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Publicly Available Assessment Report for a
Veterinary Medicinal Product

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

PRODUCT SUMMARY

EU Procedure number	IE/V/0405/001/DC
Name, strength and pharmaceutical form	Tilmovet 300 mg/ml Solution for injection
Active substance(s)	Tilmicosin
Applicant	Huvepharma NV Uitbreidingstraat 80 2600 Antwerpen Belgium
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation/ completion of procedure	13th March 2019
Target species	Cattle and sheep
Indication for use	**Cattle** Treatment of bovine respiratory disease associated with *Mannheimia haemolytica* and *Pasteurella multocida*. Treatment of interdigital necrobacillosis. **Sheep** Treatment of respiratory tract infections caused by *Mannheimia haemolytica* and *Pasteurella multocida.* *Treatment of foot rot in sheep caused by Dichelobacter nodosus and Fusobacterium necrophorum.* *Treatment of acute ovine mastitis caused by Staphylococcus aureus and Mycoplasma agalactiae.*
ATCvet code	QJ01FA91
Concerned Member States	BE, BG, DE, ES, FR, IT, NL, PL, PT, UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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

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II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 300 mg/ml tilmicosin and the excipients phosphoric acid, propylene glycol and water for injections. The container/closure system is 100 ml Type II amber glass vials, sealed with a bromobutyl stopper and aluminium cap.

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.

Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is tilmicosin, 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 has been provided.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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

F. Stability

Stability data on the active substance has 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 has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

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G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application has been submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC (a "generic" veterinary medicinal product). The candidate formulation contains tilmicosin as active substance. The reference veterinary medicinal product cited by the Applicant is Micotil 300 mg/ml Solution for Injection (VPA 10047/009/001- Elanco Animal Health, Eli Lilly and Company Limited) which was first granted a marketing authorisation in the Reference Member State (RMS) on 26/09/1990.

Warnings and precautions as listed on the product literature are consistent with those of the reference product and other similar products recently authorised within the EU and are considered adequate to ensure safety of the product for the animal, users and the environment.

III.A Safety Testing

Pharmacological Studies

It was claimed that the composition of the candidate formulation is the same as that of the reference product.

Both products are solutions for parenteral administration and they are used in the same species, for the same indications, in the same doses and using the same administration method.

Based on the data provided, an exemption from the requirement to conduct an *in vivo* bioequivalence study was justified in accordance with current guidance, section 7.1(b) of EMA/CVMP/016/00-Rev.3 (Guideline on the conduct of bioequivalence studies for veterinary medicinal products):

"For products intended for intramuscular, subcutaneous or systemically acting topical administration, bioequivalence studies are not required in cases when the product is of the same type of solution, contains the same concentration of the active substance and comparable excipients in similar amounts as the reference veterinary medicinal product, if it can be adequately justified that the difference(s) in the excipient(s) and/or their concentration have no influence on the rate and/or extent of absorption of the active substance."

Based on the information provided, the candidate product can be considered the same as the reference product and consequently, bioequivalence between the candidate and reference formulations can be assumed. Consequently, the applicant was not required to provide the results of safety tests or of pre-clinical and clinical trials.

Toxicological Studies

As this is a generic application under Article 13(1) of Directive 2001/82/EC and bioequivalence with a reference product is accepted, the omission of toxicological data was accepted.

User Safety

Given that bioequivalence with the reference product was accepted and no additional risks for the user were identified, it was accepted that the product will not present an unacceptable risk for the user when stored, handled, administered and disposed of in accordance with the recommendations included in the proposed SPC.
Warnings and precautions as listed on the product literature are considered adequate to ensure safety to users of the product.

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Environmental Risk Assessment

Phase I

The Applicant provided an environmental risk assessment as required by the legislation and has followed the Phase I decision tree.

Conclusion

Based on the data provided, the ERA can stop at Phase I. It can be concluded that the product will not present an unacceptable risk for the environment when stored, handled, administered and disposed of in accordance with the recommendations included in the proposed SPC.

Residue documentation

No residue depletion studies were conducted. As this is a generic application under Article 13(1) of Directive 2001/82/EC, bioequivalence with a reference product is accepted and given that the candidate formulation is to be administered to the same target species, using the same route of administration and the same posology as already approved for the reference product, it was accepted that studies investigating the depletion of residues are not required.

The active substance tilmicosin is included in table 1 of the Commission Regulation (EU) No. 37/2010 as follows:

	Cattle & sheep
Muscle	50 µg/kg
Liver	1000 µg/kg
Kidney	1000 µg/kg
Fat	50 µg/kg
Milk	50 µg/kg

The proposed withdrawal periods are identical to those approved for the reference product are considered adequate to ensure consumer safety.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies Pharmacology

See Part III.

Tolerance in the Target Species of Animals

As this is a generic application under Article 13(1) of Directive 2001/82/EC and as bioequivalence with a reference product is accepted, it is considered that the risk to the target species will be similar for both the test and the reference products. Consequently, the omission of target animal tolerance data was accepted.

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

Resistance

Given the legal basis of this application Article 13(1) of Directive 2001/82/EC and the fact that the product is intended to be administered to the same target species using the same posology, no difference in terms of potential for resistance development is expected between candidate and reference formulations. Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Laboratory Trials & Field Trials

As this is a generic application according to Article 13(1) of Directive 2001/82/EC and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are expected to be equivalent to those of the reference product.

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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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. 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 HPRA website.

This section 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.

Changes:

None.

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