IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Curofen 50 mg/g Premix for Medicated Feeding Stuff for Pigs

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PRODUCT SUMMARY

EU Procedure Number	IE/V/0372/001/DC
Name, Strength, Pharmaceutical Form	Curofen 50 mg/g Premix for Medicated Feeding Stuff for Pigs
Active Substances(s)	Fenbendazole
Applicant	Univet Limited Tullyvin Cootehill Co. Cavan. Ireland
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Pigs
Indication For Use	
ATC Code	QP52AC13

PUBLIC ASSESSMENT REPORT

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 product is safe for the user, the consumer and 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 product contains 50 mg/g of the active substance fenbendazole and the excipients glucose monohydrate and colloidal anhydrous silica.

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The container/closure system consists of low density polyethylene bags in pack sizes of 1 kg, 2 kg, 4 kg, 20 kg and 25 kg. Secondary packaging consists of polypropylene containers (1, 2, and 4 kg pack sizes), cardboard drums (20 kg pack size) and triple layered paper bags (25 kg pack size).

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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

C.Control of Starting Materials

The active substance is fenbendazole, an established 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 has 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

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justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods has been provided.

Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F.Stability

Stability data on the active substance has 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 has 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 has been submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC for a generic veterinary medicinal product. The reference product cited in the application is Curazole 5% w/w Premix for Medicated Feed (VPA 10990/030/001). The marketing authorisation for the reference product is also owned by the applicant. As the candidate formulation is manufactured by the same finished product manufacturer using the same manufacturing process, the candidate formulation can be accepted as being identical to that of the reference product and consequently, bioequivalence between candidate and reference product formulations can be assumed.

Warnings and precautions as listed on the product literature are in line with those approved for the reference product and are considered adequate to ensure safety of the product to users, the environment and consumers of foodstuffs from animals treated with the product.

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III.A Safety Testing Pharmacological Studies

Based upon the data provided, it was accepted that the composition of the candidate formulation is identical to that of the reference product and consequently, the omission of pharmacodynamic and pharmacokinetic data could be accepted.

Further, an exemption from the requirement to demonstrate *in-vivo*bioequivalence, in accordance with section 7.1.d of the relevant CVMP bioequivalence guidelines, was considered to have been satisfactorily justified.

Toxicological Studies

No toxicological data was provided on the basis that the candidate formulation is identical to that of the reference product. In accordance with Article 13.1, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product. It was accepted that the criteria set out in section 7.1.d of the CVMP bioequivalence guideline have been met and the candidate and reference formulations can be considered bioequivalent in the absence of *in-vivo*bioequivalence study data. Consequently, the omission of toxicological data could be accepted.

User Safety

The applicant provided a user safety assessment. As the composition of the candidate formulation is identical to that of the reference product and is to be administered to pigs using the same posology and route of administration already approved for the reference product, the potential risk to the user from handling, storing, administering or disposing of the candidate formulation will not differ (i.e. won't be greater) than that which already exists for the reference product. Warnings and precautions as listed on the product literature are considered adequate to ensure safety to users of the product.

Environmental Risk Assessment
Phase I

The applicant provided an environmental impact assessment and determined the predicted environmental concentrations of fenbendazole following proposed use of the product in weaner pigs, fattening pigs and sows (with litter).

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As all calculated $PEC_{soil\ initial}$values fall below the trigger value of 100 µg/kg and pigs are not considered as pasture animals for the purpose of an environmental risk assessment, a phase II assessment was not required and the environmental risk assessment can stop in Phase I.

Conclusion
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC. Suitable risk mitigation measures and/or advice were included in the SPC for this product and which are in line with that agreed for other similar products recently authorised via European procedures.

It was accepted that the product will not present an unacceptable risk for the environment when stored, handled, administered and disposed of in accordance with the recommendations included in the SPC.

III.B Residues Documentation Residue Studies

No residue depletion studies were conducted because the candidate formulation is identical to that of the reference product and is to be administered to the same target species using the same posology and administration route.

In accordance with Article 13.1, the applicant is not required to provide the results of residue tests if he can demonstrate that the medicinal product is a generic of a reference medicinal product.

