Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Geepenil vet 300 mg/ml Powder for Solution for Injection

Date Created: February 2022

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Geepenil vet 300 mg/ml Powder for Solution for Injection
Applicant	Orion Corporation Orionintie 1 02200 Espoo Finland
Active substance	Benzylpenicillin Sodium
ATC Vetcode	QJ01CE01
Target species	Horses
Indication for use	Infections caused by micro-organisms sensitive to benzylpenicillin in horse.

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	The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended by 2004/28/EC
Date of conclusion of the procedure	18/01/2022

I. SCIENTIFIC OVERVIEW

The application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended by 2004/28/EC.

Geepenil vet 300 mg/ml Powder for Solution for Injection contains 6.36 g benzylpenicillin sodium per vial of powder as active substance (makes 300 mg benzylpenicillin sodium per ml of reconstituted product) and no excipients. The proposed indication is for *'infections caused by micro-organisms sensitive to benzylpenicillin*' in the horse. The proposed intravenous dose is 10 – 20 mg/kg bodyweight twice a day for a duration of a minimum of 4 days.

The reference product is Novocillin vet 25.2 g powder and solution for solution for injection, marketed by Boehringer Ingelheim Danmark, which has been authorised in Sweden since 1992. Currently Geepenil vet 300 mg/ml Powder and Solvent for Solution for Injection' is authorised in the UK (in 2020; containing 24 g benzylpenicillin sodium per vial) and this is an extension application for Geepenil vet 300 mg/ml Powder for Solution for Injection' (containing 6.36 g benzylpenicillin sodium per vial).

The applicant has claimed exemption from the requirement for bioequivalence studies in accordance with section 7.1.a) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/2000-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 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

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

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 Benzylpenicillin Sodium and no excipients.

The container/closure system consists of Colourless type II glass vials (50 ml) closed with bromobutyl rubber stoppers and aluminium seal and flip-off cap.

The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the absence 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 of the powder is straight forward involving filling of the sterile powder and has been adequately described.

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 Benzylpenicillin sodium, an established active substance described in the European Pharmacopoeia. 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 copy of the current supporting European Pharmacopoeia Certificate of Suitability was provided.

The Certificate of Suitability states that the retest period for benzylpenicillin sodium is 60 months if stored in sterile double polyethylene bags in a bag of quadruplex foil placed in a cardboard box.

II.C.4. Substances of Biological Origin

Scientific data and/or certificates of suitability issued by the EDQM have been provided and 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.

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, colour, uniformity of mass, pH of solution, colour of solution, clarity of solution, particulate matter, loss on drying, identification of benzylpenicillin sodium, assay of benzylpenicillin sodium, related substances, test for sterility and 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: 3 years.
Shelf life after reconstitution according to directions: 24 hours (store in a refrigerator 2°C – 8°C).

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

Reconstituted product: Store the reconstituted product in a refrigerator (2 – 8°C).

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological and Toxicological Studies

In accordance with Article 13(1) of Directive 2001/82/EC, as amended; because this application is for a generic product, data describing the pharmacology and toxicology of the active substance, benzylpenicillin sodium, were not required.

User Safety

The user risk assessment (URA) for Geepenil 6.36 g, which is based upon that for Geepenil 24 g, is broadly in accordance with current guidance and was considered adequate. On the basis that bioequivalence with the reference product can be accepted, the minor differences in the formulation are not expected to impact upon the safety profile of the product (the active substance in the reference product is of the potassium salt), and that the generic product is to be administered to the same target species, for the same indications, at the same dose, and using the same route of administration as the reference product; the hazard, exposure and, therefore, risks to the user, are expected to be the same as those of the reference product. Furthermore, the risks to the user from the use of Geepenil 6.36 g are considered to be the same as those identified for Geepenil 24 g. The applicant has proposed the same user safety warnings as agreed recently for Geepenil 24 g.

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:,

- Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.
- Avoid skin contact with this product if you know you are sensitised, or if you have been advised not to work with such preparations.
- Handle this product with great care to avoid exposure.
- If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
- This product may cause eye irritation.
- Avoid contact with the eyes.
- In the event of accidental eye contact, rinse the affected eye(s) with plenty of clean water.
- Wash hands after use.

Environmental Safety

Phase I:

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines. The assessment ends in Phase I at Question 5 of the VICH decision tree ('Will the VMP be used to treat a small number of animals in a flock or herd?'). The product is expected to pose an acceptable risk for the environment when used as recommended. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

Residue depletion study data were not provided. This was acceptable since the generic product (Geepenil 6.36 g), like Geepenil 24 g, is contraindicated for use in food-producing animals.

Withdrawal Periods

Not authorised for use in horses intended for human consumption.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

The applicant has specified an exemption under 7.1.a) of the current CVMP 'Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2)' which states:

"The product is to be administered solely as an aqueous intravenous solution containing the same active substance as the currently approved product. However, if any excipients interact with the active substance (e.g. complex formation), or otherwise affect the disposition of the active substance, a bioequivalence study is required unless both products contain the same excipients in very similar quantity and it can be adequately demonstrated that any difference in quantity does not affect the pharmacokinetics of the active substance'.

Considering the data presented, the test formulation, when administered, can be considered the same as the reference formulation and therefore bioequivalence with the reference formulation can be assumed.

Tolerance in the Target Species

Tolerance studies were not required due to the nature of the application.

Resistance

The applicant has conducted a literature review to cover the susceptibility of some target pathogens to benzylpenicillin. Adequate warnings and precautions appear on the product literature.

IV.II. Clinical Documentation

Clinical studies were not required due to the nature 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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