IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Carprieve 20 mg Tablets for Dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0153/001/MR
Name, strength and pharmaceutical form	Carprieve 20 mg Tablets for dogs
Active substance(s)	Carprofen
Applicant	Norbrook Laboratories (Ireland) Limited, Rossmore Industrial Estate, Monaghan, Ireland
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	28 April 2004
Target species	Dogs
Indication for use	Reduction of inflammation and pain caused by musculoskeletal disorders and degenerative joint disease. As a follow up to parenteral analgesia in the management of post operative pain.
ATCvet code	QM01AE91
Concerned Member States	AT

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 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.Qualitative and Quantitative Particulars

The products contain 20 mg of carprofen and the excipients microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, povidone K30, sodium laurelsulfate and magnesium stearate.

The container/closure systems are either polypropylene snap secure tubs sealed with cotton wool and white polyethylene snap secure caps or aluminium/aluminium blister strips.The choice of the formulation is justified.
The product is an established pharmaceutical form and their 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 has been presented in accordance with the relevant European guidelines.
The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C.Control of Starting Materials

The active substance is carprofen, 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.

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

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 products.
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.

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

G.Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application is a generic application according to Article 13 of Directive 2001/82/EC, as amended.

Comparative pharmacokinetic data provided in support of the application show that the test product (Carprieve Tablets) is bioequivalent to the reference product (Rimadyl Tablets, VPA 10019/63/1-2); consequently, it can be concluded that the systemic effects of the two products in respect of safety and efficacy will be the same. To further support the safety of the final formulation, the Applicant has provided the results of a study that clearly demonstrates that the product is well tolerated in juvenile dogs when administered at up to 3 times the recommended treatment dose for 15 days. The proposed SPC for Carprieve reflects the authorised SPC of the reference product in Ireland.
In respect of user safety, the most likely route of human exposure to carprofen is through the skin or by deliberate ingestion. However, when the product is used in accordance with label recommendations the product is unlikely to result in toxicity. No specific user warnings are proposed.

The product is not expected to pose a hazard to the environment.

III.B Residues Documentation

Not applicable.

IV. CLINICAL ASSESSMENT

This application is a generic application according to Article 13 of Directive 2001/82/EC, as amended.

Comparative pharmacokinetic data provided in support of the application show that the test product (Carprieve Tablets) is bioequivalent to the reference product (Rimadyl Tablets, VPA 10019/63/1-2). The CVMP 'Guidelines for the conduct of bioequivalence studies for veterinary medicinal products' states that the aim in bioequivalence testing is 'to demonstrate that two medicinal products produce plasma concentrations similar enough to conclude that the systemic effects of the two products, in respect to efficacy (and possibly safety), are the same' i.e. there should not exist a biologically relevant difference in the rate and extent of absorption between the test and the reference product.

Based on the findings of an *in vivo* bioequivalence study, it is accepted that the carprofen kinetics following repeated oral administration of Carprieve Tablets to dogs will be similar to carprofen kinetics following repeated oral administration of the reference product. That is, the product can be considered bioequivalent.

In addition to providing data demonstrating that Carprieve Tablets are bioequivalent to Rimadyl, the Applicant has provided data to confirm that the final formulation is well tolerated when administered to dogs at doses up to three times the recommended treatment dose for 14 days. However, as a NSAID, it is acknowledged that carprofen administration may cause adverse gastrointestinal effects. Further, episodes of carprofen associated hepatic toxicosis have been reported in the published literature. Carprofen associated hepatic toxicosis is idiosyncratic and host dependant. Appropriate warning statements are included on the SPC.

The SPC for Carprieve reflects the authorised SPC of the reference product in Ireland.

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.

VI. 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 HPRA website.

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.

Changes:

Safety/Efficacy Changes

Summary of change **(Application number)**	**Approval date**
SPC amended in line with the SPC of the 100 mg tablet strength of another of the applicant's carprofen containing products (with identical formulation) recently	14th April 2010

authorised via a European procedure (Carprogesic 100 mg Tablets UK/V/0319/001/DC). IE/V/0208/001-002/II/004	