IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Preglukord 25 mg tablets for dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0615/001-003/DC
Name, strength and pharmaceutical form	Preglukord 25 mg tablets for dogs
Active substance(s)	Prednisolone
Applicant	Accord Healthcare B.V. Winthontlaan 200, Utrecht, 3526KV, Netherlands
Legal basis of application	Bibliographic application in accordance with Article 22 of Regulation (EU) 2019/6.
Date of completion of procedure	26/11/2025
Target species	Dogs
Indication for use	For the symptomatic treatment or as adjunct treatment of inflammatory and immune-mediated diseases in dogs and cats.
ATC vet code	QH02AB06
Concerned Member States	BE, IT, NL, PL, UK(NI)
Withdrawn CMS during decentralised procedure	FR, ES, DE

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in the relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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, 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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

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A. Qualitative and Quantitative Particulars

The product contains the active substance prednisolone at 25 mg/ tablet and the excipients lactose monohydrate, starch, pregelatinised, sodium starch glycolate (Type A), glycerol dibehenate, magnesium stearate and purified water. The container/closure system consists of a white polyethylene bottle with white polypropylene twist-off cap and 3 g dessicant. 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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials
The active substance is prednisolone 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 has been provided.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
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.

D. Control on Intermediate Products
In-process control tests are carried out on intermediate stages of manufacture in order to verify the consistency of the manufacturing process and the final product.
A specification was set for each intermediate and the analytical methods are described and validated, if 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 has been provided. Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

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.
Stability data on the finished product has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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III. SAFETY ASSESSMENT

No product-specific safety or toxicology studies were undertaken by the Applicant. Rather, reference was made to publicly available data from the European Medicines Agency (EMA), Committee for Veterinary Medicinal Products (CVMP), and published literature. The pharmacological and toxicological data on the active substance were reviewed previously by CVMP in the context of an application to establish an MRL (Prednisolone Summary Report, EMEA/MRL/629/99-FINAL). Therefore, in this report, reference is made to the CVMP conclusions on those data. According to Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 "*when the substance has been previously evaluated for the establishment of maximum residues limit ("MRL") to address certain safety requirements reference may be made to the European public MRL assessment reports ("EPMARs"). Where reference to EPMAR is made there is no need to submit studies already evaluated as part of the MRL evaluation.*"

Pharmacological Studies

The Applicant provided published references reviewing the pharmacology of prednisolone. It was accepted that given its longstanding use, the pharmacodynamic properties of prednisolone are well documented and are adequately described in the dossier.

Prednisolone is a synthetic corticosteroid anti-inflammatory drug belonging to the glucocorticoid family. The main effects of prednisolone are the same as those of glucocorticoids:

Anti-inflammatory action:
The anti-inflammatory properties of prednisolone are expressed at a low dose and can be attributed to:
- the inhibition of phospholipase A2, which reduces the synthesis of arachidonic acid, a precursor of many proinflammatory metabolites. Arachidonic acid is released from the phospholipid component of the cell membrane by the action of phospholipase A2. Corticosteroids indirectly inhibit this enzyme by inducing the endogenous synthesis of polypeptides, lipocortins, which have an anti-phospholipase action;
- a membrane stabilising effect, particularly in relation to lysosomes, thus preventing enzymes from being released outside the lysosomal compartment.

Immunosuppressive action:
The immunosuppressive properties of prednisolone are expressed at a higher dose impacting macrophages (slower phagocytosis, decreased flow to inflammatory foci), neutrophils and lymphocytes. Administration of prednisolone reduces the production of antibodies and inhibits several complement components.

Antiallergic action:
Like all corticosteroids, prednisolone inhibits the release of histamine from mast cells. Prednisolone is active in all manifestations of allergy as a complement to the specific treatment.

The Applicant provided a summary of the pharmacokinetics of prednisolone in in a number of species including cattle, horses, cats, dogs and humans.

Prednisolone is readily absorbed from the gastro-intestinal tract. Peak plasma concentrations are reached 0.5 to 1.5 hours after administration, with a plasma half-life of between 3 and 5 hours. It is distributed to all tissues and body fluids, even in the cerebrospinal fluid. It is extensively bound to plasma proteins, is metabolized in the liver and primarily excreted via the kidneys. It is excreted in the urine as free and conjugated metabolites and parent compound. It has a biological half-life of several hours, making it suitable for alternate-day therapy.

The pharmacological data provided by the Applicant is appropriately reflected in the SPC.

Toxicological Studies

The Applicant provided bibliographic data which are summarised below.

- The acute oral LD50 of prednisolone was 1680 mg/kg bw in male and female mice.
- A pharmacological NOEL of 20 micrograms/kg bw/day was established for induction of tyrosine aminotransferase activity in the rat.
- Studies in mice, rabbits, hamsters and rats showed that prednisolone caused malformations including cleft palate when administered parenterally. The teratogenic potential was much less when administered orally and a NOEL of 3 mg/kg bw/day was established in rats following oral dosing.
- Prednisolone is not considered to be genotoxic.
- Prednisolone is not considered to be carcinogenic.

