ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Subestin 25 microgram/ml oral solution

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Clenbuterol Hydrochloride 25 microgram
(equivalent to 22 microgram clenbuterol)

3. PACKAGE SIZE

360 ml bottle, including a syringe of 25 ml.

4. TARGET SPECIES

Horses.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For oral use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 28 days
Do not use in animals producing milk for human consumption.

8. EXPIRY DATE

EXP {month/year}
Shelf life after first opening the immediate packaging: 3 months
Once opened use by ___/____

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Floris Holding B.V.

14. MARKETING AUTHORISATION NUMBERS

Vm 56190/3003

15. BATCH NUMBER

Lot: {number}

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGE

Plastic (HDPE) bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Subestin 25 microgram/ml oral solution

2. QUANTITY OF THE ACTIVE SUBSTANCES

Each ml contains:
Clenbuterol Hydrochloride 25 microgram
(equivalent to 22 microgram clenbuterol)

3. TARGET SPECIES

Horses.

4. ROUTES OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 28 days
Do not use in animals producing milk for human consumption.

6. EXPIRY DATE

EXP {month/year}
Shelf life after first opening the immediate packaging: 3 months
Once opened use by ___/____

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Floris Holding B.V.

9. BATCH NUMBER

Lot: {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Subestin 25 microgram/ml oral solution for horses

2. COMPOSITION

Slightly viscous, colourless to slightly yellow solution.

Active Substance:
Clenbuterol Hydrochloride 25 microgram/ml
(equivalent to 22 microgram/ml clenbuterol)

Excipients:
Methyl parahydroxybenzoate (E218) 1.8 mg/ml
Propyl parahydroxybenzoate 0.2 mg/ml

3. TARGET SPECIES

Horses.

4. 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.

5. CONTRAINDICATIONS

Do not use in cases of known hypersensitivity to the active substance or any of the excipients.
Do not use in horses with known cardiac disease.
For use during pregnancy or lactation see section “special warnings in subheading Pregnancy or Lactation”.

6. SPECIAL WARNINGS

Special warnings:
None

Special precautions for safe use in the target species:
In cases accompanied by bacterial infection the administration of antimicrobial agents is recommended.
In case of glaucoma the veterinary medicinal product must only be used after a careful benefit-risk assessment by the attending veterinarian.
Special precautions should be taken in case of halothane anaesthesia, since the heart function can show increased sensitivity to catecholamines.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product contains clenbuterol, a beta-agonist, which may cause adverse effects such as increased heart rate.
Dermal exposure and accidental ingestion, including hand-to-mouth contact should be avoided. When using this veterinary medicinal product do not eat, drink or smoke to avoid accidental intake of the veterinary medicinal product.
To avoid accidental ingestion by or exposure to a child, do not leave the filled syringe unattended and close the bottle immediately and properly after use.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. Wash hands after use.
This veterinary medicinal product may cause embryotoxicity. Pregnant women should take care when handling the veterinary medicinal product. Wear gloves to avoid skin contact.
This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to any of the excipients (parabens, polyethylene glycol and/or triethanolamine) should avoid exposure to the veterinary medicinal product. In case of hypersensitivity reactions or if irritation persists, seek medical advice and show the package leaflet or label to the physician.
This veterinary medicinal product may be irritating to the skin and/or eyes. Avoid skin and/or eye contact. In case of accidental skin contact, wash skin thoroughly. In case of accidental eye contact, flush thoroughly with clean water.

Pregnancy:
If used during pregnancy, treatment must be discontinued a minimum of 4 days before the expected time of delivery, since uterine contractions may be abolished or labour may be prolonged.

Lactation:
Avoid administration to nursing mares because of excretion in the milk. The safety of the veterinary medicinal product has not been established during lactation.
A nursing foal ingests a high volume of milk relative to its body weight. Therefore, during lactation an effect of the active substance excreted in milk in the nursing foal cannot be definitely excluded.

