ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Genta-Equine 100 mg/ml Solution for Injection for Horses

PuAR correct as of 09/09/2019 when RMS was transferred to BE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0515/001/MR
Name, strength and pharmaceutical form	Genta-Equine 100 mg/ml Solution for Injection for Horses
Applicant	Franklin Pharmaceuticals Ltd Athboy Road Trim Co. Meath Ireland
Active substance(s)	Gentamicin (as gentamicin sulphate)
ATC Vetcode	QJ01GB03
Target species	Horses (non-food producing)
Indication for use	For the treatment of infections caused by Gram-negative bacteria sensitive to gentamicin and compatible with the distribution properties of gentamicin.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

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 completion of the original mutual recognition procedure	14th February 2014
Date product first authorised in the Reference Member State (MRP only)	07th July 2009
Concerned Member States for original procedure	Belgium, Denmark, Iceland, Spain

I. SCIENTIFIC OVERVIEW

Genta-Equine 100 mg/ ml Solution for Injection has been developed as a generic of Gentaject 10% Solution for Injection which was first authorised in Ireland in 1988 for Franklin Pharmaceuticals Ltd. The products are considered to be bioequivalent as they have identical formulations, manufacturing processes and composition.

Genta-Equine contains gentamicin (as gentamicin sulphate) and is indicated for the treatment of bacterial infections sensitive to gentamicin in horses. The product is contraindicated in pregnant animals, animals with renal impairment and if there is known hypersensitivity to the active or any of the excipients. The product should not be administered in amounts exceeding the proposed dose, 6.6 mg/ kg bw, provided once every 24 hours for 3-5 days. Not recommended for use in foals.

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[1].

The product is safe for the user, 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.

[1] SPC – Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The product contains 100 mg/ml gentamicin (as gentamicin sulphate) and the excipients sodium methyl parahydroxybenzoate (E219), sodium propyl parahydroxybenzoate (E217), sodium metabisulphate, sodium citrate, edetic acid, citric acid monohydrate and water for injections.

The container/closure system consists of 100 ml clear Type II glass vials sealed with a Type I 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 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.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The product is manufactured by mixing the excipients into the water for injections with the exception of citric acid. The required amount of gentamicin sulphate is then added and mixed until complete dissolution is achieved. The pH of the solution is measured and adjusted as necessary with the addition of citric acid before the remaining water for injections is added. The solution is passed through a sterilising filter before being filled into vials under aseptic conditions. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is gentamicin sulphate, an established active substance described in the European Pharmacopoeia. A Ph. Eur. Certificate of Suitability has been provided for the manufacturer of the 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.

The excipients are all manufactured according to their relevant Ph. Eur. monographs and testing is performed on receipt. Certificates of analysis have been provided.

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

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

E. Control on intermediate products

Not applicable.

F. 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. The tests include those for identification and assay of the active substance, identification and assay of the excipients, appearance, density, sterility and pH.

Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production sites have been provided demonstrating compliance with the specification.

G. 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. Stability data were provided for batches stored at 25°C/60% RH for 24 months and 40°C/75% RH for 6 months. A shelf life of 2 years has been established for the finished product.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

- Shelf-life of the finished product as packaged for sale is 2 years.
- Shelf life after first opening the immediate packaging is 28 days.
- Store in the original carton in order to protect from light..

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application submitted according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological tests are not required.

Toxicological Studies

As this is a generic application submitted according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of toxicological tests are not required.

User Safety

The applicant has not provided a user safety assessment as this is a generic application and the product is considered identical to the reference product. The user warnings are therefore the same as the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:

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.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product is intended to treat a small number of individual animals therefore environmental exposure will be very low and the risk to the environment is minimal. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

No residues studies were provided as the product is contraindicated in horses intended for human consumption. Necessary warnings are included in the SPC and product literature.

Withdrawal Periods

Do not use in horses which are intended to produce meat or milk for human consumption.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

As this is a generic application submitted according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of tolerance studies are not required.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, results of clinical studies are not required. However a different dosage regimen was proposed for this product, therefore a literature review was conducted to support the proposed administration.

It was proposed that instead of dosing every 8-12 hours as per the reference product instructions, dosing once daily would provide more effective antimicrobial therapy. Gentamicin is an aminoglycoside, which are classified as concentration-dependant antimicrobials. They exhibit peak concentration-dependant bactericidal activity and should therefore be administered once daily with higher peak levels. This increases the bactericidal activity and surviving bacteria tend not to replicate as rapidly. The review also indicated that once daily dosing reduced the nephrotoxic effects as serum concentration falls to trough levels for a longer, reducing the accumulation of gentamicin within the kidney.

As a result of the literature review a dosage regimen was determined that differed from the reference product, 6.6 mg/kg (3.3 ml per 50 kg). The product is not recommended for use in foals. The product should be administered via IV injection once every 24 hours for 3-5 days.

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.

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.

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