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College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Synthadon 5 & 10 mg/ml solution for injection for dogs and cats

Created: December 2019

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0183/001-002/DC
Name, strength and pharmaceutical form	Synthadon 5 & 10 mg/ml solution for injection for dogs and cats
Applicant	LeVet Beheer B.V. Wilgenweg 7 3421 TV Oudewater The Netherlands
Active substance(s)	Methadone
ATC Vetcode	QN02AC90
Target species	Dogs and cats
Indication for use	Analgesia in dogs and cats. Premedication for general anaesthesia or neuroleptanalgesia in dogs and cats in combination with a neuroleptic drug.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Synthadon 5 mg/ml: Hybrid application made in accordance with Article 13(3) of Directive 2001/82/EC as amended. Synthadon 10 mg/ml: Generic application made in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21 May 2014
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Synthadon 5 mg: AT, BE, CY, CZ, DK, EE, EL, ES, FI, FR, HU, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SK, UK. Synthadon 10 mg: AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SK, 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 slight reactions observed are indicated in the SPC.
The product is safe for the user, 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.

Synthadon 10 mg/ml is a generic application, and Synthadon 5 mg/ml is a hybrid application (different pharmaceutical strength). The reference products are Methadon HCL (REG NL 2594) and Comfortan 10 mg/ml solution for injection for dogs and cats (REG NL 107389), both from marketing authorisation holder Eurovet Animal Health B.V.

Synthadon 5 & 10 mg/ml solution for injection for dogs and cats	NL/V/0183/001-002/DC
Le Vet Beheer B.V.	DCP
	Publicly available assessment report

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The products contain 5 or 10 mg/ml methadone hydrochloride and the following excipients: methyl parahydroxybenzoate, propyl parahydroxybenzoate, sodium chloride and water for injection. Hydrochloric acid and sodium hydroxide are used for pH adjustment.

The product is packed in amber type I glass bottles of 50 ml, fitted with grey fluorinated polymer coated bromobutyl rubber stoppers and aluminium caps. The glass vials and stoppers are in conformity with the Ph.Eur. requirements

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.

The product is manufactured using conventional manufacturing techniques. Process validation results for two smallest commercial batches have been provided. Process validation results for two full-scale batches will be fulfilled pre-authorisation.

The tests performed during production are described.

C. Control of Starting Materials

The active substance is methadone hydrochloride, 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.

The excipients are in conformity with Ph.Eur. requirements.

The glass vials and stoppers are in conformity with the Ph.Eur. requirements

No excipients are 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, confirming the retest period 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.

The claim of 28 days stability after broaching has been justified.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

As this is a generic/hybrid application according to Article 13, and bioequivalence with the reference product has been demonstrated, results of pharmacological and toxicological tests are not required. The pharmaco-toxicological aspects of this product is/are identical to the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These user warnings include:
"Methadone can cause respiratory depression following spillage on the skin or accidental self injection. Avoid skin, eyes and mouth contact and wear impermeable gloves when handling the product. In case of spilling on the skin or splashing in the eyes, wash immediately with large amounts of water. Remove contaminated clothes.
People with known hypersensitivity to methadone should avoid contact with the veterinary medicinal product.
Methadone has the potential to cause stillbirths. Pregnant women are advised not to handle the product.
In case of

accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation may occur.

To the physician:
Methadone is an opioid whose toxicity may cause clinical effects including respiratory depression or apnoea, sedation, hypotension and coma. When respiratory depression occurs controlled ventilation should be initiated. Administration of theopioid antagonist naloxone to reverse the symptoms is recommended."

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will only be used in nonfood animals.

IV. CLINICAL ASSESSMENT (EFFICACY)

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

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 Heads of Veterinary Medicines 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.

Summary of change	**Section updated**	**Approval date**
Extension of the shelf life of the finished product as packaged for sale (supported by real time data) from 30 months to 36 months. (NL/V/0183/002/IB/001)	N/A	2 December 2015
Update DDPS of LeVet Beheer B.V. with the version 01 February 2019 for all DCP/MRP marketing authorizations.	N/A	12 June 2019
Renewal (NL/V/0183/002/R/001)	N/A	19 June 2019