Interaction with other medicinal products and other forms of interaction:
Effects including side effects may be enhanced with simultaneous use with glucocorticoids, ß2-sympathomimetics, anticholinergics and methylxanthines.
The veterinary medicinal product should not be used concomitantly with other sympathomimetics or vasodilators.
In animals treated with clenbuterol disturbances of the heart rhythm can be expected upon anaesthesia.
Simultaneous administration of narcotics containing halogens (isoflurane, methoxyflurane) increases the risk of ventricular arrhythmias.

During the use of both local and general anaesthetics one cannot exclude a further vascular dilatation and fall of blood pressure, particularly if used in combination with atropine.
Increased risk of arrhythmia with simultaneous administration of digitalis glycosides.
The veterinary medicinal product can reduce or neutralise the effects of prostaglandin F2α and oxytocin on the uterus.
Clenbuterol hydrochloride is a β -adrenergic agonist and is subsequently neutralised by β-blockers.

Overdose:
Doses of clenbuterol hydrochloride up to 4 times the therapeutic dose (orally administered) administered for 90 days caused only temporary side effects typical for $ß_2$-adrenoceptor agonists (sweating, tachycardia, muscle tremor) which did not require treatment.
In case of accidental overdose, a ß -blocker (such as propranolol) may be used as antidote.

Special restrictions for use and special conditions for use:
Not applicable.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. ADVERSE EVENTS

Horses

Rare (1 to 10 animals / 10,000 animals treated):	Sweating* Muscle tremor Tachycardia Hypotension** Restlessness

*mainly neck region
**slight

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to Floris Holding B.V. or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

The veterinary medicinal product should be administered twice a day with approximately 12 hours (minimum 8 hours) in between according to the following dosage:
Administer 0.8 micrograms clenbuterol hydrochloride per kilogram body weight (i.e. 0.7 micrograms clenbuterol per kg bodyweight), corresponding to 4 ml oral solution / 125 kg body weight, twice daily.
The duration of the treatment is a maximum of ten consecutive days.
The veterinary medicinal product is administered orally, through or over food.
This veterinary medicinal product is intended for individual animal treatment.

9. ADVICE ON CORRECT ADMINISTRATION

For animal treatment only. For oral use administered with feed.

10. WITHDRAWAL PERIODS

Meat and offal: 28 days
Do not use in animals producing milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 30 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton after EXP.
The expiry date refers to the last day of that month.
When the container is opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any veterinary medicinal product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. SPECIAL PRECAUTIONS FOR DISPOSAL

Medicines should not be disposed of via wastewater <or household waste>.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

14. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Vm 56190/3003

White HDPE bottle with white polypropylene child-resistant screw cap and LDPE syringe inlay.
The veterinary medicinal product is supplied in a carton box with a measuring device, a 25 ml syringe with polypropylene body and polyethylene plunger, capable of delivering 4 to 24 ml of the veterinary medicinal product.

Each bottle contains 360 ml.

15. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST REVISED

{DD/MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. CONTACT DETAILS

Marketing authorisation holder and contact details to report suspected adverse reactions:
Floris Holding B.V.
Kempenlandstraat 33
5262 GK Vught
The Netherlands
Tel.: +3173 656 3784
pharmacovigilance@florispharma.com

Manufacturer responsible for batch release:
Floris Veterinaire Producten B.V.
Kempenlandstraat 33
5262 GK Vught
The Netherlands

Local representatives and contact details to report suspected adverse reactions*:*

To be completed nationally. There may be national differences in the designated contact point for the reporting of suspected adverse events (MAH or local representative) which can be reflected accordingly in each national translation. If the MAH is the local contact point, contact details to report suspected adverse reactions will include an additional telephone number (Tel: +3173 656 3784) under the MAH contact details. A MAH e-mail address to report adverse events is always possible to contact in every country.

17. OTHER INFORMATION

Approved 6 July 2023