

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Anarthron 100mg/mL solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pentosan Polysulfate Sodium	100mg/ml
Benzyl Alcohol	0.01ml/ml

3. PHARMACEUTICAL FORM

Solution for injection

A clear, colourless pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Target Species

Dog

4.2 Indications for use, specifying the target species

For the treatment of lameness and pain of degenerative joint disease/osteoarthritis (non-infectious arthritis) 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 dogs with blood disorders, coagulation disorders, bleeding or malignancy (especially haemangiosarcoma). Pentosan polysulfate has an anticoagulant effect.

Do not use during the peri-operative period.

Do not use in the skeletally immature dog (i.e. dogs whose long bone growth plates have not closed).

4.4 Special warnings

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

4.5 Special precautions for use

- i. Special precautions for use in animals:

Dogs should be weighed prior to administration to ensure accurate dosing.

Use with caution in dogs with history of pulmonary lacerations. Caution is also recommended in cases of hepatic impairment.

Do not exceed the standard dose. Increasing the recommended dose may result in exacerbation of stiffness and discomfort.

No more than 3 courses of 4 injections should be administered in a 12 month period.

- ii. Special precautions to be taken by the person administering the medicinal product to animals:

Care should be taken to avoid accidental self-injection. Wash splashes from eyes and skin immediately with water. Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Emesis, diarrhoea, lethargy and anorexia have been reported following the use of pentosan polysulfate. 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 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

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.

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 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.

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 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.

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

4.9 Amounts to be administered and administration route

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

Administration: By aseptic subcutaneous injection only of 0.3ml/10kg of bodyweight. 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 should be assessed individually by the veterinarian and an appropriate treatment program determined.

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

Repeated daily overdoses of five times the recommended dose or more results in anorexia and depression, which are 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(s)

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 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 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.

5.2 Pharmacokinetic particulars

Absorption: In the dog, a peak plasma concentration of 7.40 µg-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. In studies carried out with rabbits, it has been shown that therapeutic concentrations of the active ingredient remain in the joint cartilage for 4-5 days after administration. The volume of distribution in dogs is 0.43L.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Disodium phosphate dodecahydrate
Sodium dihydrogen phosphate dihydrate
Sodium hydroxide
Hydrochloric acid
Water for injection

6.2 Incompatibilities

The product should not be administered in the same syringe with other substances.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf-life after first opening the immediate packaging: 3 months.

6.4 Special precautions for storage

Do not store above 25°C. Keep container in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

A 10 ml Ph.Eur. Type 1 clear glass vial fitted with a 20 mm rubber stopper Ph.Eur and closed by a plastic flip off seal attached to an aluminium seal.

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 materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Arthroparm Europe Limited
50 Bedford Street
Belfast
BT2 7FW
Northern Ireland

8. MARKETING AUTHORISATION NUMBER

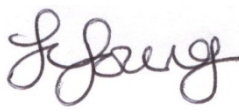
Vm 15519/4002

9. DATE OF FIRST AUTHORISATION

Date: 01 May 2007

10. DATE OF REVISION OF THE TEXT

Date: May 2013

Approved:  **17/05/2013**