User Safety

The Applicant presented a user safety assessment which was partially in accordance with the relevant guideline. Several amendments to the user safety warnings were proposed and accepted by the Applicant. The warnings and precautions as listed on the product literature (presented below) are adequate to suitably mitigate against known risks to users of the product.

'Prednisolone or other corticosteroids may cause hypersensitivity (allergic reactions).
People with known hypersensitivity to prednisolone or other corticosteroids, should avoid contact with the veterinary medicinal product.
Prednisolone may lead to gastrointestinal effects (nausea, vomiting, diarrhoea), headache, and/or hyperactivity if accidentally ingested, particularly in children.
To avoid accidental ingestion, particularly by a child, unused tablets and unused half-tablets should be returned to the container.
In case of accidental ingestion, especially by a child, seek medical advice immediately and show the package leaflet or the label to the physician.
Corticosteroids can cause foetal malformations. Pregnant women should avoid contact with the veterinary medicinal product.
Immediately wash hands thoroughly after handling the tablets.'

Environmental Risk Assessment

Phase I
An environmental risk assessment that is compliant with relevant guidance was submitted. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP is intended for use in non-food producing animals.

Conclusion
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

This application is made in accordance with Article 22 of Regulation (EU) 2019/6 (based on bibliographic data). As per this legal basis, the Applicant shall not be required to provide proprietary documentation on (safety and) efficacy if that applicant demonstrates that the active substances of the veterinary medicinal product have been in well-established veterinary use within the Union for at least 10 years, that their efficacy is documented and that they provide an acceptable level of safety. Prednisolone has been authorised for veterinary use (in dogs, cats, horses and cattle) in the Union for over 30 years and is thus considered to meet the "well-established veterinary use" criteria.

IV.A Pre-Clinical Studies

Pharmacology

See Part 3.

Tolerance in the Target Species of Animals

No proprietary target animal safety studies were presented. Rather, numerous references from published literature have been provided to support tolerance in the target species.
In line with Annex II, the information is mostly peer- reviewed and freely available. However, none of the studies were conducted or reported in accordance with VICH GL43. In addition, none of the studies were performed with the final formulation; instead, the information provided relates to a variety of different products/formulations from different manufacturers. Notwithstanding this, it is acknowledged that literature findings reflect extensive 'field' use and were relatively consistent with regards to the tolerance of prednisolone (regardless of formulation administered).
Appropriate risk management and mitigation statements are proposed with regards to the use of prednisolone.
While no safety data have been provided on use during pregnancy and lactation in the target species, evidence from laboratory animals and from humans have indicated that the substance may lead to congenital defects. Appropriate precautions and relevant information have been included under 3.7 of the SPC.

The product literature accurately reflects the type and incidence of adverse effects which might be expected in the target species under normal conditions of use.

IV.B Clinical Studies

The references provided detail the use of prednisolone in the target species, both as monotherapy or adjunct treatment for the treatment of conditions such as allergic dermatitis, pemphigus foliaceous, steroid responsive meningitis-arteritis, granulomatous meningo-encephalitis, necrotising encephalitis, hypoadrenocorticism, osteoarthritis, immune-mediated haemolytic anaemia, immune-mediated thrombocytopaenia and immune-mediated polyarthritis. acute pancreatitis, pyogranulomatous lymphadenitis, steroid-responsive meningitis-arteritis, lymphocytic cholangitis and pemphigus foliaceous. Based on the data provided, it is accepted that prednisolone, when administered orally, is effective for "the symptomatic treatment or as adjunct treatment of inflammatory and immune-mediated diseases in dogs."

While several studies, describing prednisolone use in auto-immune diseases, involve dosages of up to 4mg/kg (higher than the proposed dose range for the candidate product), the references provided generally support the proposed starting dose of 0.5-2mg/kg bodyweight once daily. A dose range is proposed allowing for the prescribing veterinarian's discretion in relation to dose to be administered and duration of treatment based on severity of presenting symptoms. For longer term treatment: when after a period of daily dosing the desired effect has been achieved, the dose should be reduced to the lowest effective dose, achieved by alternate day therapy and /or by halving the dose with intervals of 5-7 days until the lowest effective dose is reached.

While no clear overall conclusion was presented by the Applicant to support the extrapolation of clinical efficacy from the literature to the candidate product, literature findings reflect extensive 'field' use and were relatively consistent with regards to therapeutic effects of prednisolone regardless of formulation administered (the information provided relates to a variety of different products/formulations from different manufacturers). Therefore, while no data have been generated with the candidate formulation, the information that has been provided suggests that the formulation (composition in terms of excipients) is likely to have minimal impact on efficacy when prednisolone is administered orally. That is, similar effects can be expected with the candidate product is administered at the recommended treatment dose.

In conclusion, the bibliographic data provided support the well-established use of prednisolone and its efficacy for the proposed indications using the proposed posology in the target species.

In addition, both the claimed indications and posology are consistent with those included in the product information of similar prednisolone-containing veterinary medicinal products.

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.

VI. 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 HPRA website.
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.

Changes:
None.