[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Antishmania 300 mg/ml solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Meglumine antimoniate 300 mg
(equivalent to 81 mg antimony)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Potassium metabisulfite (E224)	1.6 mg
Sodium sulfite (E221)	0.18 mg
Sodium hydroxide (as pH adjuster)	
Water for injections	

Clear, pale yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Treatment of canine leishmaniasis caused by *Leishmania spp.*

3.3 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.

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
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 veterinary medicinal 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 veterinary medicinal product.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to meglumine antimoniate should avoid contact with the veterinary medicinal product.
Avoid contact between the veterinary medicinal product and skin, eyes or mouth.
If the veterinary medicinal 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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs.

Uncommon (1 to 10 animals / 1,000 animals treated):	Injection site reaction: pain, swelling, inflammation
Rare (1 to 10 animals / 10,000 animals treated):	Fever, prostration Vomiting Weakness, muscle pain[1], joint pain [2] Tachycardia, cardiac disorder[3] Renal disorder[3]

[1]Myalgia
[2]Arthralgia
[3] Prolonged use may rarely lead to renal and cardiac lesions.

Signs usually resolve upon discontinuation of treatment.

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 package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy and lactation:
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 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.

3.9 Administration routes and dosage

Subcutaneous use.

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.

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

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

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).

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

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP51DX01

4.2 Pharmacodynamics

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).

4.3 Pharmacokinetics

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: Cmax (µg/ml): 25.5, tmax (min): 85.6 e AUC0-∞ (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).

5. PHARMACEUTICAL PARTICULARS

5.1 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.

5.2 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.

5.3 Special precautions for storage

Store below 25 °C.

5.4 Nature and composition of immediate packaging

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:
Cardboard box containing 5 vials of 5 ml
Cardboard box containing 10 vials of 5 ml

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

FATRO S.p.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: DD/MM/YYYY

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
Cardboard box:
5 vials of 5 ml
10 vials of 5 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Antishmania 300 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Meglumine antimoniate 300 mg
(equivalent to 81 mg antimony)

3. PACKAGE SIZE

5 x 5 ml
10 x 5 ml

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use immediately.

9. SPECIAL STORAGE PRECAUTIONS

Store below 25 °C.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
Label:
5 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Antishmania

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each ml contains:
Meglumine antimoniate 300 mg
(equivalent to 81 mg antimony)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use immediately.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Antishmania 300 mg/ml solution for injection for dogs

2. Composition

Each ml contains:
Active substance:
Meglumine antimoniate 300 mg
(equivalent to 81 mg antimony)

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

Clear, pale yellow solution.

3. Target species

Dogs.

4. Indications for use

Treatment of canine leishmaniasis caused by *Leishmania spp*.

5. 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.

6. Special warnings

Special warnings:
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 safe use in the target species:
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 veterinary medicinal 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 veterinary medicinal product.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to meglumine antimoniate should avoid contact with the veterinary medicinal product.
Avoid contact between the veterinary medicinal product and skin, eyes or mouth.
If the veterinary medicinal 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.

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.

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.

Overdose:
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).

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.

7. Adverse events

Dogs.

Uncommon (1 to 10 animals / 1,000 animals treated):	Injection sitereaction: pain, swelling, inflammation
Rare (1 to 10 animals / 10,000 animals treated):	Fever; prostration Vomiting Weakness,muscle pain[1], joint pain [2] Tachycardia, cardiac disorder[3] Renal disorder[3]

[1]Myalgia
[2]Arthralgia
[3] Prolonged use may rarely lead to renal and cardiac lesions.

Signs usually resolve upon discontinuation of treatment.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing

authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Subcutaneous use.

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

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

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 25 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: use immediately.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Package sizes:
Cardboard box containing 5 vials of 5 ml
Cardboard box containing 10 vials of 5 ml

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
FATRO S.p.A.
Via Emilia, 285
40064 Ozzano dell'Emilia (Bologna), Italy
Tel: +39 051 6512711

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information