Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ovimel 18 mg Implantation Tablets for Sheep

Date Created: September 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Ovimel 18 mg Implantation Tablets for Sheep
Applicant	Vetpharma Animal Health S.L, Les Corts, 23 08028 Barcelona Spain
Active substance	Melatonin
ATC Vetcode	QN05CH01
Target species	Sheep
Indication for use	To improve reproductive performance in sheep intended to be mated early in the season, before the usual peak in reproductive activity.

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 8 of Veterinary Medicine Regulations (VMRs) 2013 (Schedule 1, Para 10a) as amended.
Date of conclusion of the procedure	13/06/2025

I. SCIENTIFIC OVERVIEW

The application is for an MA in Great Britain (GB) submitted in accordance with Schedule 1, Paragraph 10a of the Veterinary Medicines Regulations 2013, as amended (a 'hybrid' application). The reference product is Regulin 18 mg Implant (Vm 15052/4011), marketed by Ceva Animal Health Ltd, which has been authorised in GB since 01 January 1993. The application is submitted as a hybrid application given that bioequivalence with the reference product cannot be demonstrated through bioavailability studies.

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, 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[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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains melatonin and the excipients ethylcellulose, povidone k90, magnesium stearate, hydrogenated vegetable oil and quinoleine yellow.

The container/closure system consists of 2 PVC/Alu Blisters containing one low-density polyethylene multi-shot tag cartridge. The particulars of the containers and controls performed are provided and conform to the regulation.

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

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 regulatory 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: granulating, drying, sieving blending and filling.

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

II.C. Control of Starting Materials

The active substance is melatonin an established active substance described in the European 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.

All excipients comply with the European Pharmacopoeia monographs except dibutyl sebacate, which complies with USP.

II.C.4. Substances of Biological Origin

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.

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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product are those appropriate for this type of dosage form.

II.F. Stability

Stability data on the active substance has been provided in accordance with applicable regulatory 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 regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: use immediately.

The veterinary medicinal product does not require any special storage conditions.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

Due to the legal basis of the applications, no pharmacological or toxicological data were submitted, which is acceptable. Bioequivalence of the products to the reference products was established, based on appropriate justification.

Warnings and precautions as listed on the product literature are generally the same as those of the reference product and are adequate to ensure safety of the product to users/the environment/consumers. One addition was to include the advice to use the entire contents of the pipette immediately once opened and dispose of any used pipettes immediately after use.

III.A Safety Documentation

Pharmacological Studies

Studies have been provided which show that melatonin acts by signaling photoperiodic change to the body, i.e. variations in the day length throughout the year. Its secretion takes place during the night hours of darkness. As day length decreases, melatonin secretion increases and triggers increased reproductive activity, thus producing a natural peak in breeding performance in the autumn. This veterinary medicinal product simulates the phenomenon; each implantation tablet gradually releases melatonin for 3 to 4 months at rates comparable to those observed during the endogenous nocturnal secretion phase.

The applicant has also provided bibliographical data which show that melatonin shows good absorption after subcutaneous administration. The absolute bioavailability of melatonin released by the implant is 81% based on published results in sheep (ewes).

Fourteen days after the placement of the implant, the plasma concentrations are stable and higher than the standard diurnal levels, remaining up to three months. Melatonin is metabolized in the liver to form 6-hydroxymelatonin that is conjugated with sulfate or glucuronic acid and excreted almost exclusively by urine.

Toxicological Studies

The applicant has submitted bibliographical references to address the pharmacology and toxicology of the active substance. This approach is acceptable given the generic-hybrid nature of the application, and that the active substance has a long history of use both in human and veterinary medicine.

Based on the literature provided, it can be concluded that the studies indicate that exogenous melatonin does not produce any serious adverse effects. Also, randomised clinical studies in humans indicate that long-term administration only induces mild adverse effects comparable to a placebo treatment, such as headache or sleepiness. Melatonin is non-teratogenic, non-genotoxic, non-mutagenic and has no apparent skin irritation or sensitisation potential.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the products are not considered to present an unacceptable risk to the user when used as recommended.

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:

- Administer the veterinary medicinal product with caution to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately, and show the package leaflet or the label to the physician.
- Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The initial predicted environmental concentration (PEC) in soil is less than 100 µg/kg. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted.

MRLs

Melatonin is listed in Table 1 of Commission Regulation 37/2010 and MRLs have been established with No MRL Required.

Withdrawal Periods

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

IV. CLINICAL DOCUMENTATION

As this is a generic hybrid application, and bioequivalence with the reference product has been accepted, efficacy studies are not required. The efficacy claims, dosing regimens, and pharmacology for the product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

Pharmacology

The applicant has provided various scientific papers to document the general pharmacological effects and main mechanism of action of melatonin. Due to the legal basis of the application, the pharmacodynamics can be extrapolated from the reference product. The pharmacodynamics of melatonin have been well documented in section 4.2 of the SPC.

Tolerance in the Target Species

The applicant has conducted a controlled target animal tolerance study using multiples of the recommended dose in the target species. An authorised reference product containing the same active substance, was used as a control. All doses were administered by injection with either single dose/single period, triple dose/single period, single dose/triple period and the negative control group, which received a single dose of the control.

Parameters evaluated were the inspection of injection site, levels of CPK and AST were monitored and any internal findings at necropsy.

No adverse effects were seen following doses up to 3 times the recommended dose. The lack of a 5x dose group is considered acceptable, as the potential for such an overdose is considered extremely unlikely.

Adequate warnings and precautions appear on the product literature.

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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