IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Rimifin 50 mg Tablets for dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0184/001-003
Name, strength and pharmaceutical form	Rimifin 50 mg Tablets for dogs
Active substances(s)	Carprofen
Applicant	Chanelle Pharmaceuticals Manufacturing Limited Loughrea Co. Galway Ireland
Legal basis of application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Date of completion of the original mutual recognition procedure **Date product first authorised in the Reference Member State (MRP only)**	27 September 2006 03 March 2006
Target species	Dogs
Indication for use	Reduction of inflammation and pain caused by musculo-skeletal disorders and degenerative joint disease. As a follow up to parenteral analgesia in the management of post-operative pain following soft tissue surgery.
ATCvet code	QM01AE91
Concerned Member States	AT, CZ, DK, EE, EL, ES FI, FR, HU, IS, LV, LT, NO, PL, SE, NL

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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

• *A.1 Composition of the Veterinary Medicinal Product*

Active Substance : Carprofen (20 mg, 50 mg and 100mg)

Excipients : Lactose monohydrate
Microcrystalline cellulose
Colloidal silicon dioxide
Magnesium stearate

·*A.2 Container/Closure System*

• White HDPE twist-off plastic container with child proof tamper evident polypropylene white twist off closures

• Blister packs made up of a PVC/PVdCwith a Hard Temper Aluminium Foil

• *A.3 Clinical Trial Formula(e)*

The formulation of the batch used in key clinical studies is identical to that proposed for marketing.

• *A.4 Development Pharmaceutics*

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

• *B.1 Manufacturing Formula*

This information is commercially confidential.

• *B.2 Method of Preparation*

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

• *B.3 Validation of the Manufacturing Process*

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

C Control of Starting Materials

• C.1 Active Substance

The active substance is Carprofen, an established active substance.
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.

• *C.2 Other Substance(s)*

Other substances in the product comply with relevant European Pharmacopoeia monographs.

• *C.3 Packaging Materials*

• The product is packaged in white HDPE twist-off plastic containers and blister packs.

The packaging materials comply with relevant EU standards.

D Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
Scientific data have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

E Intermediate Products

Not applicable.

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

• G.1 Stability Studies on the Active Substance

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.2 Stability Tests on the Finished Product*

Stability data on the product 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.

H Other Information

None.

Conclusion on Quality

The manufacture of the product is adequately described and controlled. Testing methods and specifications for the raw materials and packaging components are acceptable. The control tests and specifications for the finished product are appropriate. The shelf life and storage conditions are supported by appropriate stability data.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, on the basis of essential similarity.
Comparative pharmacokinetic data provided in support of the application show that the test product (Rimifin Tablets) is bioequivalent to the reference product (Rimadyl Tablets, VPA 10019/63/1-3); 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 14 days. The proposed SPC for Rimifin 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

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, on the basis of essential similarity.
Comparative pharmacokinetic data provided in support of the application show that the test product (Rimifin Tablets) is bioequivalent to the reference product (Rimadyl Tablets, VPA 10019/63/1-3). 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.

In the *in vivo* bioequivalence study, the values for the AUC and C_{max} fell within the prescribed confidence intervals. Based on the data proved, it is accepted that the carprofen kinetics following repeated oral administration of Rimifin Tablets to dogs will be similar to carprofen kinetics following repeated oral administration of the reference product.
In addition to providing data demonstrating that Rimifin Tablets are essentially similar 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. It should be noted that episodes of carprofen associated hepatic toxicosis have been reported in the published literature. Carprofen associated hepatic toxicosis is idiosyncratic and host dependant. An appropriate warning statement is included on the SPC: 'As with other NSAIDs there is a risk of rare renal or idiosyncratic hepatic adverse events.' The SPC for Rimifin 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 risk benefit 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 veterinarymedicinal product. The current SPC is available on the HPRA website.