It was concluded that residue depletion data are not required and that the distribution and the rate and extent of depletion of residues from tissues in the target species following administration of the candidate formulation will be the same as that for the reference product.

MRLs

Fenbendazole is included in table 1 of Commission Regulation (EU) No. 37/2010 as follows:

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Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissues	Other provisions
Fenbendazole	Sum of extractable residues which may be oxidised to oxfendazole sulfone	All food-producing species except fin fish.	50 µg/kg 50 µg/kg 500 µg/kg 50 µg/kg 10 µg/kg 1300 µg/kg	Muscle Fat Liver Kidney Milk Eggs	For porcine and poultry species the fat MRL relates to 'skin and fat in natural proportions'.

Withdrawal Periods

As the candidate formulation is identical to that of the reference product and both products are manufactured using the same manufacturing process and finished product manufacturer and are to be administered using the same posology and route of administration in the same target species, no difference between candidate and reference formulations in respect of the rate or extent of depletion of residues from tissues in the target animal is to be expected. An MRL exists for the active substance and the excipients are considered as being covered by the CVMP's list of substances considered as not falling within the scope of Regulation (EC) NO. 470/2009.

It can be accepted that the 6 days withdrawal period for meat and offal approved for the reference product, is also applicable for the candidate formulation and is considered adequate to ensure consumer safety.

IV. CLINICAL ASSESSMENT

This application has been submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC for a generic veterinary medicinal product. As the candidate

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formulation is manufactured by the same finished product manufacturer using the same manufacturing process, the candidate formulation can be accepted as being identical to that of the reference product and consequently, bioequivalence between candidate and reference product formulations can be assumed.

IV.A Pre-Clinical Studies

No data provided on the basis that the candidate formulation is identical to that of the reference product. In accordance with Article 13.1, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product.
It was accepted that the criteria set out in section 7.1.d of the CVMP bioequivalence guideline have been met and the candidate and reference formulations can be considered bioequivalent in the absence of *in-vivo*bioequivalence study data. Consequently, the omission of pre-clinical study data could be accepted.

Tolerance in the Target Species of Animals

No data on target animal tolerance as provided on the basis that the candidate formulation is identical to that of the reference product. In accordance with Article 13.1, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product.

It was accepted that the criteria set out in section 7.1.d of the CVMP bioequivalence guideline have been met and the candidate and reference formulations can be considered bioequivalent in the absence of *in-vivo*bioequivalence study data.

As the candidate formulation is to be administered to the same target species using the same posology and route of administration already approved for the reference product, no difference in tolerance in the target animal is to be expected between candidate and reference product formulations. The omission of target animal tolerance data was therefore accepted.

Resistance

No data on resistance was provided on the basis that the candidate formulation is identical to that of the reference product. In accordance with Article 13.1, the applicant is not required to provide the results of safety and residue tests or of pre-

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clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product.

It was accepted that the criteria set out in section 7.1.d of the CVMP bioequivalence guideline have been met and the candidate and reference formulations can be considered bioequivalent in the absence of *in-vivo*bioequivalence study data.

As the candidate formulation is to be administered to the same target species using the same posology and route of administration already approved for the reference product, no difference in terms of risk for development of anthelmintic resistance is to be expected between candidate and reference product formulations.

Adequate warnings and precautions have been included in the product literature.

IV.B Clinical Studies

Laboratory Trials
Field Trials

No efficacy data was provided on the basis that the candidate formulation is identical to that of the reference product. In accordance with Article 13.1, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product.

It was accepted that the criteria set out in section 7.1.d of the CVMP bioequivalence guideline have been met and the candidate and reference formulations can be considered bioequivalent in the absence of *in-vivo*bioequivalence study data.

As the candidate formulation is to be administered to the same target species using the same posology and route of administration already approved for the reference product, no difference in terms of effectiveness is to be expected between candidate and reference product formulations.

It was concluded that the product will be as effective as the reference product for the proposed indications when the product is stored, handled, administered and disposed of in accordance with the recommendations included in the SPC.

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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

Note: not all variations are to be listed here, only those that materially affect the content of the original Public Assessment Report.

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:
None.

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