Institute for State Control of Veterinary Biologicals and Medicines
Hudcova 56a, 621 00 Brno, Czech Republic

(Reference Member State - CZ)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Forespix 100 mg/ml solution for injection for cattle pigs and sheep

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0166/001/DC
Name, strength and pharmaceutical form	Forespix 100 mg/ml solution for injection for cattle, pigs and sheep
Applicant	Vet-Agro Multi-Trade Company Sp. z o.o. Gliniana 32, 20-616 Lublin, Poland
Active substance(s)	Tulathromycin
ATC vet code	QJ01FA94
Target species	Cattle, pigs and sheep
Indication for use	Cattle Treatment and metaphylaxis of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida, Histophilus somni* and *Mycoplasma bovis* susceptible to tulathromycin. The presence of the disease in the group should be established before metaphylactic treatment. Treatment of infectious bovine keratoconjunctivitis (IBK) associated with *Moraxella bovis* susceptible to tulathromycin. Pigs Treatment and metaphylaxis of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae, Pasteurella multocida, Mycoplasma hyopneumoniae, Haemophilus parasuis* and *Bordetella bronchiseptica* susceptible to tulathromycin. The presence of the disease in the group should be established before metaphylactic treatment. The product should only be used if pigs are expected to develop the disease within 2–3 days. Sheep Treatment of the early stages of infectious pododermatitis (foot rot) associated with virulent *Dichelobacter nodosus* requiring systemic treatment.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application – Art. 13.1. of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	18/11/2020
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	BE, BG, DE, EL, ES, FR, HR, HU, IE, IT, LT, NL, PL, PT, RO, SI, SK

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. Qualitative and quantitative particulars

The product contains Tulathromycin 100 mg/ml and the excipients Monothioglycerol (5 mg/ml), Citric acid monohydrate, Propylene glycol, Hydrochloric acid and Sodium hydroxide (pH adjustment) and Water for injection.

The container/closure system is multilayer (coex) plastic vials (PP/HV/EVOH/HV/PP) closed with bromobutyl rubber stopper and aluminium and plastic flip capsule. The proposed pack sizes are: 50, 100 and 250 mL.

The product development is described taking into consideration the product composition, physico-chemical characteristics, method of manufacture and the choice of packaging material. The absence of preservative is justified since the formula is shown self-preserving and compliant with Ph. Eur. requirements. 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.
The product is manufactured using conventional manufacturing techniques. Process validation is provided.

C. Control of Starting Materials

The active substance is Tulathromycin which is not described in the European Pharmacopoeia neither Pharmacopoeia of EU member state. 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 using ASMF procedure and these data are deemed satisfactory. There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

The excipients Citric acid, Propylene glycol, Hydrochloric acid, Sodium hydroxide and WFI are described in Ph. Eur. monographs and these are controlled accordingly. Monothioglycerol is controlled as per USP.

The components of the product packaging comply with the relevant Ph. Eur. texts.

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 have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. 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 29 months without any storage precautions needed. The claim of 28 days stability after first broaching the vial stopper is based on the satisfactory results of the in-use stability studies.

G. Other Information

Not applicable

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

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.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the initial predicted environmental concentrations in soil were less than 100 µg/kg for all target species, both intensively reared animals (cattle and pigs) and pasture animals (cattle and sheep). The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

III.B Residues documentation

Residue Studies

This is a generic application according to article 13 (1) of Directive 2001/82/EC, as amended. The generic product has the same pharmaceutical form as the reference product and the formulation of the generic product is essentially similar to formulation of the reference product Draxxin Solution for injection, marketed by Zoetis Belgium SA, which was first authorised in EU on 11/11/2003 on the basis of the full application.

MRLs

The active substance Tulathromycin is allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissues	Other provisions	Therapeutic classification
Tulathromycin	(2R,3S,4R, 5R,8R,10R, 11R,12S, 13S,14R)-2- ethyl-3,4,10,13-tetra-hydroxy-3,5,8,10,12,14-hexamethyl-11-	Ovine, Carprine	450 µg/kg 250 µg/kg 5400 µg/kg 1800 µg/kg	Muscle Fat Liver Kidney	Not for use in animals from which milk is produced for human consumption	Anti-infectious agents/Antibiotics

	[[3,4,6-trideoxy- 3-(dimethy- lamino)-ß-D- xylo-hexopyranosyl]oxy]-1- oxa-6-azacyclopent-decan-15-one expressed as tulathromycin equivalents					
		Bovine	300 µg/kg 200 µg/kg 4500 µg/kg 3000 µg/kg	Muscle Fat Liver Kidney		
		Porcine	800 µg/kg 300 µg/kg 4000 µg/kg 8000 µg/kg	Muscle Skin and fat in natural proportion Liver Kidney		

All constituents of the intended product Forespix are included in Table 1 of Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin or are considered as not falling within the scope of Regulation (EC) No 470/2009.

Withdrawal Periods

Based on the data provided above the following withdrawals periods are established:

Cattle (meat and offal): 22 days.
Pigs (meat and offal): 13 days.
Sheep (meat and offal): 16 days.

Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals, which are intended to produce milk for human consumption, within 2 months of expected parturition.

IV. CLINICAL ASSESSMENT (EFFICACY)

Since this is a generic application submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, and the omission of bioequivalence studies has been justified, results of clinical studies are not required. The applicant has proposed the same indications as already approved for the reference product Draxxin Solution for injection, marketed by Zoetis Belgium SA, which was first authorised in EU on 11/11/2003 on the basis of the full application.

Resistance

The bibliography provided suggests that current situation and trends in resistance development are showing that resistance to tulathromycin is at a low level.
Adequate warnings and precautions appear on the product literature to ensure prudent use of the product of the concern.

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.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

None