FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
AGENCE NATIONALE DU MEDICAMENT VETERINAIRE
Agence nationale du médicament vétérinaire
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DECENTRALISED PROCEDURE
PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Alfadexx 2 mg/mL solution for injection for horses, cattle, goats, pigs, dogs and cats

DATE: 07/07/2021
# Module 1

## Product Summary

<table>
<thead>
<tr>
<th>EU Procedure number</th>
<th>FR/V/0430/001/DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name, strength and pharmaceutical form</td>
<td>Alfadexx 2 mg/ml solution for injection for horses, cattle, goats, pigs, dogs and cats</td>
</tr>
<tr>
<td>Applicant</td>
<td>Alfasan Nederland B.V. Kuipersweg 9 3449 JA Woerden The Netherlands</td>
</tr>
<tr>
<td>Active substance(s)</td>
<td>Dexamethasone (as dexamethasone sodium phosphate)</td>
</tr>
<tr>
<td>ATC Vetcode</td>
<td>QH02AB02</td>
</tr>
<tr>
<td>Target species</td>
<td>Horses, cattle, goats, pigs, dogs and cats</td>
</tr>
<tr>
<td>Indication for use</td>
<td><strong>Horses, cattle, goats, pigs, dogs and cats:</strong> Treatment of inflammation and allergic reactions. <strong>Horses:</strong> Treatment of arthritis, bursitis or tenosynovitis. <strong>Cattle:</strong> Treatment of primary ketosis (Acetonemia). Induction of parturition. <strong>Goats:</strong> Treatment of primary ketosis (Acetonemia).</td>
</tr>
</tbody>
</table>
The Summary of Product Characteristics (SPC) for this product is available on the website [http://www.anmv.anses.fr/](http://www.anmv.anses.fr/)
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 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. Composition

The product contains the active substance Dexamethasone (as dexamethasone sodium phosphate) at a concentration of 2 mg/ml and the following excipients: Benzyl alcohol, Sodium chloride, Sodium citrate dehydrate, Citric acid, Sodium hydroxide and water for injections.

The packaging of the finished product is as described on the SPC. 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.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substance is Dexamethasone (as dexamethasone sodium phosphate) 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.

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
A re-test period for the active substance is set in the certificate of suitability issued by EDQM.

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.

An in-use shelf-life as detailed on the SPC has been supported by appropriate data.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

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

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

Toxicological Studies

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

The 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.
Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline, which showed that no further assessment is required. If used as recommended, the product will have a negligible impact on the environment.

III.B Residues documentation

Residue Studies

No depletion data was provided.

MRLs

The active substance, dexamethasone, is included in table 1 of the annex of the Commission regulation (EU) No. 37/2010, as follows:

<table>
<thead>
<tr>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisons</th>
<th>Therapeutic Classification</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>Bovine, caprine, porcine, Equidae</td>
<td>0.75 µg/kg</td>
<td>Muscle</td>
<td>No entry</td>
<td>Corticoïdes/ Glucocorticoides</td>
<td>37/2010 of 22.12.2009</td>
</tr>
<tr>
<td></td>
<td>Bovine, caprine</td>
<td>0.30 µg/kg</td>
<td>Milk</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The MRL status of excipients of the product is indicated in the following table.

<table>
<thead>
<tr>
<th>Excipient</th>
<th>MRL status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl alcohol</td>
<td>Table 1, all food species, no MRL required</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>Table 1, all food species, no MRL required</td>
</tr>
<tr>
<td>Sodium citrate dihydrate</td>
<td>*</td>
</tr>
<tr>
<td>Citric acid</td>
<td>*</td>
</tr>
<tr>
<td>Sodium hydroxyde</td>
<td>*</td>
</tr>
<tr>
<td>Water for injection</td>
<td>Out of scope list</td>
</tr>
</tbody>
</table>

* Covered with food additives (substance with a valid E number approved as additives in foodstuffs for human consumption)

The composition of the product is acceptable according to the European Regulation (EC) 470/2009.

Withdrawal Periods
It is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended. The withdrawal periods are the same as those for the reference product.

**Cattle and goats:**
Meat and offal: 8 days  
Milk: 72 hours

**Pigs:**
Meat and offal: 2 days following intramuscular administration  
Meat and offal: 6 days following intravenous administration

**Horses:**
Meat and offal: 8 days  
Not authorized for use in horses producing milk for human consumption.

**IV. CLINICAL ASSESSMENT (EFFICACY)**

**IV.A Pre-Clinical Studies**

**Pharmacology**

It is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended by 2004/28/EC. The cited reference product is DEXADRESON (Intervet).

**Pharmaceutical form**

The test and the reference products have the same pharmaceutical form: solution for injection.

**Active substance qualitative and quantitative composition**

The test and reference products have the same qualitative and quantitative composition in active substance: 2.0 mg of dexamethasone per mL.

**Bioequivalence studies**

No bioequivalence study was performed. In line with the current bioequivalence guideline (EMA/CVMP/016/00 – Rev.2), an exemption from bioequivalence study is claimed based on the similar formulations of the two products.

**IV.B Clinical Studies**

As this is a generic application according to Article 13(1) of Directive 2001/82/EC, as amended by Directive 2004/28/EC, 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.