ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

RenuTend suspension for injection for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 1 ml contains:

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

Excipients:

Qualitative composition of excipients and other constituents
Dulbecco's modified eagle medium low glucose
Dimethyl sulfoxide

Clear, colourless suspension.

3. CLINICAL INFORMATION

3.1 Target species

Horses

3.2 Indications for use for each target species

To improve healing of injuries of tendons and suspensory ligaments in horses.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

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 suspensory ligament injury occurred.

A standard program of box rest and slowly increasing exercise regimen under veterinary guidance is required as part of the rehabilitation of tendon and suspensory 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. 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 intralesional injection.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Not applicable.

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 vaporizes 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.

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 label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Horses:

Very common (>1 animal / 10 animals treated):	Injection site reaction (e.g. injection site warmth, injection site pain, limb swelling and increased limb circumference) [1]

[1] Mild and occurred during the first 10 days after administration.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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.

3.8 Interaction with other medicinal products and other forms of interaction

No data available.

3.9 Administration routes and dosage

Route of administration:
Intralesional use.

Recommended dosage:
A single administration of one dose (1 ml) per animal.

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

The veterinary medicinal product is required 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 into 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 intralesionally under ultrasound guidance with chemical or physical restraint as needed according to good veterinary practice to facilitate a safe intralesional injection. After insertion of the needle into the tendon or suspensory 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No data available.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Zero days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATC vet code:

QM09AX90

4.2 Pharmacodynamics

This veterinary medicinal product contains tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells (tpMSCs). The tenogenic priming of the mesenchymal stem cells aims to promote tissue restoring and healing mechanisms in tendons, such as improving extracellular matrix production. The effects were reflected after tpMSC administration in an experimental tendon injury model in horses through improved ultrasound echogenicity and fibre scoring, higher

percentages of intact and fully aligned tendon fascicles reflected by a higher collagen type I content and a lower collagen type III and smooth muscle actin presence.

In the pivotal clinical trial, efficacy of treatment compared to a placebo group was evaluated under conditions of a standard program of box rest and slowly increasing exercise regimen under veterinary guidance. A significant improvement in fibre alignment score in the tendon lesion was demonstrated which coincided with an improvement of echogenicity and size of the cross sectional area on ultrasound examinations.

4.3 Pharmacokinetics

After injection of the veterinary medicinal product, the tpMSCs do not migrate or distribute from the treated tendon to surrounding tissues or the draining lymph node.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after thawing according to directions: Use immediately.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Cyclo-olefin co-polymer (COC) vial with a thermoplastic elastomer (TPE) stopper and a high-density polyethylene (HDPE) cap containing a single dose of stem cell suspension.

Each pack (polycarbonate container or cardboard box) contains a single dose of the veterinary medicinal product: one vial (1 ml) of stem cell suspension.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.
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 national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/282/001

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 19/04/2022

9. DATE OF THE LAST REVISION OF THE SUMMARY OF PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None.

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): 2.0–3.5×10^6

3. PACKAGE SIZE

1 x 1 ml

4. TARGET SPECIES

Horses

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intralesional use.

7. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once thawed use immediately.

9. SPECIAL STORAGE PRECAUTIONS

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

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

Boehringer Ingelheim Vetmedica GmbH

14. MARKETING AUTHORISATION NUMBERS

EU/2/22/282/001

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial containing stem cell suspension

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

RenuTend

2. QUANTITTATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

2.0–3.5×10^6 tpMSCs

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once thawed use immediately.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

RenuTend suspension for injection for horses

2. Composition

Each dose of 1 ml contains:

Active substance:
Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells (tpMSCs): 2.0–3.5×10^6

Clear colourless suspension.

3. Target species

Horses

4. Indications for use

To improve healing of injuries of tendons and suspensory ligaments in horses.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or any of the excipients.

6. Special warnings

Special warnings for safe use in the 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 suspensory ligament injury occurred.

A standard program of box rest and slowly increasing exercise regimen under veterinary guidance is required as part of the rehabilitation of tendon and suspensory 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. 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 intralesional injection.

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 vaporizes 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.

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:
No data available.

Overdose:
No data available.

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:

Very common (>1 animal / 10 animals treated):
Injection site reaction (e.g. injection site warmth, injection site pain, limb swelling and increased limb circumference) [1]

[1] Mild and occurred during the first 10 days after administration.

Reporting adverse events is important. It allows continuous safety monitoring of a 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 the marketing authorisation holder 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

For intralesional use.

Recommended dosage:
Single administration of one dose (1 ml) per animal.

9. Advice on correct administration

Preparation of the suspension for injection and method of administration:
The veterinary medicinal product must be administered intralesionally by a veterinary surgeon 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 veterinary surgeon 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 intralesionally under ultrasound guidance with chemical or physical restraint as needed according to good veterinary practice to facilitate a safe intralesional injection. After insertion of the needle into the tendon or suspensory 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 periods

Zero days.

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 precautions for disposal

Medicines should not be disposed of via wastewater.
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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/22/282/001

Each pack (polycarbonate container or carboard box) contains a single dose of the veterinary medicinal product: one vial (1 ml) of stem cell suspension.

