IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Vetimec 6 mg/g Premix for medicated feeding stuff for pigs.

PRODUCT SUMMARY

EU Procedure number	IE/V/0342/001/DC
Name, strength and pharmaceutical form	Vetimec 6 mg/g Premix for medicated feeding stuff for pig
Active substances	Ivermectin
Applicant	ECO Animal Health Europe Limited 6th Floor South Bank House Barrow Street Dublin 4 D04 TR29 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	22/01/2015
Target species	Pigs
Indication for use	Treatment of nematode or arthropod infections
ATCvet code	QP54AA01
Concerned Member State	ES, PT

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 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 product is safe for the user, the consumer of foodstuffs from treated animals 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 product contains the active substance ivermectin (6 mg/g) and the excipients propyl gallate, butylhydroxyanisole, hydrogenated castor oil, distilled monoglyceride and corn cob.

The product is packaged in foil sachets containing 333 g of product or in a foil bag inside a polypropylene/paper laminate bag containing 5.0 kg of product.

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 ivermectin, 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 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)

III.A Safety Testing

Pharmacological Studies

Pharmacodynamics
The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application, and therefore data on pharmacodynamics are not required. In support of the pharmacodynamics of ivermectin, the Clinical Expert has referred to the CVMP Summary Report (No. 5) for ivermectin (EMEA/MRL/915/04-final) which summarises the mode of action of macrolytic lactone endectocides such as ivermectin.

Pharmacokinetics
In support of this application, the applicant conducted a single *in vivo* study for the purposes of demonstrating that the product and the reference product (Ivomec Premix for Pigs) are bioequivalent.

The study demonstrated that after administration of the product to swine, at the recommended dose rate of 0.1 mg ivermectin per kg bodyweight for 7 consecutive days in diet, the mean plasma steady state concentration (Css) after the last dose was 4.45 ng/ml.The mean maximum plasma concentration (Cmax) after the last administration was 5.81 ng/ml occurring at (Tmax) approximately 5 hours after the last administration.Thereafter, mean plasma concentrations declined exponentially with the mean plasma half life (t½) up to 72 hours after the last dose representing 26 hours.By 120 hours after the last dose, mean plasma concentrations of ivermectin were below the limit of quantification of the assay in most animals.

Toxicological Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. Based on data provided in support of this application, the product has been shown to be bioequivalent to the reference product (Ivomec Premix for Pigs). Consequently, specific toxicological data relating to the active substance are not required for the test product.

The excipients in the test product are all either listed in Commission Regulation (EU) No 37/2010 for all food producing species or are considered to fall outside the scope of products requiring the establishment of MRLs.

User Safety

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application.

On the basis that bioequivalence to the reference product has been demonstrated, it is accepted that, when used in accordance with label recommendations, the test product should not pose any greater risk to the user than the risks associated with use of the reference product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I
A Phase II ERA was required as the product is an endectoparasiticide. The Phase I assessment showed that the trigger of 100 µg/kg was not exceeded.

Phase II Tier A
A Phase II Tier A assessment was conducted.

Based on the information provided it was concluded that the product would not pose a risk to organisms in the terrestrial environment. However, a potential risk to aquatic organisms was identified.
In order to further characterise the risk for the aquatic environment, a refinement of predicted exposures was undertaken.

Based upon the data provided the product will not present an unacceptable risk for the environment and a Tier B assessment was not necessary.

Conclusion
Based on the data provided the product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

In line with other ivermectin premix products, the following disposal statements have been included in section 6.6 of the SPC:

'Extremely dangerous to fish and aquatic life.Do not contaminate surface waters or ditches with the product or used container. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.'

III.B Residues Documentation

Residue Studies

No confirmatory residue studies specific to the product have been provided.Based on the findings of the bioequivalence study it is argued that overall systemic exposure is similar between the test and reference products.Consequently, it is argued that the depletion of residues following the administration of the product in the target species will, at worst, be comparable to that of the referenceproduct and that, on this basis, the withdrawal period of the reference product can be applied to Vetimec 6 mg/g Premix for medicated feeding stuff for pigs.

MRLs

Ivermectin is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

	Pigs
Muscle	30 µg/kg
Liver	100 µg/kg
Kidney	30 µg/kg
Fat/ skin	100 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 12 days for meat in pigs is justified.

IV. CLINICAL ASSESSMENT

IV.APre-Clinical Studies

Pharmacology

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application).

In vivo data provided in support of the application show that the product is bioequivalent to the reference product (Ivomec Premix for Pigs). Consequently, it can be expected that the systemic effects of the two products in respect of efficacy will be the same.

The indications for use and posology reflect those authorised for the reference product.

Tolerance in the Target Species of Animals

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. Therefore, the applicant has not provided specific target animal tolerance data for the test product. Given that bioequivalence has been demonstrated, it is argued that the tolerance profile of the active substance component of the test product will be similar to that of the reference product. Further, the excipients are either listed in Commission Regulation (EU) No 37/2010 or fall outside the scope of the MRL regulations and, consequently, are not expected to present any additional safety risk to the target species.

Given that:

- the product is an oral dose form
- bioequivalence with an authorised reference product is claimed
- the toxicological profile of the active substance is well known and has been adequately characterised in the published literature
- the excipients are recognised as being safe

the absence of tolerance studies specific to the product was accepted.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. Therefore specific clinical data for the test product have not been provided.

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.