Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Huvexxin 100 mg/ml Solution for Injection for Cattle, Pigs and Sheep

Date Created: March 2023

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Huvexxin 100 mg/ml Solution for Injection for Cattle, Pigs and Sheep
Applicant	Huvepharma N.V. Uitbreidingstraat 80 Antwerp, B-2600 Belgium
Active substance	Tulathromycin
ATC Vetcode	QJ01FA94
Target species	Cattle, Pigs and Sheep
Indication for use	<u>Cattle</u> 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 must be established before the product is used. Treatment of infectious bovine keratoconjunctivitis (IBK) associated with Moraxella bovis susceptible to tulathromycin. <u>Pigs</u> 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 must be established before the product is used. The veterinary medicinal product should only be used if pigs are expected to develop the disease within 2–3 days. <u>Sheep</u> 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 Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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 conclusion of the procedure	01/02/2023

I. SCIENTIFIC OVERVIEW

The proposed dosage is 2.5 mg tulathromycin per kilogram bodyweight as a single subcutaneous (cattle) or intramuscular (pigs and sheep) injection. A maximum injection site volume of 7.5 ml has been set for cattle. In pigs, a maximum injection site volume of 2.0 ml has been set.

The reference product for Huvemycin 100 mg/ml Solution for Injection is Draxxin 100 mg/ml Solution for Injection for Cattle, Pigs and Sheep, authorised via the centralised procedure on 11 November 2003 and marketed by Zoetis Belgium SA (EU/2/03/041/001-005). The applicant is claiming exemption from the requirement for bioequivalence studies in accordance with exemption 7.1.b) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 3-corr).

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, any reactions observed are indicated in the SPC.[1] 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 [2] 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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains Tulathromycin at 100mg/ml and the excipients monothioglycerol, propylene glycol, citric acid, hydrochloric acid, sodium, hydroxide and water for injections.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

The container/closure system consists of Type I colourless glass vials with chlorobutyl rubber stoppers and aluminium overseals. 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.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of sequential addition and dissolution of the ingredients in water for injections.

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

II.C. Control of Starting Materials

The active substance is tulathromycin, an established active substance. 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.

Supporting data was provided in the form of an ASMF. Information establishing compliance with the European Pharmacopoeia or the USNF was provided for all the excipients.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 has been provided demonstrating compliance with the specification. Control tests on the

finished product are those for: Appearance, degree of coloration, clarity, identification of tulathromycin/ monothioglycerol, pH, density, content of tulathromycin, component composition, chromatographic impurities, content of monothioglycerol, visible particles, bacterial endotoxins, sterility and extractable volume.

II.F. Stability

Stability data on tulathromycin 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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale :2 years.
Shelf life after first opening the immediate packaging: 28 days.

This veterinary medicinal product does not require any special storage conditions.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological / Toxicological Studies

In accordance with the application type, toxicological and pharmacological data have not been provided, other than to support the user risk assessment (URA). This approach was considered acceptable since bioequivalence with the reference product has been demonstrated.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that in comparison with the respective reference product, the generic products contain the same concentration of active substance and the same excipients in similar amounts, are of the same pharmaceutical form, and are administered at the same dose and by the same route of administration, to the same target animal species. Therefore, the hazard, exposure and risks from the use of the generic products will be equivalent to those of the respective reference products.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore, the following applicant's user recommendations are appropriate:

- Tulathromycin is irritating to eyes. In case of accidental eye exposure, flush the eyes immediately with clean water.
- Tulathromycin may cause sensitisation by skin contact resulting in e.g., reddening of the skin (erythema) and/or dermatitis. In case of accidental spillage onto skin, wash the skin immediately with soap and water.
- Wash hands after use.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- If there is suspicion of a hypersensitivity reaction following accidental exposure (recognised by e.g., itching, difficulty in breathing, hives, swelling on the face, nausea, vomitus) appropriate treatment should be administered. Seek medical advice immediately and show the package leaflet or the label to the physician.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The environmental risk assessment stopped in Phase I at question 17 of the decision tree because the initial predicted environmental concentration (PEC) in soil is less than 100 µg/kg. A Phase II ERA was not therefore required.

III.B.2 Residues documentation

Residue Studies

Residue depletion studies studies were not required because this is a generic application according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with a reference product has been demonstrated.

MRLs

Tulathromycin is listed in Table 1 of Regulation 37/2010 and MRLs have been established for Muscle, Liver, Kidney and Fat/Skin.

MRLs are listed below:

	Cattle	Pigs	Sheep
Muscle	300 µg/kg	800 µg/kg	450 µg/kg
Liver	4500 µg/kg	4000 µg/kg	5400 µg/kg

Kidney	3000 µg/kg	8000 µg/kg	1800 µg/kg
Fat / skin	200 µg/kg	300 µg/kg	250 µg/kg

Withdrawal Periods

As this is a generic application according to Article 13(1) of Directive 2001/82/EC as amended. Based on the data provided, the withdrawal period is the same as that for the reference product:

Meat and offal:
Cattle: 22 days
Pigs: 13 days
Sheep: 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 DOCUMENTATION

IV.I. Pre-Clinical Studies

Pre-clinical studies were not required because this is a generic application according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with a reference product has been demonstrated.

Tolerance in the Target Species

Tolerance studies were not required because this is a generic application according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with a reference product has been demonstrated.

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 benefit/risk profile of the product is favourable.

MODULE 4

POST- AUTHORISATION ASSESSMENTS

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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