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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

EKYFLOGYL (VET) 1.8 mg/ml + 8.7 mg/ml GEL FOR HORSES

DATE: 23 AUGUST 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0344/001/DC
Name, strength and pharmaceutical form	EKYFLOGYL (VET) 1.8 mg/ml + 8.7 mg/ml GEL FOR HORSES 1.8 mg prednisolone and 8.7 mg lidocaine/ml, Gel for cutaneous use
Applicant	AUDEVARD 42-46 rue Médéric 92110 Clichy FRANCE
Active substance(s)	Prednisolone (as acetate) Lidocaine (as hydrochloride monohydrate)
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 website http://www.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13.3 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	03/07/2019
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	AT, DE, DK, FI, IE, LU, NL, NO, PL, PT, SE

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 slight local reactions that may occur following the cutaneous application of the product are mentioned 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 claim for this product as described in the SPC is based on the reference product's indications for use.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

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

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.

C. Control of Starting Materials

The active substances are prednisolone (as acetate) and lidocaine (as hydrochloride monohydrate), which are established active substances described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.
The specifications of active substances are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

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

Certificates of suitability issued by the EDQM have been 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.

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

Stability data on the active substance, prednisolone acetate have been provided in accordance with applicable European guidelines, demonstrating the stability of this active substance when stored under the approved conditions.

A re-test period for the active substance, lidocaine hydrochloride monohydrate 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)

This application is submitted in agreement with the Article 13(3) as hybrid application. The cited reference product is EKYFLOGYL authorized in France since 1986.

III.A Safety Testing

Pharmacological Studies

Based on information provided in support of this application, it is accepted that the candidate product is bioequivalent to the reference product.

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

Toxicological Studies

As this is an hybrid application according to Article 13(3), 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

The applicant has provided a user safety assessment for the candidate product in compliance with the relevant guideline.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of this product:

- This product may cause allergic reactions. People with known hypersensitivity to prednisolone, lidocaine, other local anaesthetics or any of the excipients 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 (see details in section 4.9).

Environmental Risk Assessment

The environmental risk assessment can stop in Phase I, Question No. 5, because the candidate product is intended for individual treatment of horses. No phase II assessment is required. The product will not pose an unacceptable risk to the environment when used according to the SPC.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because the candidate product has an identical formulation as the reference product and is indicated in the same species at the same dosage and dose regimen.

MRLs

The active substances, prednisolone and lidocaine, are included in table 1 of the MRL regulation 470/2009, as follows:

PREDNISOLONE ADI : 0.2 µg/kg						
Marker residue	**Animal Species**	**MRL**	**Target Tissues**	**Other Provisions**	**Therapeutic Classification**	**Regulation**
Prednisolone	Horses	4 µg/kg 8 µg/kg 6 µg/kg 15 µg/kg	Muscle Fat Liver Kidney	No entry	Corticoids/ Glucorticoids	406/2013 of 02.05.2013

LIDOCAINE No ADI						
Marker residue	**Animal Species**	**MRL**	**Target Tissues**	**Other Provisions**	**Therapeutic Classification**	**Regulation**
Not applicable	*Equidae*	No MRL required	Not applicable	For local-regional anaeshesia only	No entry	37/2010 of 22.12.2009

Withdrawal Periods

According to the type of application, the withdrawal periods for the reference product are applied to this product.

Species	Tissues	**Withdrawal periods**
Horse	Meat & offal	10 days
	Milk	Not authorised for use in animals producing milk for human consumption

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

The Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-rev.2) does not apply for this topically applied product, since it is not possible to demonstrate systemic bioavailability. Bioequivalence between the reference and the candidate products is accepted as both formulations are the same, qualitatively and quantitatively, for both active substances and excipients.

Tolerance in the Target Species

The toxicological aspects of this product are identical to the reference product.
As this is a hybrid application according to Article 13(3) and bioequivalence with the reference product has been demonstrated, results of tolerance tests are not required.
The safety aspects of this product are identical to those of the reference product.

IV.B Clinical Studies

As this is a hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, efficacy studies are not required. The efficacy claim for this product is based on the indications for use 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.

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 veterinary Heads of 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.

None.