Bundesamt für
Sicherheit im
Gesundheitswesen
BASG

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Equipulmin 25 micrograms/ml Oral Syrup for Horses (AT, HU, UK)

Equipulmin vet. (DK)

Equipulmin vet. 25 micrograms/ml Oral Syrup for Horses (FI, SE)

Equipulmin 22 µg/mL syrup for horses (FR)

AT/V/0024/001/DC

(Former: UK/V/0424/001/DC)

Last update: 06/09/2023

Modules 1-3 reflect the scientific discussion for the approval of Equipulmin 25 micrograms/ml Oral Syrup for Horses. The procedure was finalised on 26/09/2012. For information on changes after this date please refer to module 4.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	AT/V/0024/001/DC
Name, strength and pharmaceutical form	Equipulmin 25 micrograms/ml Oral Syrup for Horses
Applicant	CP Pharma Handelsgesellschaft mbH Ostlandring 13 31303 Burhdorf Germany
Active substance(s)	Clenbuterol hydrochloride 25 micrograms (corresponding to 22 micrograms clenbuterol)
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
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Finland, Sweden, Hungary, Denmark

I. SCIENTIFIC OVERVIEW

This was a generic application for Equipulmin 25 microgram/ml syrup for horses, submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The product is indicated for the treatment of airway obstruction caused by bronchospasm and/or mucus accumulation is a contributing factor, and the improvement of mucocilliary clearance is required. The reference product was Ventipulmin syrup, marketed in the UK since 1991.

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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains clenbuterol hydrochloride 25 micrograms, corresponding to 22 micrograms clenbuterol and the excipients methyl parahydroxybenzoate

[1] SPC – Summary of Product Characteristics.

(E218), propyl parahydroxybenzoate, sucrose, carbomer 974P, macrogol 400, glycerol (86%), ethanol (96%), sodium hydroxide and purified water.

The container/closure system consists of a 355 ml high density polyethylene bottle closed with aluminium/polyethylene heat seals and transparent high density polyethylene caps. The product is presented in a cardboard box containing a multi-component pump dispenser which delivers 4 ml of product. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the presence of preservatives 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. The active substance and excipients are mixed appropriately, subjected to suitable tests and filled into bottles under suitably aseptic conditions.

C. Control of Starting Materials

The active substance is clenbuterol hydrochloride an established active substance described in the European Pharmacopoeia (Ph. Eur). An in-house specification was developed to accommodate tests for residual solvents. The active substance is manufactured in accordance with the principles of good manufacturing practice. All excipients are monographed in the Ph. Eur.

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.

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

Not applicable.

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. Tests include those for clarity,

colour, pH, relative density, viscosity, identity, related substances and microbial purity.

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. Additional data were provided for the finished product, which showed that the product was stable under specified conditions.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

The shelf-life of the product as packaged for sale is 2 years. Shelf-life after opening the immediate packaging is 3 months.

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 pharmacological or 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 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:

- This product contains clenbuterol hydrochloride, a beta-agonist.
- 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 was required, due to the small number of animals that will require the product, and the low dose. 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

Withdrawal Periods

No data were required for this section of the dossier, as the claim that the product was identical to the reference product was accepted. The withdrawal periods as established for the reference product and therefore relevant to the new product are as follows:

Meat and offal 28 days. Not authorised for use in lactating animals producing milk for human consumption.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, only a bioequivalence study was presented. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

The applicant provided a GLP[2] and GCP[3] controlled bioequivalence study which compared the proposed product with the reference product. A suitable number of target animals were allocated to two groups, and clinically observed for 18 days. Plasma levels of clenbuterol were taken at various time points and calculations made for a variety of statistical parameters. When the two products were compared, 90% confidence intervals for the ratios of C_{max}[4] and AUC[5] were within the range of 0.8 – 1.25, demonstrating bioequivalence.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and the product has been confirmed as being bioequivalent to the reference product, tolerance studies were not required.

Resistance

[2] GLP – Good Laboratory Practice.
[3] GCP – Good Clinical Practice.
[4] C_{max} – Maximum concentration of clenbuterol observed in blood plasma.
[5] AUC – Area under the treatment curve.

As this is a generic application according to Article 13, and the product has been confirmed as being bioequivalent to the reference product, resistance studies were not required.

IV.B Clinical Studies

As this is a generic application according to Article 13, and the product has been confirmed as being bioequivalent to the reference product, further clinical studies were not required.

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 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.

Significant changes

Summary of change (Application number)	**Approval date**
This marketing authorization was renewed unlimited. (UK/V/0424/001/R/001)	05/10/2017
Change of RMS from UK to AT	28/08/2018
Addition of CMS FR	21/05/2021
No further significant changes since last update.	