ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

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Veterinary Medicines Directorate
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(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

CIDR 1.38g Vaginal Delivery System for Cattle

PuAR correct as of 17/04/2018 when RMS was transferred to ES. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0221/001/E/001
Name, strength and pharmaceutical form	CIDR 1.38g Vaginal Delivery System for Cattle
Applicant	Zoetis UK Limited 5th Floor 6 St. Andrew Street London EC4A 3AE
Active substance	Progesterone
ATC Vetcode	QG03DA04
Target species	Cattle
Indication for use	For the control of the oestrous cycle in cycling cows and heifers, including: • Synchronisation of oestrus in groups of animals including fixed time artificial insemination (FTAI) programmes. • Synchronisation of donor and recipient animals for embryo transfer. • To be used in combination with prostaglandin F2α or analogue. • Use as recommended normally results in oestrus 48-96 hours after device removal with the majority of animals showing oestrus within 48-72 hours. For induction and synchronisation of oestrus in Fixed Time Artificial Insemination (FTAI) protocols: • In cycling and non-cycling cows and heifers. To be used in combination with prostaglandin F2α (PGF2α) or analogue. • In cycling and non-cycling cows and heifers. Gonadotrophin releasing hormone (GnRH) or analogue and PGF2α or analogue. • In non-cycling cattle. To be used in combination with PGF2α or analogue and equine chorionic gonadotrophin (eCG).

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual Recognition application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original Mutual Recognition Procedure	28 September 2011
Date product first authorised in the Reference Member State (MRP only)	20 February 2008
Concerned Member States for original procedure	Austria, Belgium, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain Addtional CMSs added for Mutual Recognition (Repeat Use) procedure Bulgaria, Denmark, Iceland, Norway, Romania, Sweden

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 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. Composition

The product contains the active substance progesterone and excipients silicone elastomer, nylon spine and polyester tail.

The devices are packed in a heat-sealed opaque low-density polyethylene bag.

Each bag contains ten devices. Sachets are re-sealable (zip-line). The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is 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 progesterone. Supporting data have been provided in the form of an Active Substance Master File (ASMF). It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

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

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

E. Control on intermediate products

There are no intermediate products.

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

The stability of progesterone is discussed in the ASMF assessment report. 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.

H. Genetically Modified Organisms

Not applicable.

I. Other Information

Shelf life:
Shelf-life of the veterinary product as packaged for sale: 2 years.

Special precautions for storage:
Store below 30° C.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

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

The pharmacological 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 / consumers

Toxicological Studies

As this is a generic application according to Article 13, 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.

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 / consumers

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which considered the main routes of exposure.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.
Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

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

The residue 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 / consumers

MRLs

Progesterone is listed in Annex II of Council Regulation 2377/90.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days for meat, offal and for milk is justified. During the treatment, mik can be used for human consumption.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

The applicant presented a comprehensive background, based on literature references, on the pharmacodynamic effects of progesterone via the intravaginal delivery system. The application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, no further information is required as it has already been presented for the reference product. Bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

Tolerance in the Target Species of Animals

The target species tolerance information provided is considered satisfactory. The incidence of reported adverse reactions is very low, demonstrating little risk of the routine use of the product. The applicant also submitted a tolerance study using inserts with 1.9g progesterone. The inserts caused ulcers and erosions and formation of cloudy or pus-filled mucus in most heifers. However these effects were transient and most heifers had few or no residual effects by 1 week after treatment and fertility at first insemination after treatment was not affected by vaginal ulcers. Therefore the fertility was more likely to be related to the progesterone levels rather than the physical presence of the inserts and the tolerance of the inserts was good.

IV.B Clinical Studies

As this is an essential similarity application, clinical field data are not required as bioequivalence has been shown between the test and reference products. However, the applicant submitted two published references that described the use of the product for 7 days to successfully synchronise return to oestrus. The indications claimed for the test product are the same as those already claimed for 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 benefit/risk 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 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.
(www.gov.uk/check-animal-medicine-licensed)