ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance
Boehringer Ingelheim Veterinary Medicine Belgium NV
Noorwegenstraat 4
9940 Evergem
BELGIUM

Name and address of the manufacturer(s) responsible for batch release
Boehringer Ingelheim Veterinary Medicine Belgium NV
Noorwegenstraat 4
9940 Evergem
BELGIUM

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substance being a principle of biological origin intended to produce passive immunity is not within the scope of Regulation (EC) No 470/2009.

The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or are considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Polycarbonate container or cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

RenuTend suspension for injection for horses

2. STATEMENT OF ACTIVE SUBSTANCES

Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells (tpMSCs): 2.0–3.5x10^6

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

One vial (1 ml) of stem cell suspension

5. TARGET SPECIES

Horses

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intra-lesional use

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and Offal: zero days.
Milk: zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP
Once thawed use immediately.

11. SPECIAL STORAGE CONDITIONS

Store and transport frozen (–90 °C to –70 °C or in liquid nitrogen).

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Read the package leaflet before use.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
GERMANY

16. MARKETING AUTHORISATION NUMBER(S)

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17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial containing stem cell suspension

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

RenuTend for injection

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

2.0–3.5×10^6 tpMSCs

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

1 ml

4. ROUTE(S) OF ADMINISTRATION

Intra-lesional use

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s): zero days.

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP
Once thawed use immediately.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
RenuTend suspension for injection in horses

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim am Rhein
Germany

Manufacturer responsible for batch release:
Boehringer Ingelheim Veterinary Medicine Belgium NV
Noorwegenstraat 4
9940 Evergem
BELGIUM

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

RenuTend suspension for injection for horses

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each dose of 1 ml contains:

Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells (tpMSCs): $2.0–3.5\times10^{6}$

Clear colourless suspension

4. INDICATION(S)

To restore fibre alignment in horses with superficial digital flexor tendon or suspensory ligament fibre disruption

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substance or any of the excipients.
Do not administer simultaneously with any other intra-lesional veterinary medicinal product

6. ADVERSE REACTIONS

Mild injection site reactions, such as increased heat, pain at palpation, limb swelling and increased limb circumference occurred very commonly during the first 10 days after administration.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Horses

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For intra-lesional use.

Dosage*:*

A single intra-lesional injection of 1 ml per animal on one occasion.

9. ADVICE ON CORRECT ADMINISTRATION

Preparation of the suspension for injection and method of administration:
The veterinary medicinal product must be administered intra-lesionally by a licensed veterinarian taking special precautions to ensure sterility of the injection process. The veterinary medicinal product must be handled and injected using sterile techniques and in a clean environment.

The following information is intended for the licensed veterinarian only:

The veterinary medicinal product needs to be administered immediately after thawing in order to maintain cell viability.

Using appropriate gloves, remove the vial from the freezer/liquid nitrogen and thaw immediately at 25 °C–37 °C, e.g. in a water bath, until the content is completely thawed (approximately 5 minutes).

If any cell clusters are visible after thawing, gently invert the vial until the suspension is clear and colourless.

Remove the cap of the vial and aspirate the suspension in a sterile syringe for injection.

Administer using a needle with a diameter greater than or equal to 22G in order to prevent cell damage.

Administer intra-lesionally under ultrasound guidance with chemical or physical restraint as needed according to good veterinary practice to facilitate a safe intra-lesional injection. After insertion of the needle into the tendon or ligament, redirect the needle, if necessary, until the lesion is reached. Slowly inject the suspension. In case of a larger lesion the needle can be slowly retracted during injection to facilitate dispersion of the cells throughout the lesion.

10. WITHDRAWAL PERIOD(S)

Meat and Offal: zero days
Milk: zero hours.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store and transport frozen (-90 °C to -70 °C) or in liquid nitrogen.
Do not use this veterinary medicinal product after the expiry date, which is stated on the labels after EXP. The expiry date refers to the last day of that month.
Shelf life after thawing according to directions: use immediately.

12. SPECIAL WARNING(S)

Special warnings for each target species:
The veterinary medicinal product has been demonstrated to be efficacious in horses with first time overstrain lesions in the superficial digital flexor tendon of the front leg, or the suspensory ligament in the back or front leg. Efficacy data are not available regarding treatment of other tendons and ligaments. Treatment of traumatic injuries with lacerations or completely ruptured tendons has not been evaluated. This veterinary medicinal product is not intended for treatment of such injuries.

The efficacy of the veterinary medicinal product was demonstrated in a pivotal field trial with horses working at training level or competition level within the disciplines dressage or show jumping, before tendon or ligament injury occurred. By day 112 post-treatment, 65% of horses treated with this product during the pivotal field trial had achieved greater than 75% fibre alignment within the affected soft tissues.

A standard program of box rest and slowly increasing exercise regimen under veterinary guidance is required as part of the rehabilitation of tendon and ligament injuries. The program should be adapted based on serial ultrasonographic monitoring and clinical signs such as lameness, heat and swelling.

The efficacy and safety of the veterinary medicinal product were demonstrated in a pivotal field trial after single administration of the veterinary medicinal product and concurrent single systemic administration of an NSAID (ketoprofen or meloxicam). According to the benefit-risk assessment of the responsible veterinarian of the

individual case a single dose systemic NSAID may be administered on the day of intra-lesional injection.

Special precautions for use in animals
A correct foot balance is critical in the management of superficial digital flexor tendon or suspensory ligament lesions.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

When the veterinary medicinal product is stored in liquid nitrogen, direct exposure to liquid nitrogen or cold nitrogen vapours can cause extensive tissue damage or burns. When liquid nitrogen vaporises, it can expand to 700-times its volume which may create an explosion hazard in unvented cryovials. Liquid nitrogen containers should be handled by properly trained personnel only. The handling of liquid nitrogen should take place in a well-ventilated area. Before withdrawing the vials from the liquid nitrogen canister, protective equipment consisting of gloves, long sleeves and a facemask or goggles should be worn.

There is only limited data available to support the human safety of this product. In particular, women of childbearing age and people with compromised immune systems should take care to avoid contact with the product. It is recommended to wear impermeable gloves at all times whilst handling and administering the product. Wash any spills off exposed skin, eyes, or mucous membranes immediately.

Take care not to accidentally self-administer this product. In case of accidental self-injection, this veterinary medicinal product can cause pain, local inflammatory reactions and swelling at the site of injection, which may persist for several weeks. Transient fever may also occur. Seek medical advice immediately and provide the package leaflet or the label to the physician.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

Do not administer simultaneously with any other intra-lesional veterinary medicinal product.

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

05/2022

Find more product information by searching for the 'Product Information Database' or 'PID' on www.gov.uk.

15. OTHER INFORMATION

For animal treatment only.

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Each pack (polycarbonate container or cardboard box) contains a single dose of the product:
one vial of stem cell suspension.

For any further information about this veterinary medicinal product, please contact:
Boehringer Ingelheim Animal Health UK Ltd.
Bracknell, RG12 8YS, UK

Approved: 19 May 2022