SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ANTISHMANIA 300 mg/ml solution for injection for dogs (ES, EL)
ANTISHMANIA solution for injection for dogs (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION (ES, EL)

Each ml contains:

Active substance:
Meglumine antimoniate.....300 mg
(equivalent to Antimony ….……..…….....81 mg)

Excipients:
Potassium metabisulfite (E224)..... 1.6 mg
Sodium sulfite (E221)……..... 0.18 mg

For the full list of excipients, see section 6.1.

QUALITATIVE AND QUANTITATIVE COMPOSITION (FR)

Each ml contains:

Active substance:
Antimony..... 81 mg
(equivalent to Meglumine antimoniate ….……300 mg)

Excipients:
Potassium metabisulfite (E224)..... 1.6 mg
Sodium sulfite (E221)..... 0.18 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, pale yellow solution.

4. CLINICAL PARTICULARS

4.1. Target species

Dogs.

4.2. Indications for use, specifying the target species

Treatment of canine leishmaniasis.

4.3. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Do not use in dogs with hepatic, renal and cardiac insufficiency.

4.4. Special warnings for each target species

If after 4 weeks of treatment no response is obtained, the strain of Leishmania is considered resistant and another treatment option should be investigated.

4.5. Special precautions for use

Special precautions for use in animals
The treatment must be accompanied by serological and etiological monitoring, indicating the prognosis of the disease and, consequently, the fate of the animal.
The treatment is to induce an improvement in clinical signs but the dog can remain a parasites source for sand-flies. The dog should be watched after the end of the administration in order to re-administer the product if necessary
Begin treatment with administration of a half dose, particularly in cases of compromised renal permeability; progressively increase until reaching the recommended dose.
In cases of intolerance, suspend the treatment and resume it at a lower dose.
Renal function must be monitored before and during treatment.
It is also recommended that liver and cardiac function be monitored during treatment**.**
In case of renal failure and/or ocular disorders (such as keratitis, uveitis, conjunctivitis), associated clinical signs must be stabilized or treated before the start of treatment.
In cases of diagnosed renal insufficiency, the associated symptoms must be treated and stabilised prior to the start of treatment with the product.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
People with known hypersensitivity to the active substance should avoid contact with the veterinary medicinal product.
Avoid contact between the product and skin, eyes or mouth.
If the product gets accidentally into the eyes or in case of accidental spillage onto skin wash thoroughly with plenty of water.
In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.
Do not eat, drink or smoke during application.

4.6. Adverse reactions (frequency and seriousness)

A painful reaction can be observed uncommonly during the injection. In addition, local reactions at injection site such as pain, swelling and inflammation have been reported following the administration of this product in uncommon cases.
The toxicity of this compound may rarely cause symptoms characterized by fever, tachycardia, vomiting, weakness, prostration, myalgia and arthralgia.
Signs usually resolve upon discontinuation of treatment.
Prolonged use may rarely lead to renal and cardiac lesions.

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 and lactation

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8. Interaction with other medicinal products and other forms of interaction

The concomitant use with agents that can prolong QT interval should be avoided, as it can increase the risk for arrhythmias.

4.9. Amounts to be administered and administration route

Administration route: subcutaneous.
The recommended daily dose of meglumine antimoniate is 100 mg/kg b.w. (equivalent to 0.33 ml of the product /kg b.w. day). If it is possible to administer several injections within the day, it is recommended that the dose daily be subdivided into two injections of 50 mg of meglumine antimoniate/kg b.w., with 12 h between administrations.
Volumes greater than 10 ml should be divided and administered at 2 different injection sites.
The initial duration of treatment is 3 weeks. If sufficient clinical improvement should not be observed, the treatment may be continued for another week.
Repeated treatments may be required to eliminate the parasites. It is therefore recommended that the clinical course of the animal be monitored.

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

Both in the literature and through clinical experience, the data regarding overdose is limited, so much so that the signs and symptoms of overdose have not been characterised.
In case of overdose, the patient must be monitored and treated symptomatically. Special attention must be paid to the potential toxic effects in the liver, heart and kidney.
There is no known antidote. Reactions at the injection site (oedema, induration) may be observed after subcutaneous injection of 200 mg/kg of meglumine antimoniate (twice the recommended dose).

4.11. Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents, Antiprotozoals. Antimony compounds.
ATC Vet Code: QP51AB01

5.1. Pharmacodynamic properties

Meglumine antimoniate is an antileishmanial antiprotozoal agent belonging to the antimoniate group, whose mechanism of action could be linked to the inhibition of certain glycolytic enzymes in the parasite. The experimental data suggest the hypothesis of metabolic conversion of pentavalent antimoniate within the macrophages into trivalent compounds, which are toxic for the amastigote stage of Leishmania. Resistant strains have been described. Resistance of the causal agent to treatment may be due to errors in the dosage and duration of treatment or to resistance due to multi-factor causes. To demonstrate real resistance, the following primary indicators must be used: absence of clinical improvement, reduction in antibody titre and maintenance of a considerable parasitic load (analysed by PCR, polymerase chain reaction).

5.2. Pharmacokinetic particulars

Meglumine antimoniate is not absorbed orally while it is absorbed completely (bioavailability >90%) intramuscularly and subcutaneously.
After subcutaneous administration of 100 mg of meglumine antimoniate/kg of body weight, the following values are obtained: C_{max} (µg/ml): 25.5, t_{max} (min): 85.6 e $AUC_{0-\infty}$ (µg/min/ml): 6481. The tissue distribution of meglumine antimoniate is very limited. The elimination half-life is short (from 20 minutes to 2 hours, depending on the administration route) and it is eliminated rapidly via the urine (over 80% in the first nine hours).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Potassium metabisulfite (E224)
Sodium sulfite (E221)
Sodium hydroxide (as pH adjuster)
Water for injections

6.2. Major incompatibilities

Do not administer with normal saline solution. 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.
Shelf life after first opening the immediate packaging: use immediately.

6.4. Special precautions for storage

Store below 25°C.

6.5. Nature and composition of immediate packaging

5 ml colourless Type I glass vial closed with a chlorobutyl rubber closure (Type I) and flip-off aluminium collar with tamper-proof polypropylene seal.

Package sizes:
Box with 5 vials.
Box with 10 vials.

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

7. MARKETING AUTHORISATION HOLDER

FATRO S.p.A. - Via Emilia 285 – Ozzano dell'Emilia (Bologna), Italy

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: *to be completed nationally.*
Date of last renewal: *to be completed nationally.*

10. DATE OF REVISION OF THE TEXT

To be completed nationally.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Dispensing conditions: **Veterinary medicinal product subject to veterinary prescription.**

Administration conditions: **Administration only by a veterinarian surgeon.**