



**Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)**

DECENTRALISED PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

**Procapen Injector
3g intramammary suspension for cattle**

Date: 06 June 2015

MODULE 1

PRODUCT SUMMARY

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| EU Procedure number | DE/V/0126/002 |
| Name, strength and pharmaceutical form | Procopen Injector 3g intramammary suspension for cattle |
| Applicant | aniMedica GmbH Im Südfeld 9 – 48308 Senden Germany |
| Active substance(s) | Benzylopenicillin, procaine 1H ₂ O |
| ATC Vetcode | QJ51CE09 |
| Target species | Cattle |
| Indication for use | For treatment of udder infection in lactating cows caused by benzylopenicillin-sensitive staphylococci and streptococci. |

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

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| Legal basis of original application | Application in accordance with Article 13(1) of Directive 2001/82/EC as amended. |
| Date of completion of the original Decentralised procedure | 21.03.2012 |
| Date product first authorised in the Reference Member State (MRP only) | n.a. |
| Concerned Member States for original procedure | CZ; EE; EL; HU; LT; LV; PL; PT; RO; SI; SK |
| Concerned Member States added during Repeat Use procedure: | ES, FI, FR, HR, IE, IS, IT, NL, SE, UK |

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.

The safety and efficacy aspects of this product are identical to the reference product. The initial application for the reference product was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITY ASPECTS

A. Composition

The product contains Benzylpenicillin, procaine 1 H₂O 3.00 g, (3-sn-Phosphatidyl)cholin (Lecithin) 0.03 g and Propylene glycol, Povidone K 25, Sodium citrate 2 H₂O, Potassium-dihydrogen phosphate and Water for injections.

The product is packed in single dose plastic injectors (intramammary syringes) of white PE closed with a twist off cap. The intramammary syringe contains 10 ml of the product.

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.

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.

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 Benzylpenicillin, procaine 1H₂O, 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 valid CEP "Benzylpenicillin, procaine, lecithin coated (1%), sterile" has been provided by the manufacturer.

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.

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.

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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL) (for pharmaceuticals only)

For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13 and bioequivalence with a reference product has been demonstrated, results of safety tests are not required.

The pharmacological and toxicological aspects of this product are identical to the reference product.

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

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

Residue Studies

No residue depletion studies were conducted as this product application is submitted in accordance with Article 13(1) of Council Directive 2001/82/EC, as amended and formulation and manufacturing process for the product are identical to the formulation and manufacturing process of the reference product,

MRLs

Procaine benzylpenicillin is a complex, which is rapidly and completely hydrolysed to procaine and benzylpenicillin; for the latter definitive MRL's have been established with benzylpenicillin itself as the marker residue and are included in Table 1 of Commission Regulation (EU) No 37/2010, in accordance with the following table:

| Pharmacologically active substance | Marker residue | Animal species | MRL | Target tissues | Other provisions | Therapeutic classification |
|------------------------------------|------------------|--------------------------------------|---|--|---|------------------------------------|
| Benzylpenicillin | Benzylpenicillin | All mammalian food producing species | 50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg | Muscle Fat Liver Kidney Milk | For fin fish the muscle MRL relates to 'muscle and skin in natural proportions'. MRLs for fat, liver and kidney do not apply to fin fish. For porcine and poultry species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which eggs are produced for human consumption. | Anti-infectious agents/antibiotics |

The CVMP has concluded that there is no need to establish a MRL for procaine when it is used as a local anaesthetic agent and as part of the complex procaine benzylpenicillin and as such, recommends its inclusion in Table 1 of Commission Regulation (EU) No 37/2010, in accordance with the following table:

| Pharmacologically active substance | Animal Species | Other provisions |
|------------------------------------|----------------------------|------------------|
| Procaine | All food producing species | |

Withdrawal Periods

The same withdrawal periods as of the reference product were accepted.

Meat and offal 5 days

Milk: 6 days

IV. CLINICAL ASSESSMENT (EFFICACY)

Procopen Injector 300mg/ml is an udder injector. Each injector contains 10ml suspension with benzylpenicillin-procain at a concentration of 300mg per ml. The product is indicated for intramammary treatment of udder infections in lactating dairy cows caused by benzylpenicillin-sensitive bacteria and shall be applied to each affected udder quarter once per 24 hours for 3 consecutive days. An improvement of the infection is to be expected after 2 days. Otherwise the diagnosis should be reviewed and treatment should be possibly changed.

The application for Procopen Injector 300mg/ml is a generic one with Procain-Penicillin-G Injektor from aniMedica serving as reference product. Because of the identical formulation in terms of active and inactive substances as well as of the identical physicochemical properties of Procopen Injector 300mg/ml and the reference product, bioequivalence of both products has been taken for granted in accordance with the exemption rules of chapter 4c of the Guidelines on the conduct of bioequivalence studies for veterinary medicinal products, EMEA/CVMP/016/00-corr-FINAL.

Based on their bioequivalence, the safety and efficacy aspects of Procopen Injector 300mg/ml are equivalent to those of the reference product.

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 risk benefit 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 Heads of Veterinary Medicinal Agencies website (www.hma.eu).

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.

Quality changes

| Summary of change (Application number) | Section updated in Module 3 | Approval date |
|--|--------------------------------|---------------|
| Submission of an updated certificate of suitability from an already approved manufacturer DE/V/0126/IA/004/G | II.A | 26.04.2013 |
| Harmonisation of product literature after finishing the repeat-use procedure (DE/V/0126/002/II/007) | | 02.02.2015 |
| Changes in Part II after repeat-use procedure: Submission of an updated certificate of suitability from an already approved active substance manufacturer Change of the name of an already approved active substance manufacturer Addition of a new specification parameter to the active substance specification (DE/V/0126/IA/008/G) | II.C | 02.02.2015 |
| Changes in Part II after repeat-use procedure: Tightening of specification limits of the finished product Addition of new specification parameters to the finished product specification with its corresponding | II.F | 02.02.2015 |

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| test methods Update (correction) of a specification parameter Minor change in a test procedure for the finished product (DE/V/0126/IB/009/G) | | |
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