College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Equipred 50 mg tablets for horses

NL/V/0276/001/DC

CMS: AT, BE, DE, DK, ES, FI, FR, HU, IE, IT, SE, UK(NI)

Created: 17 March 2022

MODULE 1

PRODUCT SUMMARY

EU Procedure number	**NL/V/0276/001/DC**
Name, strength and pharmaceutical form	**Equipred 50 mg tablets**
Applicant	CP-Pharma Handelsgesellschaft mbH Ostlandring 13 31303 Burgdorf Germany
Active substance(s)	**Prednisolone**
ATC Vet code	**QH02AB06**
Target species	**Horses**
Indication for use	**Alleviation of inflammatory and clinical parameters associated with recurrent airway obstruction (RAO – severe asthma) in horses, in combination with environmental control.**

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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).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	25 September 2019
Concerned Member States for original procedure	AT, BE, DE, DK, ES, FI, FR, HU, IE, IT, SE, UK (NI)

I. SCIENTIFIC OVERVIEW

Equipred is a hybrid product; the reference product is Equisolon 33 mg/g oral powder for horses of marketing authorisation holder Le Vet, registered by central procedure in the EEA (EU/2/14/161/004-005) in 2014.

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 tablet contains 50 mg prednisolone and the excipients lactose monohydrate, powdered cellulose, colloidal anhydrous silica, croscarmellose sodium, sodium starch glycolate type A and magnesium stearate.

The tablet is cross scored and meant to be broken in halves or quarters.

The products are packed in PVC/PVDC-Al blisters, each containing 10 tablets.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

In vivo bioequivalence between the reference and proposed product has been demonstrated.

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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.

The product is manufactured using conventional manufacturing techniques. Suitable validation results on three production scale batches have been provided. The tests performed during production are described.

C. Control of Starting Materials

The active substance prednisolone is an established active substance described in the European Pharmacopoeia.

The active substance is manufactured in accordance with the principles of good manufacturing practice.

The CEP procedures have been employed.

The active substance specification and packaging, excipients specifications and batch analytical data have been provided.

None of the starting materials used are affected by the Note for Guidance on TSE/BSE.

D. Control on intermediate products

Not applicable.

E. Control Tests on the Finished Product

The finished product specification controls 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 four batches manufactured at the proposed production site has been provided demonstrating compliance with the specification.

F. Stability

The re-test period of 3 years for prednisolone when stored under the approved conditions is evidenced by the CEP.

The re-test period of 5 years for prednisolone from another manufacturer is evidenced by the stability data.

Stability data on the finished product have been provided in accordance with applicable VICH guidelines, including photostability data. The claimed shelf life of 36 months for prednisolone 50 mg tablets is granted. The shelf life of quartered tablets is 3 days.

G. Other Information

None.

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is a hybrid application according to Article 13, and compared to the reference product, Equipred contains a different concentration and formulation of prednisolone and contains also different excipients. Therefore the applicant has conducted bioequivalence studies to support the target species safety and efficacy. 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

A pre-clinical GLP study was performed according to the Guideline on the conduct of bioequivalence studies for veterinary medicinal products. Based on the applicant's statistical analysis, the 90% confidence limits for the ratio of AUC_{0-t} and C_{max} estimated for the test and reference products fell within the pre-set acceptance bounds, from which bioequivalence was concluded.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that hypersensitivity reactions may occur, the product can be irritating to eyes and there is a risk of foetal malformation.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will be used to treat individual animals only and the initial predicted environmental concentration in soil is less than 100 µg/kg at the daily dose of 1 mg/kg for 10 days in 50% of the herd.

III.B Residues documentation

Residue Studies

The applicant has conducted residue depletion studies in horses. Animals were treated at the recommended dose for 10 consecutive days. Prednisolone residue levels were investigated in kidney, liver, muscle and fat at 1, 2, 3 and 5 days post-treatment. All residue levels are below the MRL from 2 days post-treatment for edible tissues. Based on a safety margin of 10-30%, this would result in a 3-day withdrawal period. The proposed withdrawal period by the applicant of 10 days for meat of horses is identical to the withdrawal period for the reference product.

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MRLs

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

	Equidae
Muscle	4 µg/kg
Liver	6 µg/kg
Kidney	15 µg/kg
Fat	8 µg/kg

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

Excipient	**MRL status**
Lactose monohydrate	Table 1, no MRL required
Cellulose, powdered	Table 1, no MRL required
Silica, colloidal anhydrous	Table 1, no MRL required
Croscarmellose sodium	Table 1, no MRL required
Sodium starch glycolate Type a	Out of Scope list
Magnesium stearate	Table 1, no MRL required

Withdrawal Periods

Based on the data provided above, a withdrawal period of 10 days for meat and offal in horses is justified. The product is not authorised for use in mares producing milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

This is a hybrid application according to Article 13. Bioequivalence with the reference product has been demonstrated in pre-clinical studies. Additionally, a multi-centre placebo-controlled field study has been conducted to demonstrate the efficacy and safety of the product.

IV.A Pre-Clinical Studies

Pharmacology

The applicant has conducted studies to show bioequivalence (see Pharmacologic studies under Safety Testing) and to further support the pharmacokinetics. The pharmacokinetics study established a plasma pharmacokinetic profile of prednisolone after repeated oral administrations, demonstrating high variability for all parameters, and the absence of accumulation when dosed at the intended dose. Results from this study are implemented in the SPC.

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IV.B Clinical Studies

Field Trials

The applicant has conducted a multi-centre placebo-controlled field study in 72 horses with RAO without other obvious health problems. Regarding suppression of typical RAO signs, a significant difference between treated and untreated animals was observed for cough, nostril flare and abdominal lift, when the treatment was dosed as recommended. For the negative control, the positive effect of prednisolone treatment was also recorded during a post-placebo period, during which animals received treatment according to the recommended dosage. Treatment results were also significant in comparison with results of placebo treatment. Oral administration of Equipred tablets for 10 consecutive days at the proposed dose is safe and has demonstrated a positive effect on the recovery of RAO.

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 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.

Summary of change	**Section updated**	**Approval date**
NL/V/0276/IA/001/G B.III.1.a Updated certificate of suitability from an already approved manufacturer B.III.1.a Updated certificate of suitability from an already approved manufacturer	N/A	30 May 2020
NL/V/0276/001/IA/002 B.II.d.2.a Minor changes to an approved test procedure	N/A	27 February 2021