15. Date on which the package leaflet was last revised

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:
Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

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

Local representatives and contact details to report suspected adverse reactions:

België/Belgique/Belgien
Boehringer Ingelheim Animal
Health Belgium SA
Avenue Arnaud Fraiteurlaan 15-23,
1050 Bruxelles/Brussel/Brüssel
Tél/Tel: + 32 2 773 34 56

Република България
Boehringer Ingelheim RCV GmbH & Co KG
Dr. Boehringer Gasse 5-11
A-1121 Виена, Австрия
Tel: +359 2 958 79 98

Česká republika
Boehringer Ingelheim spol. s r.o.
Purkyňova 2121/3
CZ - 110 00, Praha 1
Tel: +420 234 655 111

Lietuva
Boehringer Ingelheim RCV GmbH & Co KG
Lietuvos filialas
Dr. Boehringer Gasse 5-11
A-1121 Vīne, Austrija
Tel: +370 5 2595942

Luxembourg/Luxemburg
Boehringer Ingelheim Animal
Health Belgium SA
Avenue Arnaud Fraiteurlaan 15-23,
1050 Bruxelles/Brussel/Brüssel
Tél/Tel: + 32 2 773 34 56

Magyarország
Boehringer Ingelheim RCV GmbH & Co KG
Magyarországi Fióktelep
Lechner Ö. Fasor 10.
H-1095 Budapest
Tel: +36 1 299 8900

Danmark
Boehringer Ingelheim Animal Health Nordics A/S
Weidekampsgade 14
DK-2300 København S
Tlf: + 45 3915 8888

Deutschland
Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Tel: 0800 290 0 270

Eesti
Boehringer Ingelheim RCV GmbH & Co KG
Eesti filiaal
Dr. Boehringer Gasse 5-11
A-1121 Viin, Austria
Tel: +372 612 8000

Ελλάδα
Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim/Rhein, Γερμανία
Τηλ: +30 2108906300

España
Boehringer Ingelheim Animal Health España, S.A.U.
Prat de la Riba, 50
08174 Sant Cugat del Vallès (Barcelona)
Tel: +34 93 404 51 00

France
Boehringer Ingelheim Animal Health France, SCS
29, avenue Tony Garnier
69007 Lyon
Tél : +33 4 72 72 30 00

Hrvatska
Boehringer Ingelheim RCV GmbH & Co KG
Dr. Boehringer Gasse 5-11
A-1121 Beč, Austrija
Tel: +385 1 2444 600

Ireland
Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim/Rhein, Germany
Tel: +353 1 291 3985

Malta
Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim/Rhein, il-Ġermanja
Tel: +353 1 291 3985

Nederland
Boehringer Ingelheim Animal Health Netherlands bv
Basisweg 10
1043 AP Amsterdam
Tel: +31 20 799 6950

Norge
Boehringer Ingelheim Animal Health Nordics A/S
Weidekampsgade 14
DK-2300 København S
Tlf: +47 66 85 05 70

Österreich
Boehringer Ingelheim RCV GmbH & Co KG
Dr. Boehringer Gasse 5-11
A-1121 Wien
Tel: +43 1 80105-6880

Polska
Boehringer Ingelheim Sp. z o.o.
ul. Józefa Piusa Dziekonskiego 3
00-728 Warszawa
Tel.: + 48 22 699 0 699

Portugal
Boehringer Ingelheim Animal Health Portugal, Unipessoal, Lda.
Avenida de Pádua, 11
1800-294 Lisboa
Tel: +351 21 313 5300

România
Boehringer Ingelheim RCV GmbH & Co KG
Sucursala Bucureşti
Dr. Boehringer Gasse 5-11
A-1121 Viena, Austria
Tel: +40 21 302 28 00

Slovenija
Boehringer Ingelheim RCV GmbH & Co KG
Podružnica Ljubljana
Dr. Boehringer Gasse 5-11
A-1121 Dunaj, Avstrija
Tel: +386 1 586 40 00

Ísland
Vistor
Hörgatún 2
210 Garðabær
Sími: + 354 535 7000

Italia
Boehringer Ingelheim Animal Health
Italia S.p.A.
Via Vezza d'Oglio, 3
20139 Milano
Tel: +39 02 53551

Κύπρος
Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim/Rhein, Γερμανία
Τηλ: +30 2108906300

Latvija
Boehringer Ingelheim RCV GmbH & Co KG
Latvijas filiāle
Dr. Boehringer Gasse 5-11
A-1121 Viena, Austrija
Tel: +371 67 240 011

Slovenská republika
Boehringer Ingelheim RCV GmbH & Co KG, o.z.
Dr. Boehringer Gasse 5-11
A-1121 Viedeň, Rakúsko
Tel: +421 2 5810 1211

Suomi/Finland
Vetcare Oy
PL/PB 99
24101 Salo
Puh/Tel: + 358 201443360

Sverige
Boehringer Ingelheim Animal Health Nordics A/S
Weidekampsgade 14
DK-2300 København S
Tel: +46 (0)40-23 34 00

United Kingdom (Northern Ireland)
Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim/Rhein, Germany
Tel: +353 1 291 3985