SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Osteopen 100 mg/ml Solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Pentosan Polysulphate Sodium 100 mg/ml

Excipients:
Benzyl Alcohol E1519 10.45 mg/ml
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.
A clear pale yellow aqueous solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

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

4.3 Contraindications

Do not use in the treatment of septic arthritis. In this 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 known cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in the skeletally immature dog (i.e. dogs whose long bone growth plates have not closed).

As pentosan polysulphate has an anticoagulant effect, do not use in dogs with blood disorders, coagulation disorders, bleeding, trauma or malignancy (especially haemangiosarcoma) or during the peri-operative period within 6 – 8 hours of surgery.
Do not use in arthritides of immunological origin (e.g. rheumatoid arthritis).

4.4 Special warnings for each target species

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

4.5 Special precautions for use

Special precautions for use in animals
Do not exceed the standard dose. Increasing the recommended dose may result in exacerbation of stiffness and discomfort.
Because of the fibrinolytic action of pentosan polysulphate sodium, the possibility of internal bleeding from a tumour or vascular abnormality should be considered and appropriate therapeutic action taken.
It has been reported that a dog which had suffered pulmonary lacerations twelve months previously had severe pulmonary bleeding after an injection of pentosan polysulphate sodium. Use with caution in dogs with a history of pulmonary lacerations.
Caution is also recommended in cases of hepatic impairment.
Pentosan polysulphate sodium has an anticoagulant effect.
It is recommended that the Packed Cell Volume (PVC) and capillary filling time should be monitored, when the product is used.
Avoid intramuscular injection because of the risk of haematoma at the injection site.
No more than three courses of four injections should be administered in a twelve month period.
It is recommended that the animal should be monitored for signs of blood loss and treated appropriately. Interrupt the treatment if signs of increased bleeding occur.

Special precautions to be taken by the person administering the veterinary medicinal product to animals. The preservative, benzyl alcohol, can cause hypersensitivity (allergic) reactions in sensitised people. If you know that you are sensitised, care should be taken when handling this product. If accidental skin or eye contact occurs, rinse affected area immediately with water.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Rarely, reaction to the injection may occur within 24 hours in an apparently healthy animal. In these circumstances treatment should be discontinued and symptomatic relief given.
Experience indicates that in very rare cases, dogs may vomit immediately after injection with pentosan polysulphate.
Such dogs generally require no medical treatment and make an uneventful recovery.
Further treatment with pentosan polysulphate is not recommended.

A further very rare side effect following administration of pentosan polysulphate sodium in dogs is an apparent mild depression and lethargy lasting up to 24 hours.

Emesis, diarrhoea, lethargy and anorexia have been reported following the use of pentosan polysulphate. These signs may be the result of a hypersensitivity reaction and may require appropriate symptomatic treatment including antihistamine administration. Administration of the product at recommended dose rates results in increases of activated partial thromboplastin time (aPTT) and thrombin time (TT) which 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 polysulphate 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

Bleeding disorders such as nasal bleeding, haemorrhagic diarrhoea and haematomas have been reported.

Local reactions such as a transient swelling have been observed post injection.

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

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 or lactating animal has not been studied, therefore use is not recommended in pregnant or lactating animals.
The product should not be used at the time of parturition due to its anticoagulant effects.

4.8 Interaction with other medicinal products and other forms of interaction

NSAIDs and in particular aspirin should not be used in combination with pentosan polysulphate 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 polysulphate sodium. Furthermore, use of anti-inflammatory drugs may result in a premature increase in the dog’s activity, which may interfere with the analgesic and regenerative effects 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 in conjunction with heparin and other anti-clotting agents.

4.9 Amounts to be administered and administration route

3 mg pentosan polysulphate sodium / kg bodyweight (equivalent to 0.3 ml/10kg bodyweight) on four occasions, with an interval of 5-7 days.
Administer by aseptic subcutaneous injection only. An appropriately graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting small volumes.
To establish the appropriate dosage, the weight of the individual animal should be determined prior to administering the veterinary medicinal product.

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

At three times the recommended dose a transient increase in bleeding time of about 3 to 4 hours duration has been observed. 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.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids
ATC vet code: QM01AX90

5.1 Pharmacodynamic properties

The product contains Pentosan Polysulphate 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 similar to therapeutic doses, 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.
Pentosan polysulphate sodium has fibrinolytic, lipolytic and mild anti-coagulant activities. Pentosan polysulphate sodium has an effect on blood coagulation due to its heparin-like structure and fibrinolytic activity that lasts for up to 6-8 hours after administration.

5.2 Pharmacokinetic particulars

Absorption: In the dog, a peak plasma concentration of 7.40 μg-eq pentosan polysulphate sodium/mL is achieved 15 minutes after subcutaneous administration.
Distribution: Pentosan polysulphate sodium binds many plasma proteins with a variable strength of association and dissociation resulting in a complex equilibrium between bound and unbound drug. Pentosan polysulphate sodium is concentrated in the liver and kidneys and reticuloendothelial system. Low levels occur in connective tissue and muscle. The volume of distribution in dogs is 0.43 L.

Biotransformation: Desulfation of pentosan polysulphate 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol E1519
Disodium phosphate dodecahydrate
Sodium dihydrogen phosphate dihydrate
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
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: 4 years
Shelf life after first opening the immediate packaging: 84 days

6.4 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Colourless glass vial fitted with a grey chlorobutyl stopper and sealed by a lacquered aluminium cap.
Package size:
1 x 10ml
1 x 20ml
Not all pack sizes may be marketed.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.
Loughrea
Co. Galway
Ireland.

8. MARKETING AUTHORISATION NUMBER

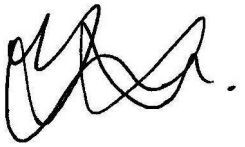
Vm 08749/4086

9. DATE OF FIRST AUTHORISATION

19 July 2018

10. DATE OF REVISION OF THE TEXT

January 2023



Approved: 23 January 2023