1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oapent 100 mg/ml Solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Pentosan Polysulfate Sodium 100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	0.01 ml
Disodium phosphate dodecahydrate	-
Sodium dihydrogen phosphate dihydrated	-
Sodium hydroxide	-
Hydrochloric acid, concentrated	-
Water for injection	-

Clear, pale-yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs

3.2 Indications for use for each target species

For the treatment of lameness and pain of degenerative joint disease/osteoarthritis (non-infectious arthrosis) in the skeletally mature dog.

3.3 Contraindications

Do not use in the treatment of septic arthritis. In that case, appropriate antimicrobial therapy should be instigated.
Do not use in dogs with advanced liver or kidney impairment, or evidence of infection.
Do not use in dogs with blood disorders, blood clotting disorders, bleeding or malignant tumours (in particular haemangiosarcoma). Pentosan polysulfate has an anticoagulating effect.
Do not use during the perioperative period. Do not use in the skeletally immature dog (i.e. dogs whose long bone growth plates have not closed).
Do not use in cases of hypersensitivity to the active substance or to any of the excipient(s).

3.4 Special warnings

A clinical effect may not be observed until after the second injection of the course of treatment.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use with caution in dogs with a history of pulmonary lesions.
Caution is also advised in cases of liver disease.
Do not exceed the standard dose. Exceeding the recommended dose can result in an increase in stiffness and discomfort.
Do not administer more than 3 treatments of 4 injections each over a 12-month period.

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

Pentosan polysulfate may cause anticoagulant and gastrointestinal effects. Caution is advised to prevent accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Pentosan polysulfate and benzyl alcohol may cause hypersensitivity reactions. People with known hypersensitivity to pentosan polysulfate sodium or benzyl alcohol should administer the veterinary medicinal product with caution. If contact occurs, wash the affected area immediately. If you develop symptoms following exposure, such as a skin rash, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Undetermined frequency (cannot be estimated from the available data):	Anorexia[1], vomiting[1], diarrhoea[1]; Lethargy[1]; Prolonged activated partial thrombin time (aPTT)[2], prolonged thrombin time (TT)[2]; Bleeding disorders (e.g. nasal bleeding, bloody diarrhoea, haematoma); Injection site swelling[3]

[1] Due to hypersensitivity reaction; may require symptomatic treatment, including antihistamine administration.

[2] May persist for up to 24 hours after administration in healthy dogs. This very rarely results in clinical effects, but because of the fibrinolytic action of pentosan polysulfate sodium, the possibility of internal bleeding from a tumour or vascular abnormality should be considered if signs develop. It is recommended that the animal should be monitored for signs of blood loss and treated appropriately.

[3] Transient

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

Pregnancy and lactation
Laboratory studies in rabbits showed embryotoxic effects associated with a primary effect on the parent at repeated daily doses 2.5 times the recommended dose.
The safety of the product in the pregnant bitch has not been studied; therefore, use is not recommended in these circumstances.
The product should not be used at the time of parturition due to its anticoagulant effects.

3.8 Interaction with other medicinal products and other forms of interaction

NSAIDs, and in particular aspirin, should not be used in combination with pentosan polysulfate sodium as they may affect thrombocyte adhesion and potentiate the anticoagulant activity of the product.
Corticosteroids have been shown to be antagonistic to a number of actions of pentosan polysulfate sodium. Furthermore, use of anti-inflammatory drugs may result in a premature increase in the dog's activity, which may interfere with the therapeutic activity of the product.
Do not use concurrently with steroids or non-steroidal anti-inflammatory drugs, including aspirin and phenylbutazone or within 24 hours of such administration.

Do not use concurrently with heparin, warfarin or other anti-coagulants.

3.9 Administration routes and dosage

Subcutaneous use.

To ensure a correct dosage, body weight should be determined as accurately as possible.

3 mg pentosan polysulfate sodium / kg bodyweight (equivalent to 0.3 ml/10kg bodyweight) on four occasions, with an interval of 5-7 days between each administration.

Administer by aseptic subcutaneous injection only of 0.3 ml/10 kg body weight. An appropriately graduated syringe must be used to allow accurate administration of the required dose volume.
This is particularly important when injecting small volumes.
Each case must be assessed on an individual basis by the veterinarian, and an appropriate treatment program should be established.

The cap may be safely punctured up to 40 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Repeated daily overdoses of five times the recommended dose or more resulted in anorexia and depression, which were reversible upon withdrawal of the drug.

At overdose there may be hepatocellular damage and an associated, dose-dependent, elevation in ALT.

Increases in aPTT and TT are dose-dependent. At repeated doses greater than five times that recommended, these increases may persist beyond 1 week after administration in healthy dogs. Signs associated with these defects may include bleeding into the gastro-intestinal tract, body cavities and ecchymoses. At repeated doses greater than ten times that recommended there may be fatality as a result of gastro-intestinal haemorrhage.

If overdose occurs dogs should be hospitalised and observed, and supportive therapy provided as deemed necessary by the veterinarian

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QM01AX90

4.2 Pharmacodynamics
The product contains Pentosan Polysulfate Sodium (NaPPS), a semi-synthetic polymer with a mean molecular weight of 4000 Daltons.

In a model of osteoarthritis in dogs, when NaPPS was administered at doses similar to therapeutic ones, levels of metalloproteinases in cartilage were reduced and levels of tissue inhibitor of metalloproteinase (TIMP) increased, thereby preserving proteoglycan content and protecting cartilage matrix from degradation.

In dogs with osteoarthritis administration of NaPPS caused fibrinolysis, lipolysis and decreased platelet aggregability.

In *in vitro* studies and *in vivo* studies in laboratory species using doses above those proposed for therapeutic use, NaPPS suppressed levels of anti-inflammatory mediators and stimulated hyaluron synthesis from fibroblasts.

4.3 Pharmacokinetics
Absorption: In the dog, a peak plasma concentration of 7.40 mg-eq pentosan polysulfate sodium/mL is achieved 15 minutes after subcutaneous administration.

Distribution: Pentosan polysulfate sodium binds many plasma proteins with a variable strength of association and dissociation resulting in a complex equilibrium between bound and unbound drug. Pentosan polysulfate sodium is concentrated in the liver and kidneys and reticuloendothelial system. Low levels occur in connective tissue and muscle. Studies conducted with rabbits have shown that the therapeutic concentration of the active substance remains in the cartilage of the joint approximately 4-5 days after administration. The volume of distribution in dogs is 0.43 L.

Biotransformation: Desulfation of pentosan polysulfate sodium occurs in the hepato-reticulo-endothelial system, the liver being the main site of activity.
Depolymerisation may also occur in the kidney.

Elimination: The product is eliminated with a half-life of approximately 3 hours in the dog. Forty-eight hours after injection approximately 70% of the dose administered is eliminated via urine.

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: 2 years
Shelf life after first opening the immediate packaging: 90 days

5.3 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions. Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Clear glass vial (Ph. Eur. type I) closed with rubber stopper. The vial is sealed with aluminium cap equ ipped with a polypropylene “flip-off” seal.

Pack sizes:
Cardboard box with 1 vial of 10 ml
Cardboard box with 1 vial of 20 ml

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

VETPHARMA ANIMAL HEALTH, S.L

7. MARKETING AUTHORISATION NUMBER(S)

VPA10516/026/001

8. DATE OF FIRST AUTHORISATION

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

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).