DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dalmaprost 0.075 mg/ml solution for injection for cattle, pigs and horses (AT, BE, BG, HR, CY, CZ, DK, EE, ES, FR, DE, EL, HU, IS, IE, IT, LV, LT, LU, MT, NL, PL, PT, RO, SK, SI, UK(NI))

Dalmaprost vet 0.075 mg/ml solution for injection for cattle, pigs and horses (FI, NO, SE)

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0305/001/DC
Name, strength and pharmaceutical form	Dalmaprost 0.075 mg/ml solution for injection forcattle, pigs and horses (AT, BE, BG, HR, CY, CZ, DK, EE, ES, FR, DE, EL, HU, IS, IE, IT, LV, LT, LU, MT, NL, PL, PT, RO, SK, SI, UK(NI)) Dalmaprost vet 0.075 mg/ml solution for injection for cattle, pigs and horses (FI, NO, SE)
Applicant	FATRO S.p.A.
Active substance(s)	(+)-Cloprostenol
ATC Vetcode	QG02AD90
Target species	Cattle (cows), pigs (sows) and horses (mares)
Indication for use	Cows: Synchronisation or induction of oestrus; Induction of parturition after day 270 of gestation; Treatment of ovarian dysfunction (persistent corpus luteum, luteal cyst); Treatment of clinical endometritis with the presence of a functional corpus luteum and pyometra; Treatment of delayed uterine involution; Induction of abortion up to day 150 of gestation; Expulsion of mummified foetuses. Sows: Induction of parturition after day 114 of gestation. Mares: Induction of luteolysis with a functional corpus luteum.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13.1 of Directive 2001/82/EC as amended.
Date of completion of the decentralised procedure	31/07/2019
Date product first authorised in the ReferenceMemberState (MRP only)	-
Concerned Member States for original procedure	AT, BE, BG, HR, CY, CZ, DK, EE, FI, FR, DE, EL, HU, IS, IE, IT, LV, LT, LU, MT, NL, NO, PL, PT, RO, SK, SI, SE, UK(NI)

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 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 product contains 0.075 mg of (+)-cloprostenol (equivalent to 0.079 mg of (+)-cloprostenol sodium) as active substance and as excipients: chlorocresol (preservative), sodium hydroxide, citric acid, ethanol (96 per cent) and water for injections.

The container/closure system are colourless type I glass vial (2 ml), colourless type II glass vials (10 ml and 20 ml) and high density polyethylene (HDPE) container (100 ml) closed with a chlorobutyl type I stopper and a flip-off aluminium collar, in a cardboard box.

The choice of the formulation and presence of preservative are justified.

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 substance is (+)-cloprostenol (sodium), it is not described in the European/British Veterinary Pharmacopoeia but the monograph for the racemic form of the active substance is found in the British Pharmacopeia (Veterinary) and in USP. The information on the active substance is provided according to the Active Substance Master File (ASMF) procedure. 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.

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

D. Control on intermediate products

Not 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 have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance have 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 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.

Appropriate in-use stability data have been also provided to support the proposed in-use shelf-life period of 28 days for the medicinal product.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, results of safety tests are not required.

The safety and residues aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of toxicological studies and other requirements are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the exposure, hazards and risks from the use of the product will be similar to those for the reference product, and for that reason, the same mitigation measures are included in the SPC and product literature.

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 a small number of animals in a flock or herd.

Nevertheless, d-cloprostenol is a prostaglandin-like substance that might have an effect in the sexual function of fish. However, although the risk for fish exists the

exposure is not likely to surpass the effect level. To address this concern the following warning was including in the SPC to avoid the direct exposure of the active substance to the water compartment: “The product should not enter water courses as this may be dangerous for fish and other aquatic organisms”.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted on the basis that bioequivalence with the reference product has been demonstrated. Taking into account that both products have the same qualitative and quantitative composition, it is expected to have the same residues depletion profile, and the withdrawal periods will be the same.

MRLs

(+)-Cloprostenol is listed in table 1 of the annex to Commission Regulation (EU) No 37/2010.

MRLs are listed below:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
R-Cloprostenol	Not applicable	Bovines, porcine, caprine and *Equidae*	No MRL required	Not applicable	No entry

The excipients are classified as follows:

Excipient	Status
Ethanol	Included in table 1 of Commission Regulation (EU) No 37/2010 – No MRL required
Chlorocresol	
Sodium hydroxide	
Citric acid, anhydrous	
Water	Included in the list of substances considered as not falling within the scope of Council Regulation (EC) No. 470/2009.

Withdrawal Periods

The withdrawal periods for the proposed product are the same as those of the reference product:

Cattle:
Meat and offal: zero days.
Milk: zero hours.

Pigs:

Meat and offal: 1 day

Horses:
Meat and offal: 2 days.
Milk: zero hours.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

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,