Subestin 25 microgram/ml oral solution for horses	NL/V/0362/001/DC
Floris Holding BV	DCP
	Publicly available assessment report

College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

SUBESTIN 25 microgram/ml oral solution for horses

Date:
September 2023

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0362/001/DC
Name, strength and pharmaceutical form	SUBESTIN 25 microgram/ml oral solution for horses
Applicant	Floris Holding BV Kempenlandstraat 33 5262 GK Vught The Netherlands
Active substance(s)	Clenbuterol Hydrochloride
ATC Vetcode	QR03CC13
Target species	Horses
Indication for use	Treatment of respiratory disease in horses where it is considered that airway obstruction due to bronchospasm and/or accumulation of mucus is a contributing factor, and improved mucociliary clearance is desirable. To be used alone or as adjuvant therapy.

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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) and in the Union Product Database (UPD).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	9 February 2022
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Old CMS: AT, BE, DK, FR, IE, IT, SE, UK(NI) New CMS: DE

I. SCIENTIFIC OVERVIEW

SUBESTIN 25 microgram/ml oral solution for horses 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.
SUBESTIN 25 microgram/ml oral solution for horses 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.

The quality, safety and efficacy aspects of SUBESTIN 25 microgram/ml oral solution for horses is based on bioequivalence with the Reference Product Ventipulmin Siroop REG NL 2529.
Warnings statements and precautions are adopted from the (EU) Reference Product.
Additional statements have been added, based on increased knowledge and the current state of science. Adverse events and contraindications are indicated in the SPC.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

SUBESTIN 25 microgram/ml oral solution for horses is an oral solution containing 25 µg/ml of the active substance Clenbuterol hydrochloride. Excipients included are Methyl parahydroxybenzoate, Propyl parahydroxybenzoate, Carbomer (974P), Sucrose, Macrogol 400, Glycerol, Ethanol 96%, Trolamine and Purified water.

The oral solution is packaged in a HDPE bottle and closed with a PP Child Resistant closure with LDPE syringe inlay containing 360 ml oral solution. A graduated syringe of 25 ml is supplied.

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The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. Dosing accuracy of the 25 mL syringe has been demonstrated.

The claimed biowaiver can be granted.

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. However, suitable pre-approval validation results on two production scale batches have been provided.

The tests performed during production are described.

C. Control of Starting Materials

The active substance Clenbuterol hydrochloride is an established substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Use has been made of the ASMF procedure.

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 are in conformity with the Ph. Eur. requirements.

None of the starting materials used are affected by the Note for Guidance on TSE/BSE.

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. All tests in the specification 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 has been provided demonstrating compliance with the specification.

F. Stability

The retest period of 2 years for Clenbuterol hydrochloride when stored under the approved conditions is justified.

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Stability data on the finished product has been provided in accordance with applicable VICH guidelines. According to the stability results provided the claimed shelf life of 36 months can be granted.

Satisfactory in-use stability results on a recent batch have been provided and in-use stability studies will be performed on a batch approaching end of shelf life.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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

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. Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

III.A Safety Testing

User Safety

Being a generic procedure the applicant refers to the reference product for information on this section.

Additionally, the applicant has provided a user safety assessment in compliance with the relevant guideline. Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

The environmental risk assessment can stop in Phase I because this product is intended for use in horses, in individual animals, and a Phase II assessment is not deemed necessary.

The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

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III.B Residues documentation

Residue Studies

Being a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, results of residue studies are not required.

MRLs

Clenbuterol hydrochloride is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

	Equidae
Muscle	0.1 microgram/kg
Liver	0.5 microgram/kg
Kidney	0.5 microgram/kg

Withdrawal Periods

The withdrawal period of SUBESTIN 25 microgram/ml oral solution for horses is identical to the withdrawal period of the reference product Ventipulmin Siroop REG NL 2529.

Based on the data provided above, a withdrawal period of 28 days is justified.

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.

Tolerance in the Target Species of Animals

Additionally to the above, based on increased knowledge and the current state of science, warning statements and precautions have been added to the product literature ensuring safety to the target animals. Adverse events, warnings and contraindications are indicated in the SPC.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when SUBESTIN 25 microgram/ml oral solution for horses 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 SUBESTIN 25 microgram/ml oral solution for horses 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) and in the Union Product Database (UPD).

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 these products.

Summary of change (Application number)	**Section updated in**	**Approval date**
NL/V/0362/001/A/001 VRA classification G.I.18 - One-off alignment of the product information with version 9.0 of the QRD templates i.e. major update of the QRD templates in accordance with Regulation (EU) 2019/6, for veterinary medicinal products placed on the market in accordance with Directive 2001/82/EC or Regulation (EC) No 726/2004.	Product Information	2 April 2023
NL/V/0362/001/E/001 SRP	New CMS: DE	26 June 2023
NL/V/0362/001/A/002 (VRA-R: F.II.f.1.a.1 - Change in the shelf-life or storage conditions of the finished product) VNRA 9882: C.8 - Implementation of changes in the SPC as a result of the SRP (NL/V/0362/001/E/001)	Part II Product information	28 September 2023