IPAR

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vetmulin 162 mg/ml Solution for Injection for pigs
IE/V/0225/001/DC

1 PRODUCT SUMMARY

EU Procedure number	IE/V/0225/001/DC
Name, strength and pharmaceutical form	Vetmulin 162 mg/ml Solution for Injection for pigs
Applicant	Huvepharma NV Uitbreidingsstraat 80 2600 Antwerpen Belgium
Active substance	Tiamulin
ATC Vet Code	ATC Vet Code: QJ01XQ01 Pharmacotherapeutic group: Antibacterials for systemic use, pleuromutilins
Target species	Pigs
Indication for use	For treatment and prevention of swine dysentery caused by *Brachyspira hyodysenteriae*. The product is not appropriate for use for the prevention of disease at the level of herd treatment but should only be used for prevention of swine dysentery in individual animals with a known history of exposure to diseased animals. For the treatment of enzootic pneumonia caused by tiamulin-susceptible *Mycoplasma hyopneumoniae* and mycoplasmal arthritis caused by tiamulin-susceptible *Mycoplasma hyosynoviae.*

2 PUBLIC ASSESSMENT REPORT

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic, Article 13(1) Reference product: Tiamutin 200mg/ml Solution for Injection (Novartis)
Date of completion of the	Not applicable.

original mutual recognition procedure	
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	AT,BE,CZ,DE,DK,EL,ES,FR,HU,IT,NL,PL,PT,UK,BG,RO

2.1 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.

2.2 Quality Aspects

Composition

The product contains 162 mg/ml tiamulin base in a formulation also containing ethanol, propyl gallate, butylated parahydroxybenzoate and sesame oil.

Containers
Composition: type I amber glass provided with a nitrile stopper and sealed by an aluminium cap.

Pack size: 100 ml vials

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

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 have been presented in accordance with the relevant European guidelines.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

Control of Starting Materials

The active substance is Tiamulin 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

No materials of animal origin are used in the product.

Control on intermediate products

Not applicable.

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.

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 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.

Genetically Modified Organisms

Not applicable.

Other Information

Not applicable.

2.3 Safety and residues assessment (pharmaco-toxicological)

III.A Safety Testing

Pharmacological Studies

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application). Vetmulin 162 mg/ml Solution for Injection for pigs contains the same qualitative and quantitative composition in terms of active ingredient as the reference product Tiamutin 200mg/ml Solution for Injection. The applicant conducted a single GLP *in vivo* study to compare the pharmacokinetics of tiamulin following administration of Vetmulin 162 mg/ml Solution for Injection for pigs and the reference product Tiamutin 200mg/ml Solution for Injection. The confidence intervals for the pivotal pharmacokinetic parameters (Cmax and AUC) fell within the acceptable ranges according to the relevant guideline and the two products can be considered bioequivalent.

Toxicological Studies

As this application is made in accordance with Article 13(1) of Directive 2001/82/EC as amended, and the product is bioequivalent to the reference product, no toxicological studies are required.
The applicant conducted a residue study in pigs, a secondary objective of which was to determine the local tolerance of the test product. The test product was well tolerated in pigs. Local irritation was noted at the site of administration in some animals. Appropriate warnings are included in the SPC.

User Safety

The provisions of the Guideline on user safety for veterinary medicinal products (EMEA/CVMP/543/03-FINAL) do not apply to applications made in accordance with Article 13(1) of the Directive. However the applicant provided a brief user safety assessment. It is accepted that for Vetmulin 162 mg/ml Solution for Injection for pigs, user safety will be similar to the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

An environmental risk assessment in compliance with the relevant guidelines was presented. It is accepted that the product when used in accordance with label recommendation does not present an unacceptable risk to the environment. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

As this is a generic application according to Article 3(1) of Directive 2001/82/EC, and bioequivalence with a reference product has been demonstrated, results of safety and residue tests are not required. However, as this product is for intramuscular administration, in addition to a bioequivalence study the applicant has provided a GLP residue study to determine residue depletion rates at the injection site.
Following intramuscular administration of the product, no marker residue (sum of metabolites that may be hydrolysed to 8-□-hydroxymutilin) was detected at the injection site of any animal up to 14 days post administration. Residues of the parent active substance (Tiamulin) were identified at the injection site up to 14 days post administration. The withdrawal period was determined using an ADI approach and inclusion of an appropriate safety factor of 25%.

MRLs

Tiamulin is listed in Annex I of Council Regulation 2377/90. The marker substance is the sum of metabolites that may be hydrolysed to 8-α-hydroxymutilin.

MRLs are listed below:

	Porcine
Muscle	100 µg/kg
Liver	500 µg/kg

Withdrawal Periods
Based on the data provided above a withdrawal period of 21 days was agreed.

2.4 Clinical Assessment

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

An *in vivo* bioequivalence study has been presented in support of the application and shows that the test product (Vetmulin 162 mg/ml Solution for Injection for pigs) is bioequivalent to the reference product (Tiamutin 200mg/ml Solution for Injection). Consequently, it can be concluded that the systemic effects of the two products in respect of efficacy and target animal tolerance will be the same.

2.5 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.