical and clinical trials are not required.

IV.A Pre-Clinical Studies
Pharmacology
Pharmacodynamics
No pharmacodynamic data for the active substance has been supplied. Inductofol 10mg/ml Emulsion for Injection for Cats and Dogs has the same qualitative and quantitative composition, and is the same pharmaceutical form as the reference product. Propofol is one of a group of alkylphenols with anaesthetic properties. Distribution is extensive and elimination rapid, the main site of metabolism being the liver to produce water soluble glucuronide and sulphate conjugates which are excreted in the urine.

Pharmacokinetics
A comparative *in vivo* bioavailability study was conducted in dogs. This study demonstrated bioequivalence between Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs and the reference product.

Tolerance in the Target Species of Animals
Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of bioequivalence new tolerance data is not required as it has already been presented for the reference product. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies
The results of clinical trials are not a requirement for this type of application. However, a bioequivalence study was conducted in dogs. This study demonstrated the bioequivalence of Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs

with the reference product. Acceptable justification for the omission of an *in vivo* bioequivalence study conducted in cats was provided.

The qualitative and quantitative composition and pharmaceutical form of Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs and the reference product are very similar and the dissolution and dispersion of propofol in the blood are the same. Bioequivalence has been adequately demonstrated between the product and the reference product. Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs is accepted as having comparable safety and efficacy to 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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.