DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Doxatib 500 mg/g powder for use in drinking water for pigs and chickens (BE, BG, CZ, DE, EE, ES, GB, HR, HU, IE, LT, LV, NL, PL, PT, RO, SI, SK)

Doxatib 433 mg/g powder for use in drinking water for pigs and chickens (FR)
**PRODUCT SUMMARY**

<table>
<thead>
<tr>
<th>EU Procedure number</th>
<th>SI/V/0001/001/DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name, strength and pharmaceutical form</td>
<td>DOXATIB 500 mg/g prašek za dajanje v vodo za pitje za prašiče in piščance</td>
</tr>
<tr>
<td>Applicant</td>
<td>KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia</td>
</tr>
<tr>
<td>Active substance(s)</td>
<td>Doxycycline hyclate</td>
</tr>
<tr>
<td>ATC Vetcode</td>
<td>QJ01AA02</td>
</tr>
<tr>
<td>Target species</td>
<td>Pigs and chickens (broilers, pullets, broiler breeders)</td>
</tr>
<tr>
<td>Indication for use</td>
<td>Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by Actinobacillus pleuropneumoniae, Pasteurella multocida, and Mycoplasma hyopneumoniae susceptible to doxycycline. Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by Pasteurella multocida or to reduce morbidity and lesions in respiratory infections caused by Ornithobacterium rhinotracheale (ORT).</td>
</tr>
</tbody>
</table>
Doxatib 500 mg/g powder for use in drinking water for pigs and chickens

**Product name**

SI/V/0001/001/DC

**Manufacturer**

KRKA, d. d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

**Reference**

DCP

**Publicly available assessment report**

**MODULE 2**

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website ([http://www.HMA.eu](http://www.HMA.eu)).
Doxatib 500 mg/g powder for use in drinking water for pigs and chickens

Product name

KRKA, d. d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Publicly available assessment report

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 July 2016

Date product first authorised in the Reference Member State (MRP only)

Not applicable

Concerned Member States for original procedure

BE, BG, CZ, DE, EE, ES, FR, HR, HU, IE, LT, LV, NL, PL, PT, RO, SK, 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.

It has been shown that the product can be safely used in the target species; the slight 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 risk/benefit analysis is in favour of granting a marketing authorisation.
II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 500 mg of doxycycline hyclate (corresponding to 433 mg of doxycycline) and tartaric acid as the only excipient.

The container/closure system consists of heat sealed bags of 100 g, 1000 g and 5000 g composed of PET/AL/PE foil or PET/AL/PET/PE foil. The particulars and specification for both type of foil is provided and the certificates of analysis presented and conform to the regulation.

The choice of the formulation is 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 at 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 doxycycline hyclate, an established 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.

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

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 have been provided.

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

F. Stability
Stability data on the active substances 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 finished product throughout its shelf life when stored under the approved conditions. The results are reflected in the established shelf-life data information provided in the SPC.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13(1) of the Directive 2001/82/EC, and bioequivalence with a reference product has been demonstrated, results of safety tests are not required.

The safety aspects of this product are identical to the reference product.

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

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13(1) of the Directive 2001/82/EC, and bioequivalence with a reference product has been demonstrated, results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application according to Article 13(1) of the Directive 2001/82/EC, and bioequivalence with a reference product has been demonstrated, results of toxicological studies are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the product is not expected to pose a risk for users when used as recommended.

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

Environmental Risk Assessment
Phase I:

The applicant provided a Phase I of the environmental risk assessment in compliance with the relevant guideline. PEC_{soil} values exceed the trigger value of 100 µg/kg for pigs and for intensively reared broilers. Based on exposure calculations, the phase II assessment was required.

Phase II:

A Phase II Tier A assessment was conducted.

Based upon the data obtained in the Phase II studies, the use of this product would not lead to unaccepted risk for the terrestrial and aquatic compartment.

The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

**III.B Residues documentation**

**Residue Studies**

Bioequivalence of Doxatib 500 mg/g powder for use in drinking water for pigs and chickens and the reference product Soludox 500 mg/g powder for use in drinking water for pigs and chickens is demonstrated and therefore residue depletion studies were not required.

**MRLs**

Doxycycline is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>Doxycycline</td>
<td>Porcine, poultry</td>
<td>100 µg/kg</td>
<td>Muscle</td>
<td>Not for use in animals from which eggs are produced for human consumption.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>300 µg/kg</td>
<td>Fat</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>300 µg/kg</td>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>600 µg/kg</td>
<td>Kidney</td>
<td>For porcine and poultry species the fat MRL relates to ‘skin and fat in natural proportions’.</td>
</tr>
</tbody>
</table>

**Withdrawal Periods**

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

Pigs:
- Meat and offal: 4 days
Doxatib 500 mg/g powder for use in drinking water for pigs and chickens Product name  
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Chickens:
- Meat and offal: 3 days, (at a dose rate of 10 mg/kg b.w.).
- Meat and offal: 9 days, (at a dose rate of 20 mg/kg b.w.).
- Eggs: Not authorised for use in laying birds producing eggs for human consumption. Do not use within 4 weeks of onset of the laying period.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product 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.
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 Medicines 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.

None