Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ekyflogyl 1.8mg/ml + 8.7mg/ml Gel for Horses

Date Created: October 2021

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Ekyflogyl 1.8mg/ml + 8.7mg/ml Gel for Horses
Applicant	AUDEVARD, 42-46 rue Médéric, 92110 CLICHY, 92110, FRANCE
Active substance	Lidocaine Hydrochloride, Prednisolone
ATC Vetcode	Qm02AX99
Target species	Horses
Indication for use	For the alleviation of pain and inflammation associated with localised musculoskeletal disorders.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic 'hybrid' application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	7th September 2021

I. SCIENTIFIC OVERVIEW

This was an application for a generic 'hybrid' application, in accordance with Article 13 (3) of Directive 2001/82/EC as amended, as plasma-level bioequivalence cannot be assessed for topically applied products. The product is indicated for use in horses, for the treatment of for the alleviation of pain and inflammation associated with localised musculoskeletal disorders. The reference product is Trinodol Gel, marketed in France since 1986.

The dose is 11 to 32 ml twice daily, corresponding to 6 to 18 actuations of the pump dispenser, depending on the nature of the lesion. The treatment can be continued until the clinical signs are resolved, but the product may not be used for more than 12 days.

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, any reactions observed are indicated in the SPC.[1] 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 [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.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 1.8 mg/ml prednisolone (as acetate), and 8.7 mg/ml lidocaine (as hydrochloride monohydrate), and the excipients dimethyl sulfoxide, Hydroxyethylcellulose and purified water.

The container/closure system consists of a brown Type III glass bottle with a dosing pump made of high density polyethylene/polypropylene, and a dip tube made of low density polyethylene/polypropylene. The cap is a polypropylene screw-fit. A box of one 125 ml bottle. 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 and heating and cooling of the ingredients, followed by packaging of the product.

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

II.C. Control of Starting Materials

The active substances are prednisolone acetate and lidocaine hydrochloride monohydrate, established active substances described in the European Pharmacopoeia (Ph. Eur). 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. Appropriate Certificates of Suitability were provided. The excipients are cited in Ph. Eur, and packaging is suitably controlled.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

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 product are those for: appearance, identification. Impurities and microbiological quality.

II.F. Stability

Stability data on the active substances have 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: 3 years.
Shelf life after first opening the immediate packaging: 30 days.
Do not store above 30°C.
Store in the outer carton in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Due to the nature of the application, toxicological and pharmacological studies were not required. A user risk assessment and environmental assessment were provided.

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:

This product may cause allergic reactions. People with known hypersensitivity to prednisolone, lidocaine, other local anaesthetics or dimethyl sulfoxide (DMSO) should not handle the product.
- Prednisolone may cause harm to the unborn foetus. Pregnant women should therefore not handle this product.
- This product may be harmful after dermal and oral exposure. Lidocaine may form genotoxic metabolites in humans. A long-term toxicology study in rats has shown evidence that these metabolites can also induce carcinogenic effects at high doses. The product is also irritating to the skin (reactions including erythema and pruritus) and to the eye.
- Avoid contact with skin, eye and mouth, including hand-to-mouth and hand-to-eye contact. Wash hands after use. In the event of accidental contact with the skin or eyes, rinse thoroughly with water.
- Personal protective equipment consisting of impermeable single-use protective gloves should be worn when handling the veterinary medicinal product or touching the treated area.
- Prevent children from touching the treated horse during the period of treatment and 12 days after the end of the treatment.
- Do not touch the treated area. If this is necessary for horse care, wear impermeable single-use protective gloves.
- In the event of accidental ingestion or persistent skin or eye irritation, seek medical advice immediately and show the package leaflet or the label to the physician.
- Additional material or devices used to apply the product such as a brush should be cleaned up thoroughly or disposed of according to local requirements.
- Keep the bottle with the dosing pump in the outer carton and in safe place out of the sight and reach of children until ready to use. The device should be locked after each use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines. The product will be used to treat a small number of animals and as such environmental exposure will be low. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the product is contraindicated for use in horses intended for human consumption.

Withdrawal Periods

Not authorised for use in horses intended for human consumption.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Pharmacodynamics

No *in vitro* or *in vivo* studies were conducted by the applicant. The product will have the same pharmacodynamic properties after topical application to horses. The proposed SPC reflects that of the reference product.

Pharmacokinetics

The test and reference products are intended for topical administration and are locally active. Exemption was claimed from providing *in vivo* bioequivalence studies. Due to the nature of the application, this was accepted. Therefore, bioequivalence studies have not been provided in accordance with the legal base.

Tolerance in the Target Species

Tolerance studies were not required due to the nature of the application.

Resistance

Resistance studies were not required due to the nature of the application.

IV.II. Clinical Documentation

Clinical studies were not required due to the nature of the application.

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.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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