MINISTERIO
DE SANIDAD, POLÍTICA SOCIAL
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

SUBDIRECCIÓN GENERAL
DE MEDICAMENTOS
DE USO VETERINARIO

# Agencia Española de Medicamentos y Productos Sanitarios

Parque Empresarial Las Mercedes
Edificio 8
C/Campezo 1,
28022 – Madrid
España
**(Reference Member State)**

**DECENTRALISED PROCEDURE**

# [DRAFT] PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

## ACEGON 50 McG/ML

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# MODULE 1

## PRODUCT SUMMARY

| | |
|---|---|
| EU Procedure number | ES/V/0158/001/DC |
| Name, strength and pharmaceutical form | ACEGON, 50 µg/ml, solution for injection for cattle |
| Applicant | Lab. Syva, S.A. |
| Active substance(s) | Gonadorelin acetate |
| ATC Vet code | QH01CA01 |
| Target species | Cattle: cows, heifers |
| Indication for use | Treatment of ovarian follicular cysts.<br>In association with artificial insemination to optimise the time of ovulation. |

# 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 original decentralised procedure | 26/01/2011 |
| Date product first authorised in the Reference Member State (MRP only) | |
| Concerned Member States for original procedure | DE, FR, HU, IT, NL, PL, UK |

## 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, 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 52,5 mcg of gonadorelin acetate and excipients benzyl alcohol, potassium dihydrogen phosphate, dipotassium hydrogen phosphate, sodium chloride and water for injections.

The container/closure system is colourless glass vials Type II, closed with Type I bromobutyl rubber stoppers and aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the preservatives 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 gonadorelin, an established active substance described in the European Veterinary 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 have been provided.

CEP (No. R0-CEP 2005-022-Rev 00).

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

Scientific data and/or 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> (pharmaceuticals)*

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

### *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 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.

### *H. Genetically Modified Organisms*

### *J. Other Information*

# III. SAFETY AND RESIDUES ASSESSMENT

As this is a generic application according to Article 13 of Directive 2001/82/EC, as amended, and bioequivalence with a reference product has been demonstrated, results of safety tests are not required.

The safety 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*

The applicant has provided bibliographical data which show that Gonadorelin stimulates the synthesis and release of the pituitary gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH).

The applicant has provided bibliographical data which show that in cows after intramuscular administration gonadorelin is rapidly absorbed from the injection site, there is a fast distribution to the adenohypophysis, the compound is rapidly metabolized into smaller inactive peptides and aminoacids and the main excretion route is renal.

### *Toxicological Studies*

The applicant has not conducted laboratory studies which show that relevant acute and chronic toxicity, reproductive, mutagenicity and carcinogenicity since this is a generic application according to Article 13 of Directive 2001/82/EC, as amended.

### *User Safety*

The applicant has provided a user safety assessment in compliance with the relevant guideline on User Safety for Pharmaceutical Veterinary Medical Products EMEA/CVMP/543/03.

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 EMEA/CVMP/592/98-FINAL which showed that no further assessment is required. The assessment concluded that Gonadorelin is a synthetic gonadorelin physiologically and chemically identical to the natural gonadorelin released by the hypothalamus in mammalian species. No warnings regarding Acegon 5 mg/ml are therefore required.

## *III.B Residues documentation*

### *Residue Studies*

The applicant has provided bibliographical data which show that they have equivalent depletion residue and the data for the authorised product can be applied to Acegon.

### *MRLs*

In accordance with Regulation (EC) No 470/2009 and Comission Regulation (EU) No 37/2010, Gonadorelin is not required MRL as shown below:

| Pharmacologically active substance | Marker residue | Animal species | MRL | Target tissues | Other provisions According to article 14(7) of regulation (EC) No 47072009 | Therapeutic classification |
|---|---|---|---|---|---|---|
| Gonadotrophin releasing hormone | Not applicable | All food producing species | No MRL required | Not applicable | Not entry | Not entry |

### *Withdrawal Periods*

Based on the data provided above, a withdrawal period of zero days for meat in cattle and zero hours for milk are justified.

# IV. CLINICAL ASSESSMENT (EFFICACY)

Acegon 50 mcg/ml solution for injection for cattle and contains 50 mg/ml of gonadorelin (as gonadorelin acetate ). It is a solution for injection intended for an intramuscular use and it is recommended for treatment of ovarian follicular cysts and optimization the conception rate after the insemination in cows and heifers. The recommended dosage is 100- 150 µg of gonadorelin /animal as follows.

- *Treatment of ovarian follicular cysts*: 100-150 µg of gonadorelin (as acetate) per animal (i.e. 2- 3 ml of the product per animal). If necessary, treatment can be repeated at intervals of 1-2 weeks.
- *In association with artificial insemination to optimise the time of ovulation, improving the chances that the treated cow will become fertile***:** 100 µg of gonadorelin (as acetate) per animal (i.e. 2 ml of the product per animal). It must be administered at the same time as artificial insemination and/or 12 days after this.

This is a generic application according to Article 13.1 of Directive 2001/82/EC, as amended, and no bioequivalence with a reference product has been carried out as both products are the same (It's an autogeneric ).

The applicant has submitted a Declaration of identical composition of the veterinary medicinal products GONASYL and ACEGON . The former authorised on 09-03-2001 in Spain for the same Laboratory applicant: Syva, S.A.

The target specie safety and efficacy aspects of this product are therefore identical to the reference product.

## *IV.A Pre-Clinical Studies (pharmaceuticals only)*

### *Pharmacology*

No studies are needed as the product is generic and identical to the reference product Gonasyl.

The applicant has provided bibliographical to address this section.

### *Tolerance in the Target Species of Animals*

No studies are needed as the product is generic and identical to the reference product Gonasyl.

### *Resistance*

Not applicable

## *IV.B Clinical Studies*

No studies are needed as the product is generic and identical to the reference product Gonasyl.
The applicant has provided bibliographical to address this section.

## 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).