ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem suspension for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml dose contains:

Active substance:

Equine umbilical cord mesenchymal stem cells (EUC-MSCs) 7.5×10^6

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Cloudy homogenous cellular suspension

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

Reduction of pain and lameness associated with osteoarthritis in dogs.

4.3 Contraindications

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

4.4 Special warnings for each target species

The veterinary medicinal product was demonstrated to be efficacious in dogs affected by osteoarthritis in elbow or hip. No efficacy data are available regarding the treatment of other joints.

The onset of efficacy may be gradual.

In a laboratory study, 50% of dogs treated with a single dose developed antibodies towards the xenogeneic mesenchymal stem cells. The potential influence of these antibodies on the efficacy of the product has not been evaluated. Efficacy data are available after single dose. No efficacy data are available regarding the treatment in more than one arthritic joint at the same time or after repeated doses.

4.5 Special precautions for use

Special precautions for use in animals

Correct placement of the needle is crucial to avoid accidental injection into blood vessels and an associated risk of thrombosis.

The safety of the veterinary medicinal product has only been investigated in dogs at least one year old and weighing more than 15 kg.

In the clinical field study, a single dose of NSAIDs was administered concomitantly to all the dogs at the time of product administration. The treatment with a systemic dose of NSAIDs the same day as the intra-articular administration of the medicinal product may be considered according to the benefit-risk evaluation performed by the veterinarian for each individual case.

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

Care should be taken to avoid accidental self-injection.

Wash hands after use.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Lameness and pain have been reported commonly:

Marked increase of lameness and pain was reported between 24 hours and 1 week after administration of the veterinary medicinal product. Complete remission in the following few to several weeks. Symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs) was administered.

Mild to moderate increase of lameness 24h after product administration. Complete remission was observed within few days, without the need of anti-inflammatory medication.

Signs of inflammation of the joint were also commonly observed in the clinical studies:

Marked increase in joint effusion was observed 24 hours after product administration in the pivotal field study.

Moderate increase in joint effusion and heat at the injection site was observed 24 hours after product administration in an exploratory field study

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).

4.7 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.

4.8 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.

4.9 Amounts to be administered and administration route

Route of administration:

Intra-articular use.

Dosage:

A single intra-articular injection of 1 ml (7.5×10^6 equine umbilical cord mesenchymal stem cells) into the affected joint.

Method of administration:

The veterinary product must be administered intra-articularly, only by a veterinary surgeon, taking special precautions to ensure the sterility of the injection process. The product must be handled and injected following sterile techniques and in a clean environment.

Swirl gently before use in order to ensure the contents are well mixed.

Use a 23G needle in the elbow and a spinal needle (20G or 23G) in the hips joints with sterile technique and materials. Immediately after product administration a single subcutaneous dose of NSAIDs may be administered.

Intra-articular placement should be confirmed by the appearance of synovial fluid in the hub of the needle.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No data available.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other drugs for disorders of the musculo-skeletal system.
ATCvet code: QM09AX90

5.1 Pharmacodynamic properties

Mesenchymal stem cells have immunomodulatory and anti-inflammatory properties attributed to their paracrine activity, e.g. prostaglandin secretion.

Prostaglandin secretion and immunomodulatory and anti-inflammatory properties have been demonstrated in proprietary studies conducted with the product.

The response to treatment and the duration of effect may be variable.

In the pivotal field trial 51% of the DogStem-treated dogs and 5% of the placebo-treated dogs demonstrated treatment success regarding the primary endpoint (improvement based on force plate gait analysis 8 weeks after product administration). Efficacy was also observed 12 weeks after product administration (secondary endpoint) although de success rate at this time point decreased to 39% in the DogStem-treated group vs. 11% in the placebo group. Efficacy was also evaluated in an uncontrolled long-term follow-up study lasting up to 18 months. Overall, in dogs responding to treatment, data indicate a duration of effect between 8 weeks and more than 12 months.

5.2 Pharmacokinetic particulars

The extent of persistence of EUC-MSCs from this product after intra-articular administration to dogs is not known, as no proprietary biodistribution studies have been conducted with DogStem.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Adenosine
Dextran-40
Lactobionate
HEPES N-(2-hydroxyethyl) piperazine-N´-(2-ethanesulfonic acid)
Glutathione
Sodium salts
Chlorine salts
Bicarbonate salts
Phosphate salt
Potassium salts
Glucose
Sucrose
Mannitol
Calcium salts
Magnesium salts
Trolox (6-hydroxyl-2,5,7,8- tetramethylchroman-2-carboxylic acid)
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 21 days.

Shelf life after first opening the immediate packaging: use immediately.

6.4 Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).
Do not freeze.

6.5 Nature and composition of immediate packaging

Cyclic olefin vial closed with a bromobutyl rubber stopper and a flip-off aluminium cap.

