FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

TYLAXEN 200 MG/ML SOLUTION FOR INJECTION FOR CATTLE, SHEEP, GOATS AND PIGS

Date:
12/02/2013

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0240/001/DC
Name, strength and pharmaceutical form	TYLAXEN 200 mg/ml solution for injection for cattle, sheep, goats and pigs
Applicant	HUVEPHARMA NV UITBREIDINGSTRAAT 80, 2650 ANTWERPEN BELGIUM
Active substance(s)	Tylosin
ATC Vetcode	QJ01FA90
Target species	Cattle, sheep, goats, pigs.
Indication for use	Infections caused my microorganisms susceptible to tylosin. **Cattle (adult):** - Treatment of respiratory infections, metritis caused by Gram-positive micro-organisms, mastitis caused by *Streptococcus* spp., *Staphylococcus* spp. or *Mycoplasma* and interdigital necrobacillosis", i.e. panaritum or foot rot. **Calves**: - Treatment of respiratory infections and necrobacillosis. **Pigs**: - Treatment of enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis. - Treatment of arthritis caused by *Mycoplasma* and *Staphylococcus* spp. **Sheep and goats:** Treatment of respiratory infections, metritis caused by Gram-positive microorganisms, mastitis caused by Gram+ microorganisms or *Mycoplasma* spp.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

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 decentralized procedure	21/12/2012
Concerned Member States for original procedure	AT, BG, DE, DK, EL, ES, HU, IE, IT, PL, PT, RO

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

II. QUALITY ASPECTS

A. Composition

The product contains tylosin (200000UI/ml) and excipients benzyl alcohol, propylene glycol and water for injections.

The container/closure system is a glass vial closed with bromobutyl stopper. 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 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

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.

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

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The test product is bioequivalent to the reference product TYLAN 200 of LILLY. An exemption from the requirement to provide bioequivalence studies is accepted.

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required.

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

Toxicological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

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

User Safety

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

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

Ecotoxicity

The applicant has submitted a Phase I and Phase II Environmental Risk Assessment which showed that no risk for the aquatic and terrestrial compartments is expected.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted since the tested product is bioequivalent to the reference product and since their formulations have been considered sufficiently similar.

MRLs

a. active substances

The active substance, tylosin, is included in table 1 of the MRL regulation 37/2010, as follows:

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

b. excipients

The MRL status of excipients of the product 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 tested product will be applied identical withdrawal periods than the reference product that is:

Cattle
Meat and offal: 28 days.
Milk: 108 hours.

Sheep and goats:
Meat and offal: 42 days.
Milk: 108 hours

Pigs:
Meat and offal: 14 days.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

The applicant has not provided tolerance study which is acceptable because the tested product and the reference product have similar formulations and are bioequivalent.

The tolerance aspects of this product are identical to the reference product. Based on the conclusion made for the reference product, the product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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.