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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Prednizol 5 mg Tablets for Dogs and Cats

Created: February 2020

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0351/001
Name, strength and pharmaceutical form	Prednizol 5 mg Tablets for Dogs and Cats
Applicant	Millpledge Europe BVBA 38 Verrekijker 8750 Wingene Belgium
Active substance(s)	Prednisolone
ATC Vetcode	QH02AB06
Target species	Dogs and cats
Indication for use	For the symptomatic treatment of inflammatory or allergic conditions in dogs and cats.

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MODULE 2

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (3) of Directive 2001/82/EC as amended
Date of completion of the original decentralised procedure	25/09/2019
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	Belgium, France, Germany, United Kingdom (Northern Ireland)

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, Prednizol 5 mg Tablets for Dogs and Cats. The reference product is Prednisolone Tablets B.P. (Vet) 5 mg, also marketed by Millpledge Ltd, authorised in the UK since August 1997.

The product is indicated for the symptomatic treatment of inflammatory or allergic conditions in dogs and cats. For oral administration 0.1 - 2.0 mg per kg bodyweight per day. The dose and total duration of treatment is determined by the veterinarian for each individual case, depending on the severity of symptoms. The lowest effective dose must be used. For longer term treatment: when after a period of daily dosing, the desired effect has been achieved, the dose should be reduced until the lowest effective dose is reached. The reduction of the dose should be made by alternate day therapy and/or by halving the dose with intervals of 5 - 7 days, until the lowest effective dose is reached. The tablets are not intended to be divided. For animals requiring a dose below 5 mg an alternative or lower strength product should be used.

Dogs should be treated in the morning and cats in the evening on account of differences in day rhythm.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The product is safe for the user, and for the environment, when used as recommended.

[1] SPC – Summary of product Characteristics.

Suitable warnings and precautions are indicated in the SPC. The efficacy [2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTIUENTS

II.A. Composition

The product contains (per tablet), 5 mg prednisolone and the excipients lactose monohydrate, maize starch, pregelatinised starch, stearic acid, talc and magnesium stearate.

The product is supplied in cardboard boxes containing PVC aluminium/PVC foil blisters as well as white high- density polyethylene bottles containing 250 tablets, sealed with a white, child-resistant, polypropylene closure. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the absence of preservative are justified.

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

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of a mixing, milling, drying, blending and compression process. The tablets are then suitable packaged.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is prednisolone, an established active substance described in the European Pharmacopoeia (Ph. Eur) and is produced in accordance with a Certificate of Suitability. 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.

All excipients are monographed in the Ph. Eur. Packaging meets the appropriate requirements.

[2] Efficacy – The production of a desired or intended result.

II.C.4. Substances of Biological Origin

Appropriate data were provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 site have been provided demonstrating compliance with the specification. Control tests on the finished tablets are those for: appearance, identification, weight, loss on drying, thickness, hardness, friability, disintegration, dissolution, uniformity of dosage units, related substances and microbiological quality.

II.F. 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.

G. Other Information

- Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
- This veterinary medicinal product does not require any special storage conditions.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

The proposed product was deemed to be identical to the reference product and therefore, additional pharmacological and toxicological data were not required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore, the following applicant's user recommendations are appropriate:

- Pharmacological effects of prednisolone cannot be excluded following accidental ingestion of the product. The product is supplied in a container with a child-resistant closure. The cap of the container must be securely engaged after use.
- **If smaller quantities are dispensed from the pack, they must be supplied in a container with a child-resistant closure**. If appropriate containers are not available, the product must be supplied in the original container. Store the product safely, out of the sight and reach of children.
- In case of accidental ingestion seek medical attention and show product label and/or pack insert to the doctor.
- Immediately wash hands thoroughly after handling the tablets.
- People with known hypersensitivity to prednisolone or other corticosteroids should avoid contact with the veterinary medicinal product.
- Corticosteroids can cause foetal malformations; therefore, it is recommended that pregnant women avoid contact with the veterinary medicinal product.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Due to the nature of the application, no additional data were required.

Pharmacodynamics

Prednisolone is a synthetic corticosteroid anti-inflammatory drug belonging to the glucocorticoid family. It has relatively slight mineralocorticoid effects. The action of glucocorticoids in suppressing inflammation may be therapeutic in a variety of conditions. The anti-inflammatory potency differs between glucocorticoids, that of prednisolone being about four times greater than hydrocortisone but about five times less than betamethasone. Anti-inflammatory actions are mediated via the glucocorticoid receptor (GR). In particular, glucocorticoids repress transcription of many genes encoding pro-inflammatory cytokines and chemokines, cell adhesion molecules and key enzymes involved in the initiation and/or maintenance of the host inflammatory response.

Pharmacokinetics

Prednisolone is readily absorbed from the gastro-intestinal tract and peak plasma levels are reached within 1 to 2 hours. It spreads throughout all tissues and body fluids, it crosses the placental barrier, and is excreted in small amounts in milk. Prednisolone is extensively bound to plasma proteins. The half-life varies between 2 to 4 hours and the parent plus metabolites are excreted in the urine.

Tolerance in the Target Species

Due to the nature of the application, additional data were not required for this section.

IV.II. Clinical Documentation

A biowaiver confirming the bioequivalence of the proposed and reference products undersection 7.1.d) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2) was accepted. Therefore, there was no requirement for further data for this section.

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 of the product is favourable.

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MODULE 4

POST-AUTHORISATION ASSESSMENTS

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

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.

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Summary of change (procedure number)	**Section updated**	**Approval date**
Change in the RMS from UK (procedure number UK/V/0683/001/DC) to NL (procedure number NL/V/0351/001).	Module 1 procedure number, applicant, Module 3 CMS's	12 February 2020
NL/V/0351/IB/001/G - Type IA: A.z: add a carton as secondary packaging. Type IB: C.II.6.b: to amend the concertina label and package leaflet layout. QRD text has not been amended.	Module 4	3 September 2020
NL/V/xxxx/IA/048/G - Type IAin: C.I.9.a : Change(s) to an existing pharmacovigilance system as described in the detailed description of the pharmacovigilance system (DDPS). Change in the QPPV and/or QPPV contact details and/or back-up procedure due to a change in QPPV activities from the UK to the EU due to Brexit. C.I.9.b : Change(s) to an existing pharmacovigilance system as described in the detailed description of the pharmacovigilance system (DDPS).	Module 4	24 October 2020
NL/V/0351/II/002/G – Type IA: B.II.b.5.b Change to inprocess test(s) or limits applied during the manufacture of the finished product B.II.d.1.z Change in the specification parameters and/or limits of the finished product B.III.1.a.2 To update the Ph. Eur. Certificate of Suitability for prednisolone from R0-CEP 2014-153-Rev 01 to R1-CEP 2014-153-Rev 01.The name and address of the manufacturer of the active substance remain unchanged. Type II: B.II.d.1.e Change outside the approved specifications limits range	Module 4	22 May 2021
NL/V/0351/001/VNRA with submission id: 3675: Replacement of GB batch release site by EU site (Millpledge Europe BVBA) ; Replacement of batch control site. Deletion of batch control site; Batch size change; Immediate package change: HDPE bottle, PP closure; 3676: Deletion of batch control site; 3677; Deletion of batch control site.	Module 3, 4	16 November 2022

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NL/V/0351/001/A/004 - VRA-S: F.II.d.1.a - Change in the specification parameters and/or limits of the finished product	-	10 June 2023
NL/V/0351/A/005/G - VRA-R: F.II.e.1.b.1 - Update stability data; VRA-R: F.II.e.5.a - Introduction of a blister pack.	Module 3	13 September 2023