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 substances:

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

Excipients:

Qualitative composition of excipients and other constituents
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

Cloudy homogenous cellular suspension

3. CLINICAL INFORMATION

3.1 Target species

Dogs

3.2 Indications for use for each target species

Reduction of pain and lameness associated with osteoarthritis in dogs.

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 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.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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 non-steroidal anti-inflammatory drugs (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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Lameness[1,2], pain[1] Joint inflammation Joint effusion[3] Injection site warmth[4]

[1] Marked increase, reported between 24 hours and 1 week after administration. Complete remission in the following few to several weeks. Symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs) was administered.
[2] Mild to moderate increase, 24 hours after administration. Complete remission was observed within few days, without the need of anti-inflammatory medication.
[3] Moderate/marked increase, observed 24 hours after administration
[4] Moderate increase, observed 24 hours 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 systemhttps://www.ema.europa.eu/documents/template-form/qrd-appendix-i-adverse-event-phv-mss-reporting-details_en.docx. 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.

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

3.9 Administration routes and dosage

Intra-articular use.

Dosage:
A single intra-articular injection of 1 ml 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 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.

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

For administration only by a veterinarian.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QM09AX90

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

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

5.3 Special precautions for storage

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

5.4 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.

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

EquiCord S.L.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/285/001

8. DATE OF FIRST AUTHORISATION

30/11/2022

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

OUTER CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

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

3. PACKAGE SIZE

1 x 1 ml

4. TARGET SPECIES

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For intra-articular use.

Swirl gently before use.

To be administered only by a veterinary surgeon.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {dd/mm/yyyy}

Once opened use immediately.

9. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Do not freeze.

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

EquiCord S.L.

14. MARKETING AUTHORISATION NUMBERS

EU/2/22/285/001

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DogStem

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

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

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {dd/mm/yyyy}

Once opened use immediately.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

DogStem suspension for injection for dogs

2. Composition

Each 1 ml dose contains:

Active substance:

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

Excipients:

Qualitative composition of excipients and other constituents
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

Cloudy homogenous cellular suspension

3. Target species

Dogs

4. Indications for use

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. Special warnings

Special warnings:

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 safe use in the target species:

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 interaction:

No data available.

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

Overdose:

No data available.

Special restrictions for use and special conditions for use:

For administration only by a veterinarian.

7. Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Lameness[1,2], pain[1] Joint inflammation Joint effusion[3] Injection site warmth[4]

[1] Marked increase, reported between 24 hours and 1 week after administration. Complete remission in the following few to several weeks. Symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs) was administered.
[2] Mild to moderate increase, 24 hours after administration. Complete remission was observed within few days, without the need of anti-inflammatory medication.
[3] Moderate/marked increase, observed 24 hours after administration
[4] Moderate increase, observed 24 hours 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 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

Intra-articular use.

Dosage

A single intra-articular injection of 1 ml 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 use DogStem 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 periods

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 carton and the vial.

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/2/22/285/001

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.

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, manufacturer responsible for batch release and contact details to report suspected adverse reactions:

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