



**ASSURING THE SAFETY, QUALITY AND EFFICACY
OF VETERINARY MEDICINES**

**United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS**

MUTUAL RECOGNITION PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

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

**PuAR correct as of 10/10/2018 when RMS was transferred to IE. Please contact
the RMS for future updates.**

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0440/001/MR
Name, strength and pharmaceutical form	Inductofol 10 mg/ml Emulsion for Injection for Cats and Dogs
Applicant	Norbrook Laboratories Limited Station Works Camlough Road Newry Co. Down BT35 6JP Northern Ireland
Active substance(s)	Propofol
ATC Vetcode	QN01AX10
Target species	Dogs and cats
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

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

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 completion of the original mutual recognition procedure	27 th June 2012.
Date product first authorised in the Reference Member State (MRP only)	9 th January 2009.
Concerned Member States for original procedure	Denmark, France, Ireland, Italy, Norway, Sweden.

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.¹ 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.

¹ SPC – Summary of Product Characteristics.

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 particulars of the containers and controls performed are provided and conform to the regulation.

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 from 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 container is a clear, colourless Type I, glass bottle containing 20 ml or 50 ml of the solution. The containers are closed with bromobutyl bungs and a crimped aluminium seal is then applied. The packaging materials are stated to meet the requirements of the relevant monographs of the Ph. Eur. for containers for parenteral products. The secondary pack is a printed cardboard box containing one vial and a package leaflet.

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

A declaration and Format 3 statement in compliance with revised CVMP guidelines was provided. 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 were provided by the active substance manufacturer. The data supported a 24 month retest interval.

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.

A shelf life of 2 years was considered justified under the appropriate storage conditions: Do not store above 25°C. Protect from light.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years. Withdrawn product should be used immediately. Product remaining in the container should be discarded. Do not store above 25°C, do not freeze.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

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 (EFFICACY)

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.

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.

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