Irish Medicines Board
(Reference Member State)

DECENTRALISED PROCEDURE
PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT
Marbonor 100 mg/ml Solution for Injection for Cattle and Pigs
**PRODUCT SUMMARY**

<table>
<thead>
<tr>
<th>EU Procedure number</th>
<th>IE/V/0296/001/DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name, strength and pharmaceutical form</td>
<td>Marbonor 100 mg/ml Solution for Injection for Cattle and Pigs</td>
</tr>
<tr>
<td>Applicant</td>
<td>Norbrook Laboratories Limited</td>
</tr>
<tr>
<td>Active substance(s)</td>
<td>Marbofloxacin</td>
</tr>
<tr>
<td>ATC Vetcode</td>
<td>QJ01MA93</td>
</tr>
<tr>
<td>Target species</td>
<td>Cattle and Pigs</td>
</tr>
<tr>
<td>Indication for use</td>
<td><strong>Cattle</strong>&lt;br&gt;Treatment of respiratory infections caused by sensitive strains of <em>Pasteurella multocida</em>, <em>Mannheimia haemolytica</em> and <em>Mycoplasma bovis</em>.&lt;br&gt;Treatment of acute mastitis caused by <em>Echerichia coli</em> strains sensitive to marbofloxacin during the lactation period.&lt;br&gt;<strong>Sows</strong>&lt;br&gt;Treatment of Metritis Mastitis Agalactia Syndrome (postpartum dysgalactia syndrome, PDS) caused by bacterial strains sensitive to marbofloxacin.</td>
</tr>
</tbody>
</table>
The Summary of Product Characteristics (SPC) for this product is available on the veterinary Heads of Agencies website (www.hma.eu).
## MODULE 3

### PUBLIC ASSESSMENT REPORT

<table>
<thead>
<tr>
<th>Legal basis of original application</th>
<th>A generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.</th>
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</thead>
<tbody>
<tr>
<td>Date of completion of the original decentralised procedure</td>
<td>26th September 2012.</td>
</tr>
<tr>
<td>Date product first authorised in the Reference Member State (MRP only)</td>
<td>N/A</td>
</tr>
<tr>
<td>Concerned Member States for original procedure</td>
<td>AT, BE, BG, CY, CZ, DE, EE, EL, ES, FI, FR, HU, IT, LU, LV, NL, PL, PT, RO, SI, SK and UK</td>
</tr>
</tbody>
</table>
I. **SCIENTIFIC OVERVIEW**

This application for a marketing authorisation has been submitted by Norbrook Laboratories Limited, Northern Ireland. This application has been submitted in accordance with Article 13(1) of Directive 2001/82/EC as amended, that is, as a generic application. The reference product cited in this application is Marbocyl 10% Injection for Cattle and Pigs (Vetoquinol SA) as authorised in the UK (Vm 06462/4003).

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 (transient local reactions such as pain and swelling at the injection site and inflammatory lesions which may persist for at least 12 days after injection) 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 by claiming bioequivalence with the reference product. The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. **QUALITY ASPECTS**

A. **Composition**

The product contains the active substance marbofloxacin 100 mg/ml and excipients monothioglycerol, metacresol, disodium edetate, gluconolactone and water for injections.

The container/closure system amber type II glass vials (20 ml, 50 ml, 100 ml 250 ml and 500 ml) and amber co-ex plastic (polypropylene) vials (60 ml, 100 ml, 250 ml and 500 ml).

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.

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 marbofloxacin, 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.

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 sites have been provided demonstrating compliance with the specification.
G. Stability

Stability data on the active substance has 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

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

As this is a generic application according to Article 13.1 of Directive 2001/82/EC, as amended and bioequivalence with a reference product has been claimed, results of the safety and residue tests or of the pre-clinical and clinical trials are not required.

In order to justify the omission of comparative bioavailability studies, the applicant provided the results of a comparative analysis conducted on the reference and candidate formulations. The results of the comparative analyses demonstrated the essential similarity between generic and reference products in terms of active substance content, excipients, impurity profile and physicochemical properties. It was accepted that there will be no difference between formulations in terms of the rate and/or extent of absorption of the active substance. The absence of bioequivalence studies was considered justified and bioequivalence in both target species could be assumed.

Warnings and precautions as listed on the product literature are in line with those of the reference product and other similar products recently authorised via European procedures and are adequate to ensure safety of the product to users/environment/consumers.
III.A Safety Testing

Pharmacological Studies
Toxicological Studies

No data provided. The application has been submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application). Given that essential similarity of the candidate formulation with the reference product has been claimed, the omission of pharmacological and toxicological data was accepted.

