Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

SynVet-50; 50 mg solution for injection for horses

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each 2.5 ml syringe contains:

Sodium Hyaluronate 50 mg
(equivalent to hyaluronic acid) 47 mg

Excipients:

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Clear colourless viscous solution

4 CLINICAL PARTICULARS

4.1 Target Species

Horse

4.2 Indications for use, specifying the target species

For adjunctive intra-articular treatment of joint disease associated with non-infectious synovitis in horses.

4.3 Contraindications

Do not use in cases of joint infections.
Do not use in cases of known hypersensitivity to exogenous sodium hyaluronate or to any of the excipients of the product.

4.4 Special warnings for each target species

The treated horse should be box-rested for 2 days before gradually resuming a normal exercise pattern.

4.5 Special precautions for use

i) Special precautions for use in animals

Excess synovial fluid should be removed whenever possible prior to injection.
The injection should be administered under strict aseptic conditions through healthy undamaged skin.
Appropriate investigations should be carried out in cases of acute, severe lameness to ensure that the joints are free from fractures, OCD fragments and infections.

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

In case of accidental contact with skin, wash with soap and water.
In case of accidental contact with eyes, blurred vision may occur because of the viscous nature of the product. Rinse immediately with plenty of clean water.

In the event of accidental self-injection, seek medical advice immediately and show the package leaflet of the label to the physician.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

The most commonly reported adverse reaction are transient mild swelling and/or heat occurring in approximately 2.7% of the treated joints. These self-limiting local signs typically resolve spontaneously within 48 hours. However, since the early signs of septic arthritis may be similar, it is advised that a thorough clinical examination and monitoring are carried out if these clinical signs occur. Consideration should be given to appropriate further investigations.

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 product has not been established in pregnant and lactating mares.Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

No data available regarding the interaction with other medicinal products. It is described that hyaluronic acid competes with other high molecular weight polysaccharides such as chondroitin sulphate for receptor binding and thus for uptake in the articular cartilage tissue.

4.9 Amounts to be administered and administration route

For single intra-articular injection: 2.5 ml intra-articularly into medium sized and large joints. More than one joint may be treated at the same time.
A sterile dressing and clean bandage should be applied after injection, as appropriate for the particular joint treated.

If necessary, re-treatment of the joint can be considered at 2-3 weeks after the first-treatment.

Single dose syringes made ready for injection shall be used immediately; any unused portion of a syringe is to be discarded.

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

None observed

4.11 Withdrawal period(s)

Meat and offal: zero days
Milk: zero hours

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: sodium hyaluronate (hyaluronic acid)
ATCvet Code: QM09AX01.

5.1 Pharmacodynamic properties

A bacterial fermentation process produces the active substance in the product. Sodium hyaluronate is extracted from the capsule of *Streptococcus spp*. and purified, resulting in a form which is free of protein, pyrogen and nucleic acids. Sodium hyaluronate is the sodium salt of hyaluronic acid, a non-sulphated acid, high-viscosity mucopolysaccharide or

glycosaminoglycan of high molecular weight composed of equimolar amounts of D-glucuronic acid and N-acetylglucosamine linked by glycosidic bonds.

Hyaluronate is a physiological natural substance of connective tissues in all mammals and its chemical structure is the same in all species.
High concentrations of hyaluronate are especially found in the synovial fluid, the vitreous of the eye and the umbilical cord. Hyaluronic acid is also found in the articular cartilage matrix.

Apart from its physical and rheological properties, hyaluronic acid has anti-inflammatory, analgesic, lubricant and anti-oxidant activities. Its biochemical activities are distinct from its physical and rheological properties. It is an effective free radical scavenger, a potent inhibitor of leucocytes and macrophage migration and aggregation, and enhances healing of connective tissue.

Intra-articularly administered sodium hyaluronate alleviates aseptic joint inflammation and enhances joint lubrication. The mechanism of action of the active substance is not fully understood. The molecular weight of the active ingredient in SynVet-50 sodium hyaluronate ranges from >1 million to 1.8 million Dalton.

5.2 Pharmacokinetic particulars

Studies with radio labelled hyaluronic acid in rabbit and sheep indicate that hyaluronic acid is cleared from the joint within 4 to 5 days after intra-articular injection.

Elimination half-life from synovial fluid after intra-articular injection of any joint was highly variable, however the mean T1/2, determined in only a few horses, was approximately 8-24 hours.
Intra-articular administered HA moved into and disappeared from the circulation at a first-order rate.
Uptake is primarily via the lymphatics. Hyaluronate is taken up and metabolized in liver endothelial cells, where it is broken down into C1 units of the carbon cycle before being re-utilised in the body. The main metabolites are H_2O, CO_2, lactate, D-glucosamine-N-acetyl-D-glucosamine, low weight HA and monosaccharides.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Disodium Phosphate Dodecahydrate
Citric Acid Monohydrate
Water for Injections

6.2 Major incompatibilities

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

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Any solution remaining in the syringe following withdrawal of the required dose should be discarded.

6.4 Special precautions for storage

Do not store above 25°C
Store in the original container
Store in a dry place

6.5 Nature and composition of immediate packaging

Single-dose glass syringe barrel with luer tip and rigid tip cap
Type 1 glass syringe, lubricated with dimethicone.
Styrene-butadiene rubber cap.

Bromobutyl rubber plunger.

Available in single cartons or packs of 6 single cartons overwrapped with plastic film.
Not all pack sizes may be marketed.

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

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

7 MARKETING AUTHORISATION HOLDER

Equi Pharma Ltd
Aspen Lodge
Notabile Road
Mriehel
Birkirkara BKR1870
Malta

8 MARKETING AUTHORISATION NUMBER(S)

VPA22962/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 July 2014
Date of last renewal: 18 July 2019

10 DATE OF REVISION OF THE TEXT

October 2021