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

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

FATRO S.p.A.
Via Emilia, 285
Ozzano Emilia - Bologna
Italy.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

(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, anhydrous (E221) 0.18 mg.

(FR)
Each ml contains:
Active substance: Antimony 81 mg (equivalent to Meglumine antimoniate 300 mg) - **Excipients:** Potassium metabisulfite (E224) 1.6 mg - Sodium sulfite, anhydrous (E221) 0.18 mg.

Clear, pale yellow solution

4. INDICATIONS

Treatment of canine leishmaniasis.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in dogs with hepatic, renal and cardiac insufficiency.

6. ADVERSE REACTIONS

A painful reaction can be observed 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 occasionally cause symptoms characterized by fever, tachycardia, vomiting, weakness, prostration, myalgia and arthralgia.
Signs usually resolve upon discontinuation of treatment.

Prolonged use may 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)) during the course of one treatment)
- 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).

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs.

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

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.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIODS

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store below 25°C.
After first opening use immediately.
Do not use this veterinary medicinal product after the expiry date which is stated on the vial label after “EXP”.

12. SPECIAL WARNINGS

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.

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.
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.

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

Interaction with other medicinal products and other forms of interaction
No data available.

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).

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

May 2019

15. OTHER INFORMATION

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).

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).

Pack sizes:
5 x 5 ml vials
10 x 5 ml vials

Not all pack sizes may be marketed.