Pack size: cardboard box with 1 vial containing 1 ml.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

EquiCord S.L.
103-D Loeches
Polígono. Industrial Ventorro del Cano
Alcorcón
28925 Madrid
Spain
Tel: +34 (0) 918284238
E-mail: info@equicord.com

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/285/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30/11/2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURERRESPONSIBLE 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

EquiCord S.L.
103-D Loeches
Polígono Industrial Ventorro del Cano
Alcorcón
28925 Madrid
Spain

Name and address of the manufacturer(s) responsible for batch release

EquiCord S.L.
103-D Loeches
Polígono Industrial Ventorro del Cano
Alcorcón
28925 Madrid
Spain

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

OUTER CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem suspension for injection for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1 ml dose contains 7.5×10^6 equine umbilical cord mesenchymal stem cells

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

1 x 1 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For intra-articular use.

Swirl gently before use.

To be administered only by a veterinary surgeon.

8. WITHDRAWAL PERIOD (S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated.

Do not freeze.

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

Disposal: read package leaflet.

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.

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

EquiCord S.L.
103-D Loeches
Polígono Industrial Ventorro del Cano
Alcorcón
28925 Madrid
Spain

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/285/001

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem suspension for injection for dogs

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

7.5 x 10^6 / ml equine umbilical cord mesenchymal stem cells

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

1 ml

4. ROUTE(S) OF ADMINISTRATION

Intra-articular use

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP

8. THE WORDS "FOR ANIMAL TREATMENT ONLY "

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
DogStem suspension for injection for dogs

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

EquiCord S.L.
103-D Loeches
Polígono Industrial Ventorro del Cano
Alcorcón
28925 Madrid
Spain
Phone: +34 (0) 914856756
E-mail: info@equicord.com

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem suspension for injection for dogs

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

Each 1 ml dose contains:

Active substance:
7.5×10^6 equine umbilical cord mesenchymal stem cells

Excipients:
Adenosine
Dextran-40
Lactobionate
HEPES N-(2-hydroxyethyl) piperazine-N´-(2-ethanesulfonic acid)
Glutathione
Sodium salts
Chlorine salts
Bicarbonate salts
Phosphate salt
Potassium salts
Glucose
Sucrose
Mannitol
Calcium salts
Magnesium salts
Trolox (6-hydroxyl-2,5,7,8- tetramethylchroman-2-carboxylic acid)
Water for injections

Suspension for injection

Cloudy homogenous cellular suspension

4. INDICATION(S)

Reduction of pain and lameness associated with osteoarthritis in dogs.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Lameness and pain have been reported commonly:

Marked increase of lameness and pain was reported between 24 hours and 1 week after administration of the veterinary medicinal product. Complete remission in the following few to several weeks. Symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs) was administered.

Mild to moderate increase of lameness 24h after product administration. Complete remission was observed within few days, without the need of anti-inflammatory medication.

Signs of inflammation of the joint were also commonly observed in the clinical studies:

Marked increase in joint effusion was observed 24 hours after product administration in the pivotal field study.

Moderate increase in joint effusion and heat at the injection site was observed 24 hours after product administration in an exploratory field study

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

Dogs.

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

Route of administration
Intra-articular use.

Dosage
A single intra-articular injection of 1ml (7.5×10^6 equine umbilical cord mesenchymal stem cells) into the affected joint.

Method of administration
The veterinary product must be administered intra-articularly, only by a veterinary surgeon, taking special precautions to ensure the sterility of the injection process. The product must be handled and injected following sterile techniques and in a clean environment.

Swirl gently before use in order to ensure the contents are well mixed.

Use a 23G needle in the elbow and a spinal needle (20G or 23G) in the hip joint with sterile technique and materials. Immediately after product administration a single subcutaneous dose of NSAIDs may be administered.

9. ADVICE ON CORRECT ADMINISTRATION

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

Use a 23G needle.

Intra-articular placement should be confirmed by the appearance of synovial fluid in the hub of the needle.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store and transport refrigerated (2 °C – 8 °C).

Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the vial label.

12. SPECIAL WARNINGS

Special warnings for each target species:
The veterinary medicinal product was demonstrated to be efficacious in dogs affected by osteoarthritis in elbow or hip. No efficacy data are available regarding the treatment of other joints.

The onset of efficacy may be gradual.

In a laboratory study, 50% of dogs treated with a single dose developed antibodies towards the xenogeneic mesenchymal stem cells. The potential influence of these antibodies on the efficacy of the product has not been evaluated. Efficacy data are available after single dose. No efficacy data are available regarding the treatment in more than one arthritic joint at the same time or after repeated doses.

Special precautions for use in animals:

Correct placement of the needle is crucial to avoid accidental injection into blood vessels and an associated risk of thrombosis.

The safety of the veterinary medicinal product has only been investigated in dogs at least one year old and weighing more than 15 kg.

In the clinical field study, a single dose of NSAIDs was administered concomitantly to all the dogs at the time of product administration. The treatment with a systemic dose of NSAIDs the same day as the intra-articular administration of the medicinal product may be considered according to the benefit-risk evaluation performed by the veterinarian for each individual case.

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

Care should be taken to avoid accidental self-injection.

Wash hands after use.

In case of accidental self-injection, 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 according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interactions:

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

Overdose (symptoms, emergency procedures, antidotes):

No data available.

Incompatibilities:

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with any 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 or household waste.
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

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency: http://www.ema.europa.eu/

15. OTHER INFORMATION

Cyclic olefin vial closed with a bromobutyl rubber stopper and a flip off aluminium cap.
Pack size: cardboard box with 1 vial containing 1ml.