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AGENCE NATIONALE DU MEDICAMENT VETERINAIRE**

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

TYLUCYL 200 mg/ml solution for injection for cattle and pigs

DATE: 11 April 2016

French agency for food, environmental and occupational health safety– French Agency for Veterinary Medicinal Products
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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0289/001/DC
Name, strength and pharmaceutical form	TYLUCYL 200 mg/ml solution for injection for cattle and pigs
Applicant	VETOQUINOL SA Magny-Vernois 70200 Lure FRANCE
Active substance(s)	Tylosin
ATC Vetcode	QJ01FA90
Target species	Cattle Pigs
Indication for use	<p>For the treatment of specific infections conditions (stated below) caused by microorganisms susceptible to tylosin.</p> <p>Cattle (adult): -Respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by <i>Streptococcus spp</i>, <i>Staphylococcus spp</i> or <i>Mycoplasma spp</i> and interdigital necrobacillosis, i.e. panaritium or foot root.</p> <p>Calves: -Respiratory infections and necrobacillosis.</p> <p>Pigs (more than 25 kg): -Enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis. -Arthritis caused by <i>Mycoplasma spp</i>. and <i>Staphylococcus spp</i>. For information regarding swine dysentery see section 4.5.</p>

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website <http://mri.medagencies.org/veterinary/>

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	27/01/2016
Concerned Member States for original procedure	AT – BE – CY – CZ – DE – DK – EE – EL – ES – FI – HR – HU – IE – IT – LT – LU – LV – MT – NL – PL – PT – RO – SE – SI – SK – UK

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 reactions that may be observed are indicated in the SPC, with information on the frequency.

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 claims for these products are equivalent to those of the reference product with taking also into account the decision of the European Commission in a referral on oral products containing Tylosin to be used in pigs.

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

II. QUALITY ASPECTS

A. *Composition*

The product contains 200 000 IU/ml of tylosin and the following excipients: benzyl alcohol, propylene glycol and water for injections.

The product is packed in glass vials. The particulars of the containers and controls performed are provided and conform to the regulation.

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 from a licensed manufacturing site.

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

C. Control of Starting Materials

The active substance is tylosin, 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.

D. 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.

E. Control on 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

A re-test period for the active substance is set in the certificate of suitability issued by EDQM.

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.

An in-use shelf-life as detailed on the SPC has been supported by appropriate data.

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H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT

Based on exemption 7.1. b) of the “Guidelines on the conduct of bioequivalence studies for veterinary medicinal products” (EMA/CVMP/016/00-Rev.2), it is accepted that the test product is bioequivalent to the reference product TYLAN 200 marketed by LILLY FRANCE and authorized in France since 15/12/1980. As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests are not required.

III.A Safety Testing

Pharmacological Studies

The pharmacological aspects of this product are identical to those of the reference product.

Toxicological Studies

The toxicological aspects of this product are identical to those of the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that all PEC soil values were below the trigger threshold of 100 µg/kg.

No warnings to ensure safety to the environment are therefore required when the product is used as directed.

III.B Residues documentation

Residue Studies

No residue depletion studies were required, based on exemption 7.1. b) of the “Guidelines on the conduct of bioequivalence studies for veterinary medicinal products” (EMA/CVMP/016/00-Rev.2) and in accordance with the CVMP guideline “Approach towards harmonisation of withdrawal periods” (EMEA/CVMP/036/95).

MRLs

The active substance tylosin is listed in table 1 of Council Regulation 37/2010. The marker substance is Tylosin A.

MRLs are listed below:

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification	Regulation
Tylosin A	All food producing species	100 µg/kg 100 µg/kg 100 µg/kg 100 µg/kg 50 µg/kg 200 µg/kg	Muscle Fat Liver Kidneys Milk Eggs	For fin fish the muscle MRL relates to « muscle and skin in natural proportions ». MRLs for fat, liver and kidney do not apply for fish. For porcine and poultry species, the fat MRL relates to “skin and fat in natural proportions”.	Anti-infectious agents/ Antibiotics	37/2010 of 22.12.2009

The MRL status of excipients is indicated in the following table :

Excipient	MRL status
Benzyl alcohol	Table1, no MRL required
Propylene glycol	Table1, no MRL required
Water for injection	Out of scope

Withdrawal Periods

The same withdrawal periods as the reference product are accepted :

Species	Tissues	Withdrawal periods
Bovine	Meat & offal	28 days
	Milk	108 hours
Pigs	Meat & offal	14 days

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

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IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated based on exemption 7.1. b) of the “Guidelines on the conduct of bioequivalence studies for veterinary medicinal products” (EMA/CVMP/016/00-Rev.2), efficacy studies are not required.

IV.A Pre-Clinical Studies

Pharmacology

The pharmacological aspects of this product are identical to those of the reference product.

Tolerance in the Target Species of Animals

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

Resistance

The bibliography regarding the susceptibility or resistance to tylosin for pathogens but also for commensal bacteria, provided in a context of prudent use of antimicrobials and responsible attitude of the applicant, is difficult to interpret in the absence of clinical break points for tylosin.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

The efficacy claims for this product are equivalent to those of the reference product and take also into account the decision taken by the European Commission in a referral on oral products containing Tylosin to be used in pigs.

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 are acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

None

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 veterinary Heads of Agencies website. <http://mri.medagencies.org/veterinary/>