Microbiological Studies

No data provided. The application has been submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application). Given that essential similarity of the candidate formulation with the reference product has been claimed, the omission of microbiological study data was accepted.

User Safety

The applicant has provided a user safety assessment. Given that the candidate formulation is considered to be essentially similar to the reference product, it is not expected that Marbonor 100 mg/ml Solution for Injection will present any greater risk to the user than that already posed by the reference product. As such, it was accepted that the proposed product will not present an unacceptable risk to the user when the product is used in accordance with the recommendations proposed for inclusion in the SPC.

User safety warnings are considered adequate to ensure user safety and are in line with those agreed for other similar products recently authorised via European procedures.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. All PEC_{sol initial} values were below the trigger value of 100 µg/kg and further assessment was not required. It was therefore accepted that the product is not expected to present an unacceptable risk for the environment when the product is used in accordance with the recommendations included in the proposed SPC. As the candidate formulation has been demonstrated to be essentially similar to that of the reference product, no difference in risk for the environment is expected between the candidate and reference product formulations.
**III.B Residues documentation**

**Residue Studies**

No data provided. The application has been submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application). In accordance with Article 13.1, ‘the applicant shall not be required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product…’.

The excipients included in the generic product are all present in the authorised reference product (evident from section 6.1 of the SPC of the reference product). Based upon the results of the comparative analysis conducted by the applicant on the candidate and reference products, these excipients are included at the same concentrations in both formulations.

**MRLs**

Marbofloxacin is included in table 1 of 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 tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marbofloxacin</td>
<td>Marbofloxacin</td>
<td>Bovine, porcine</td>
<td>150 µg/kg</td>
<td>Muscle</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50 µg/kg</td>
<td>Fat</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>150 µg/kg</td>
<td>Liver</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>150 µg/kg</td>
<td>Kidney</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bovine</td>
<td>75 µg/kg</td>
<td>Milk</td>
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</table>

**Withdrawal Periods**

No residue depletion studies have been conducted with the candidate formulation on the basis that the formulation was claimed to be identical to that of the reference product. Based upon the results of the comparative analyses of the candidate and reference products conducted by the applicant, it was accepted that the rate of depletion of marbofloxacin from the injection site in cattle (intramuscular or subcutaneous) and in pigs (intramuscular) will not differ between formulations. The applicant’s proposal to apply the same withdrawal periods as approved for the reference product (Marbocyl 10% Injection for Cattle and Pigs (Vetoquinol SA)) were considered appropriate.
The following withdrawal period information was accepted:

**Cattle**
- Meat and offal: 6 days
- Milk: 36 hours

**Pigs**
- Meat and offal: 4 days

**IV. CLINICAL ASSESSMENT (EFFICACY)**

As this is a generic application according to Article 13.1, and bioequivalence with a reference product has been claimed, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

**IV.A Pre-Clinical Studies**

**Pharmacology**

The application has been submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application). Given that essential similarity of the candidate formulation with the reference product has been claimed, the omission of pharmacodynamic data was considered appropriate.

**Tolerance in the Target Species of Animals**

No data provided. Given that the candidate formulation has been demonstrated to be essentially similar to that of the reference product by way of a comparative analyses conducted on both reference and generic formulations, there is no reason to suggest that tolerance to the candidate formulation in the target species will differ from that of the reference product and the omission of tolerance studies conducted using the candidate formulation was accepted.

**Resistance**

Given that essential similarity of the candidate formulation with the reference product has been claimed, it was accepted that the concentration of the active substance marbofloxacin will be the same in the candidate formulation as included in the reference product formulation. Furthermore, the proposed posology, routes of administration and target species will be the same for the candidate formulation as those approved for the reference product.

The intended use of the product will be the same as the reference product and therefore no difference in the risk of development of antimicrobial resistance is to be expected between the candidate product and the reference product. The omission of specific data on resistance development was considered appropriate.
for this generic application. Adequate warnings and precautions appear on the product literature.

**IV.B Clinical Studies**  
**Laboratory Trials**  
**Field Trials**

No data presented. The application has been submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application). In accordance with Article 13.1, *‘the applicant shall not be required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product…’*.

Given that the candidate formulation has been demonstrated to be essentially similar to that of the reference product, the omission of field studies conducted using the candidate formulation was accepted. The proposed indications, posology, routes of administration and target species are the same for the candidate formulation as those approved for 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 benefit/risk 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

None.