ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dilaterol 25 micrograms/ml Syrup for Horses

PuAR correct as of 25/03/2019 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0423/001/DC
Name, strength and pharmaceutical form	Dilaterol 25 micrograms/ml Syrup for Horses
Applicant	Le Vet Beheer B.V. Wilgenweg 7 3421 TV Oudewater 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.

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	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	26th September 2012
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, Finland, France, Hungary, Iceland, Ireland, Italy, Luxembourg, Norway, Poland, Protugal, Romania, Slovakia, Spain and Sweden.

I. SCIENTIFIC OVERVIEW

This was a generic application for Dilaterol 25 microgams/ml Syrup for Horses, in accordance with Article 13(1) of Directive 2001/82/EC as amended. The reference product was Ventipulmin Syrup 25 micrograms/ml authorised since 29th January 1991.

The product is indicated for horses as a treatment for bronchospasm due to allergies or infection, and as an aid to mucociliary clearance. 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[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 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 clenbuterol hydrochloride (0.025mg/ml) and the excipients carbomer 974P, ethanol, glycerol, methyl hydroxybenzoate, polyethylene glycol 400, propyl hydroxybenzoate, sodium hydroxide, sucrose and purified water.

[1] SPC - Summary of Product Characteristics

The container/closure system is a 355 ml HDPE bottle sealed with an aluminium/PE heat seal and a transparent HDPE cap. The product is supplied in a carton box with a multi-component mechanical pump dispenser capable of delivering 4 ml of the product. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and presence of preservative are 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, and the product is manufactured in accordance with the European Pharmacopoeia.

C. Control of Starting Materials

The active substance is clenbuterol hydrochloride, an established 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, along with an Active Substance Master File (ASMF).

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

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. Tests include HPLC tests for identity of the active ingredient and excipients, assay of the active ingredient and excipients, and impurities, as well as pH, clarity and colour in accordance with Ph. Eur. Methods.

The applicant has undertaken an in-use stability study on two batches of the product. For batch 1, in-use stability was started after the samples had been stored at 25°C/60% RH for three months and for batch 2, in-use stability was started after the samples had been stored at 25°C/60% RH for nine months.

The data provided show that the proposed in-use shelf life of three months can be accepted. In addition, APE testing was undertaken on an opened bottle from batch 2 that had been stored at 25°C/60% RH for two years and this met the requirements of the Ph. Eur.

H. Genetically Modified Organisms

N/A

J. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life after first opening the immediate packaging: 3 months

Storage Precautions: Do not store above 25°C. Protect from light.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)
For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, and bioequivalence with a reference product has been successfully claimed, results of pharmacological and toxicological 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 and consumers.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that user safety is the same for that of the reference product.

Wear gloves to avoid skin contact. In case of accidental skin contact, wash affected area thoroughly. If irritation occurs/persists seek medical advice. Wash hands thoroughly after using the product.

Take care to avoid eye contact. In the case of accidental eye contact, flush thoroughly with clean water and seek medical advice.

Do not eat, drink or smoke when using this product. In case of accidental ingestion, seek medical advice immediately and show the package leaflet to the healthcare professional.

People with known hypersensitivity to clenbuterol should avoid contact with the veterinary medicinal 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, as the product is unlikely to be used on more than a small number of animals at one time. 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

Since there is evidence for bioequivalence with the reference product, the applicant has not provided residues depletion data as part of this application. The applicant has also proposed that the horse meat withdrawal period should be the same as that approved for the reference product, 28 days.

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Clenbuterol HCl	Clenbuterol	Equidae	0.1	Muscle	None
			0.5	Liver	

It is noted that there is no MRL for clenbuterol in horses' milk. All the excipients included in this product have been evaluated by the CVMP; MRLs were not considered necessary.

IV CLINICAL ASSESSMENT (EFFICACY)

For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, 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.

In accordance with Directive 2001/82/EC Article 13 (1) as amended by Directives 2004/28/EC and 2009/9/EC the applicant is not required to provide pharmacological, toxicological, tolerance, resistance or clinical trial data for a product that is demonstrated to be a generic of a reference medicinal product that has been authorised within a Member State for at least 10 years.

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)