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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dophatyl-ject IM 200 000 IU/ml solution for injection for cattle, sheep, goats, and pigs

FR_V_0481_001_DC

Date:
6 May 2024

PRODUCT SUMMARY

EU procedure number	FR_V_0481_001_DC
Name, strength and pharmaceutical form	Dophatyl-ject IM 200 000 IU/ml solution for injection for cattle, sheep, goats, and pigs
Applicant	DOPHARMA RESEARCH / ZALMWEG 24 – 4941 VX RAAMSDONKSVEER – PAYS-BAS
Active substance(s)	Tylosin
ATC vetcode	QJ01FA90
Target species	Cattle, sheep, goats and pigs
Indication for use	Cattle (adult): - Treatment of respiratory infections, metritis caused by Gram-positive micro-organisms, mastitis caused by *Streptococcus* spp., *Staphylococcus* spp. and interdigital necrobacillosis i.e. panaritium or foot rot. Calves: - Treatment of respiratory infections and necrobacillosis. Sheep and goats: - Treatment of respiratory infections, metritis caused by Gram-positive micro-organisms and mastitis caused by Gram-positive micro-organisms and *Mycoplasma* spp. Pigs: - Treatment of enzootic pneumonia, haemorrhagic enteritis, erysipelas and metritis. - Treatment of arthritis caused by *Mycoplasma* and *Staphylococcus* spp.

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Tylan 200 000 UI/ml
Marketing authorisation holder	ELANCO
MS where the RP is or has been authorised	FRANCE
Marketing authorisation number EU procedure number	FR/V/0474355 6/1980
Date of authorisation	15/12/1980
Concerned Member States for original procedure	NL

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains 200 000 IU/ mL of tylosin for veterinary use and the excipients propylene glycol, benzyl alcohol and water for injections.

The container/closure system is colourless type I glass vial closed with a bromobutyl rubber stopper and sealed by aluminium cap.

The choice of the formulation and presence of preservative are justified.

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

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

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

C. Production and control of starting materials

The active substance is tylosin for veterinary use, an established active substance described in the European Pharmacopeia. 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.

Scientific data have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

D. Control tests carried out on isolated intermediates during the manufacturing process

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 VMP.

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.

F. Stability tests

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 VMP 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.

G. Other information

Not applicable.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of toxicological tests are not required.

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

A. Safety tests

Pharmacological studies

See part IV

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that the risks for the user are similar for candidate and reference product.
Warnings and precautions as listed on the product literature have been updated and are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

According to the Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6 (EMA/CVMP/ERA/622045/2020), as a generic (Pharmasin 200 mg/ml solution) has been approved in 2012, an ERA for the product under application is not needed.

B. Residues documentation

Residue tests

No residue depletion studies were conducted on the basis that bioequivalence with the reference product has been demonstrated.
The absence of residue data is acceptable given that:
- bioequivalence with the reference product is satisfactory documented,
- the formulation of the candidate product is very similar to that of the reference product, has the same physicochemical properties and will be administered at the same posology.

Maximum Residue Limits

Tylosin is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions	Regulation
Tylosin	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”.	37/2010 of 22.12.2009

The composition of the tested product is acceptable according to the European Regulation (EC) No 470/2009.

Withdrawal Periods

The same withdrawal periods approved for the reference product was proposed to be applied to the candidate product.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

The tested product is a solution for injection containing tylosin.
This application is for a generic product, submitted in accordance with Article 18 of Regulation (EU) No. 2019/6, using the decentralised procedure. The reference product is TYLAN 200 000 UI/ml marketed by ELANCO and was first authorised in France on 15/12/1980

A. Pre-Clinical Studies

Pharmaceutical form
The test and the reference products have the same pharmaceutical form: solution for injection

Active substance qualitative and quantitative composition
The test and reference products have the same qualitative and quantitative composition in active substance: 200 000 IU of tylosin per mL.

Bioequivalence studies
The bioequivalence between the test and reference product is satisfactory demonstrated according to the point 7.1 of the GL EMA/CVMP/016/2000-Rev.4*.

Pharmacology

As details on pharmacodynamics and pharmacokinetics have been sufficiently described in the file of the reference product, no further documentation is needed.

Development of resistance and related risk in animals

The applicant provided adequate bibliography. Adequate warnings and precautions appear on the product literature.

Dose determination and confirmation

No dose determination or confirmation studies were provided.

Tolerance in the target species of animals

As bioequivalence is accepted and target animal safety (TAS) has been evaluated for the reference product, the applicant is not required to provide TAS data.
The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

No clinical trials were performed.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.