United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Equigent 100 mg/ml Solution for Injection for Horses
Equigent, 100 mg/ml Solution for Injection for horses (Estonia)

Date Created: November 2018

PuAR correct as of 12/03/2019 when RMS was transferred to CZ. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0659/001/DC
Name, strength and pharmaceutical form	Equigent 100 mg/ml Solution for Injection for horses
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd. Dublin Road, Loughrea Co. Galway Ireland
Active substance(s)	Gentamicin (as gentamicin sulfate)
ATC Vetcode	QJ01GB03
Target species	Horses.
Indication for use	For the treatment of infections of the lower respiratory tract in horses caused by aerobic Gram-negative bacteria susceptible to gentamicin.

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 decentralised procedure	23rd October 2018
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Belgium, Czech Republic, Estonia, Poland, Slovakia

I. SCIENTIFIC OVERVIEW

This was a generic application for Equigent 100 mg/ml Solution for Injection for Horses, authorised in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference product is Gentaject 10% Solution for Injection for Horses, marketed in Ireland since October 1988.The UK has also authorised Genta-Equine 100 mg/ml Solution for Injection for Horses. Authorised in the UK since 2009. Genta-Equine was produced as a generic of Gentaject. Both Gentaject and Genta-Equine are produced by the same Marketing Authorisation Holder.

The product is indicated for use in horses, for the treatment of infections of the lower respiratory tract in horses caused by aerobic Gram-negative bacteria susceptible to gentamicin. The product is administered by slow intravenous injection, at a dose rate of 6.6 mg gentamicin/kg bodyweight, (equivalent to 0.066 ml/kg bodyweight of the product), given intravenously once daily for 3–5 consecutive days. Bodyweight must be determined as accurately as possible to avoid under- or over-dosing. The dosing regimen must not be exceeded.
The use of gentamicin in foals and neonates is not recommended.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto 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 and for the environment, when used as recommended. Suitable warnings and precautions

[1] SPC – Summary of product Characteristics.

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 100 mg/ml gentamicin, 9as gentamicin sulphate), and the excipients sodium methyl hydroxybenzoate (E219), sodium propyl hydroxybenzoate (E217), sodium metabisulphite, sodium citrate (for pH adjustment), disodium edetate and citric acid monohydrate (for pH adjustment).

The container/closure system consists of 100 ml and 250 ml clear, Type II glass vials sealed a bromobutyl bung and aluminium overseal. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.
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 the mixing of the ingredients at suitable time points and under suitable conditions, checking of pH and clarity of the solution, filtration, sterilisation and filling into vials.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substance is gentamicin sulphate, an established active substance described in the European Pharmacopoeia (Ph. Eur). 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. A specification and Certificate of Suitability were provided.

All excipients are described in the Ph. Eur. The packaging for the active substance complies with Commission Regulation 10/2011 and with a specific

[2] Efficacy – The production of a desired or intended result.

Ph. Eur monograph. Suitable specifications were provided for the finished product.

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 have been provided demonstrating compliance with the specification. Control tests on the finished product are those for: appearance, identification of active gentamicin sulphate and key excipients. pH, density, assay of active substance, microbiological assay of the active substance, preservatives and antioxidant assays, identification of antioxidant, sterility test and identification of bacterial endotoxins.

II.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 when stored under the approved conditions.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 30 months

Shelf-life after first opening the immediate packaging: 28 days

Keep the vial in the outer carton, in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

The generic and reference product are essentially similar given that both products are of the same qualitative composition in terms of active substance, containing gentamicin sulfate (100 mg/ml). Both products are to be administered at a rate of 6.6 mg/kg body weight. A minor difference to one excipient has no impact on the safety and efficacy of the proposed product. Therefore, the results of pharmacological and toxicological tests were not required. A User Risk Assessment (URA) and Environmental Risk Assessment (ERA) were provided.

User Safety

A user risk assessment was provided 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. Therefore the following applicant's user recommendations are appropriate:

- Gentamicin may cause hypersensitivity (allergic) reactions following exposure. People with known hypersensitivity to gentamicin should avoid contact with the product.
- Administer the product with caution.
- In case of accidental self-injection, 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[3] and CVMP[4] guidelines.

The product will only be used in non-food animals, (non-food producing horses), and as a result environmental exposure will be low. A Phase II ERA was not

[3] VICH – International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.
[4] CVMP – Committee for Medicinal Products for Veterinary Use.

required. Disposal advice as shown in the SPC and product literature is satisfactory.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the product is not intended for food-producing horses.

Withdrawal Periods

Not authorised for use in horses producing meat or milk for human consumption.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Due to the nature of the application, no pharmacodynamic or pharmacokinetic studies were required. Full details of relevant pharmacodynamic and pharmacokinetic considerations are available in the SPC.

Pharmacodynamics

Gentamicin sulfate exerts concentration-dependent bacterial killing characteristics. The rate of killing increases as the gentamicin concentration increases above the minimum concentration (MIC) for a given Gram-negative pathogen, with optimal maximum serum concentration (Cmax) to MIC ratio of 8-10.

Pharmacokinetics

Gentamicin sulfate is poorly absorbed from the gastrointestinal tract, and must be administered parenterally for systemic action. It is primarily distributed within extracellular fluids, does not distribute to the cerebrospinal fluid, and does not penetrate intracellularly, or into abscesses.

After parenteral administration, gentamicin is distributed to synovial, perilymph, pleural, peritoneal and peri-cardial fluid. It does not cross the placenta of late-term mares.

Gentamicin is eliminated unchanged by the kidney via glomerular filtration, including 85–95% of the dose.

The plasma elimination half-lives range from 1 to 3 hours in adult animals, but this is increased in animals with renal dysfunction.

Tolerance in the Target Species

Tolerance studies were not required because of the nature of the application. The proposed product has the same safety profile as the reference product.

Resistance

Full details appear on the SPC and product literature. The dosing regimen must not be exceeded. Use of the product deviating from the instructions given in the SPC increases the risk of nephrotoxicity, and may increase the prevalence of bacteria resistant to gentamicin.

IV.II. Clinical Documentation

It was concluded that the proposed test product met the criteria defined under Section 7.1a) of the current CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2), and are essentially similar. The proposed product and the reference product have the same qualitative and quantitative composition. Any minor differences in formulation were not considered to impact the efficacy or tolerance of the active substance.

Given the legal base of the MA application for the test product and the fact that a waiver from the requirement to conduct bioequivalence studies can be accepted, the applicant was not required to submit further preclinical or clinical data to support of the application.

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.

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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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