SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HorStem suspension for injection for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml dose contains:

Active substance:
Equine umbilical cord mesenchymal stem cells (EUC-MSCs) 15x106

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection. Cloudy colourless suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Horses.

4.2 Indications for use, specifying the target species

Reduction of lameness associated with mild to moderate degenerative joint disease (osteoarthritis) in horses.

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 horses affected by osteoarthritis in the metacarpo-phalangeal joint, distal interphalangeal joint, and tarsometatarsal/ distal intertarsal joint. No efficacy data are available regarding the treatment of other joints.

No efficacy data are available regarding the treatment in more than one arthritic joint at the same time.

The onset of efficacy may be gradual. Efficacy data demonstrated an effect from 35 days after treatment.

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 horses at least two years old.

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)

Very common:
Acute synovitis with an acute onset of severe lameness, joint effusion and pain on palpation was reported 24 hours after administration of the veterinary medicinal product. Substantial improvement was shown in the next 48 hours and complete remission in the following two weeks. In case of severe inflammation, administration of symptomatic treatment with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) could be necessary.

Common:
Moderate joint effusion with no associated lameness has been observed 24 hours after HorStem administration. Complete remission was observed over the following two weeks without any symptomatic treatment.
An increase in mild lameness was observed 24 hours after HorStem administration. Complete remission was observed within 3 days, without any symptomatic treatment.

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

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer simultaneously with any other intraarticular veterinary medicinal product.

4.9 Amounts to be administered and administration route

Route of administration:
Intraarticular use.

Dosage:
A single intraarticular injection of 1 ml (15x106 equine umbilical cord mesenchymal stem cells) into the affected joint.

Method of administration:

The veterinary product must be administered intraarticularly, 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 20G needle.

Intraarticular 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

Intraarticular administration of a 2x dose (30x106/2ml) of HorStem to 4 years old and older healthy horses led to lameness in 5/6 animals and to signs of inflammation in all animals. In 5/6 horses, the adverse reactions were mild and resolved spontaneously within 28 days. One horse required symptomatic treatment (NSAID) and its lameness resolved by day 14.

A second administration of the product at the recommended dose to healthy young horses in the same joint, 28 days after the first administration at the recommended dose, led to an increase in frequency and severity of inflammation related to the treated joint (8/8 horses) and to an increase in the severity of the lameness observed (3/8 horses; up to grade 4/5 according to the American Association of Equine Practitioners lameness scale (AAEP)) compared to the first treatment. In one case, symptomatic treatment (NSAID) was required. Adverse reactions in the other horses resolved spontaneously within a maximum of 21 days; lameness lasted for up to three days.

4.11 Withdrawal period(s)

Zero days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Not yet assigned
ATCvet code: QM09AX90

5.1 Pharmacodynamic properties

Mesenchymal stem cells have immunomodulatory and anti-inflammatory properties that may be attributed to their paracrine activity, -e.g. prostaglandin (PGE2) secretion, and can possess tissue regenerative properties. These pharmacodynamic properties may be also relevant for equine umbilical cord derived MSCs (EUC-MSCs) but have not been demonstrated in proprietary studies conducted with the product.

The potential of EUC-MSCs to secrete PGE2 with and without stimulation by synovial fluid has been demonstrated in studies in vitro.

5.2 Pharmacokinetic particulars

To what extent EUC-MSCs from this product persist after intraarticular administration to horses is not known as no proprietary biodistribution studies have been conducted with HorStem.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Adenosine
Dextran-40
Lactobionic acid
HEPES N-(2-hydroxyethyl) piperazine-N´-(2-ethanesulfonic acid)
Sodium hydroxide
L- Glutathione
Potassium chloride
Potassium bicarbonate
Potassium phosphate
Dextrose
Sucrose
Mannitol
Calcium chloride
Magnesium chloride
Potassium hydroxide
Sodium hydroxide
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

8. MARKETING AUTHORISATION NUMBER

Vm 46422/5000

9. DATE OF FIRST AUTHORISATION

19 June 2019

10. DATE OF REVISION OF THE TEXT

December 2021

Approved: 31 December 2021