ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Arti-Cell Forte suspension for injection for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 2 ml contains:

Active substance:
Chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells:
$1.4 – 2.5 \times 10^6$

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Dimethyl sulfoxide	
Dulbecco's Modified Eagle Medium Low Glucose	
Solvent:	
Equine allogeneic plasma (EAP)	1 ml

Stem cells: clear colourless suspension.
Solvent: clear yellow suspension.

3. CLINICAL INFORMATION

3.1 Target species

Horses

3.2 Indications for use for each target species

Reduction of mild to moderate recurrent lameness associated with non-septic joint inflammation 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 product has been demonstrated to be efficacious in horses showing mild to moderate lameness in the fetlock joint. Efficacy data are not available regarding treatment of other joints.

The efficacy of the product was demonstrated in a pivotal field trial after single administration of the product and concurrent single systemic administration of an nonsteroidal anti-inflammatory drug (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 intraarticular injection.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In order to avoid thrombosis in small vessels when administering intra-articular injections, the correct placement of the needle is critical.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
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 product can cause pain, local inflammatory reactions and swelling at the site of injection, which may persist for several weeks and possibly cause fever. Seek medical advice immediately and show the package leaflet or the 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):	Lameness[1,2] Injection site reaction[1] (e.g. joint swelling[3], injection site warmth[2])

1 Occurring in the first week after use of the product.
2 Mild
3 Mild to moderate

In the pivotal clinical field study a single systemic administration of an NSAID was given concurrently to treatment with Arti-Cell Forte.

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 accordingly to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

No data available.
Do not administer simultaneously with any other intra-articular veterinary medicinal product.

3.9 Administration routes and dosage

Intra-articular use.

Recommended dosage*:*
A single intra-articular injection of 1 dose (2 ml) per animal.

Preparation of the suspension for injection:
The veterinary product must be administered intra-articularly by a veterinary surgeon taking special precautions to ensure sterility of the injection process. The product must be manipulated and injected using sterile techniques and in a clean environment.

The product needs to be administered immediately after thawing to prevent significant cell death.

Using appropriate gloves, remove the two vials (one vial of cells (1 ml) and one vial of EAP (1 ml)) from the freezer/liquid nitrogen and thaw immediately at 25 °C – 37 °C, e.g. in a water bath, until the contents in each are completely thawed (approximately 5 minutes).

If any cell clusters are visible in either of the vials after thawing, gently shake the vial concerned until the suspension is clear and colourless (stem cell suspension) or clear and yellow (equine allogeneic plasma suspension: the solvent).

Remove the cap of the vial that thawed first and aspirate the suspension in a syringe, then remove the cap of the other (thawed) vial and aspirate the suspension in the same syringe. Then mix both the suspensions in the same syringe to produce one dose of the product (2 ml).

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

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 ATCvet code:

QM09AX90

4.2 Pharmacodynamics

This product contains chondrogenic induced equine mesenchymal stem cells and equine allogeneic plasma (EAP). The addition of the EAP to the stem cells after thawing and just before injection of the product increases the viability of the stem cells.

The chondrogenic induction of the mesenchymal stem cells aims to activate chondroprotective mechanisms, such as the production of extracellular matrix. In an experimental model of osteoarthritis in horses these effects were reflected through parameters related to cartilage turnover.

4.3 Pharmacokinetics

After injection of the product the stem cells do not migrate or distribute from the treated joint and synovia to tissues surrounding the synovial space.

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: 3 years.
Shelf life after reconstitution 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

Each pack (polycarbonate container) contains a single dose of the product: one vial of chondrogenic induced mesenchymal stem cell suspension and one vial of equine allogeneic plasma (EAP) suspension (solvent).

Nature of vials: cyclo-olefin co-polymer (COC) vial with a thermoplastic elastomer (TPE) stopper and a high-density polyethylene (HDPE) cap.

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

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 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/2/18/228/001

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 29/03/2019

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

{MM/YYYY}

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 (2 vials of 1 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Arti-Cell Forte suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells:
$1.4 – 2.5 \times 10^6$

3. PACKAGE SIZE

1 ml vial of stem cells
1 ml solvent vial of equine allogeneic plasma

4. TARGET SPECIES

Horses

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intra-articular use.

7. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once reconstituted 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/2/18/228/001

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

1 ml vial containing the stem cell suspension

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Arti-Cell Forte

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

1 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

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

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

1 ml vial containing the solvent

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Solvent for Arti-Cell Forte

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

1 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Arti-Cell Forte suspension for injection for horses

2. Composition

Each dose of 2 ml contains:

Active substance:
Chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells:
$1.4 – 2.5 \times 10^6$

Solvent: Equine allogeneic plasma (EAP), 1 ml

Stem cells: clear colourless suspension.
Solvent: clear yellow suspension.

3. Target species

Horses.

4. Indications for use

Reduction of mild to moderate recurrent lameness associated with non-septic joint inflammation in horses.

5. Contraindications

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

6. Special warnings

The product has been demonstrated to be efficacious in horses showing mild to moderate lameness in the fetlock joint. Efficacy data are not available regarding treatment of other joints.

The efficacy of the product was demonstrated in a pivotal field trial after single administration of the product and concurrent single systemic administration of a nonsteroidal anti-inflammatory drug (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 intra-articular injection.

Special precautions for safe use in the target species:
In order to avoid thrombosis in small vessels when administering intraarticular injections, the correct placement of the needle is critical.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
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 product can cause pain, local inflammatory reactions and swelling at the site of injection, which may persist for several weeks and possibly cause fever. Seek medical advice immediately and show 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 accordingly to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
No data available.
Do not administer simultaneously with any other intra-articular veterinary medicinal product.

Overdose:
No data available.

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

7. Adverse events

Horses:

Very common (> 1 animal / 10 animals treated): Lameness[1,2],
Injection site reaction[1] (e.g. joint swelling[3], injection site warmth[2])

1 Occurring in the first week after use of the product.
2 Mild
3 Mild to moderate

In the pivotal clinical field study a single systemic administration of an NSAID was given concurrently to treatment with Arti-Cell Forte.

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: {national system details}.

8. Dosage for each species, routes and method of administration

For intra-articular use.

Recommended dosage:
Single administration of 1 dose (equivalent to 2 ml) per animal.

9. Advice on correct administration

Preparation of the suspension for injection:
The veterinary product must be administered intra-articularly by a veterinary surgeon taking special precautions to ensure sterility of the injection process. The product must be manipulated and injected using sterile techniques and in a clean environment.

The following information is intended for the veterinary surgeon only:
The product needs to be administered immediately after thawing to prevent significant cell death.

Using appropriate gloves, remove the two vials (one vial of cells (1 ml) and one vial of EAP (1ml)) from the freezer/liquid nitrogen and thaw immediately at 25 °C – 37 °C, e.g. in a water bath, until the contents in each are completely thawed (approximately 5 minutes).

If any cell clusters are visible in either of the vials after thawing, gently shake the vial concerned until the suspension is clear and colourless (stem cell suspension) or clear and yellow (equine allogeneic plasma suspension: the solvent).

Remove the cap of the vial that thawed first and aspirate the suspension in a syringe, then remove the cap of the other (thawed) vial and aspirate the suspension in the same syringe. Then mix both the suspensions in the same syringe to produce one dose of the product (2 ml).

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

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 reconstitution according to directions: use immediately.

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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/18/228/001

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

15. Date on which the package leaflet was last revised

{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:
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:

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Health Belgium SA
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