SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINE

GLUCANTIME 1.5 g/5 ml, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Meglumine antimoniate 1.5000g
Corresponding amount of antimony 0.4050g
For a 5 ml ampoule.
Excipients with known effect: Potassium disulphite, anhydrous sodium sulphite
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL DATA

4.1. Therapeutic indications

Treatment of visceral leishmaniasis (Kala azar) and cutaneous leishmaniasis (except Leishmania aethiopica resistant).

4.2. Dosage and method of administration

Visceral leishmaniasis:

Intramuscular injection of 20 mg/kg/day of antimony (i.e. 75 mg/kg/day of antimonate meglumine), without exceeding 850 mg of antimony, for at least 20 consecutive days. The treatment should be continued until the parasites have disappeared in punctures of the spleen carried out at intervals of 14 days.

In case of recurrence, the cure must be immediately restarted with the same doses daily.

Cutaneous leishmaniasis:

- With the exception of Leishmania braziliensis and Leishmania amazonensis forms:

Lesion injections should only be considered in the early stage. The infiltration must be deep until complete bleaching at the base of the lesion.

Systemic treatment is necessary when the lesions are too numerous, inflamed, ulcerated or located in a place where scars could be unsightly or incapacitating, especially if there is obstruction of the lymphatic channels or cartilage damage.

Local treatment: Injection of 1 to 3 ml at the base of the lesion, repeated once (or twice in no apparent result), at intervals of 1 or 2 days.

General treatment: Intramuscular injection of 10 to 20 mg/kg/day of antimony (i.e. 37 to 75 mg/kg/day of meglumine antimonate) until clinical cure or disappearance of the parasite from the dermal juice collected by scarification, then a few days beyond.

- For Leishmania braziliensis (cutaneous and mucocutaneous leishmaniasis) and Leishmania amazonensis (mucocutaneous leishmaniasis):

Intramuscular injection of 20 mg/kg/day of antimony (i.e. 75 mg/kg/day of meglumine antimonate) until recovery and during:

  - at least 4 weeks for Leishmania braziliensis,
  - several months for Leishmania amazonensis

4.3. Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1,
- kidney, heart or liver failure.

4.4. Special warnings and precautions for use

Warnings

Due to the risk of antimony intolerance, it is advisable to monitor liver function and kidneys throughout treatment (see sections 4.8 and 4.9). In case of abnormalities, reduce the doses. Meglumine antimonate can cause QT prolongation and severe arrhythmia. Monitoring of the ECG tracing is advised and caution should be exercised when using meglumine antimonate in patients with known risk factors for causing prolongation of the QT interval such as, for example:

- uncorrected electrolyte imbalance (eg, hypokalemia, hypomagnesemia)
- congenital long QT syndrome
- heart disease (eg myocardial infarction, bradycardia)
- concomitant use of medicinal products known to induce prolongation of the QT interval (for example, certain class IA and III antiarrhythmics, certain tricyclic antidepressants, certain macrolides, some antipsychotics, other antiparasitics) (see sections 4.5, 4.8, and 4.9).

Hypersensitivity reactions (including anaphylactic shock and type IV hypersensitivity reactions); sometimes severe, have been reported with the use of meglumine antimoniate. If signs and symptoms of allergic reactions occur, treatment with GLUCANTIME should be discontinued and appropriate symptomatic treatment should be instituted (see section 4.3).

This medicine contains “sulphite” and may, in rare cases, cause reactions severe hypersensitivity and bronchospasm.

Special precautions for use

A high-protein diet should be administered throughout treatment being preceded if possible by the correction of any iron deficiency or any other deficiency specific.

4.5. Interactions with other medicinal products and other forms of interaction

+ Drugs known to induce QT interval prolongation

Meglumine antimonate should be used with caution in patients receiving medicines known to induce prolongation of the QT interval (for example certain class IA and III antiarrhythmics, certain tricyclic antidepressants, certain macrolides, certain antipsychotics, other antiparasitics) (see section 4.4.).

4.6. Fertility, pregnancy and lactation

Pregnancy

Preclinical data available in the literature suggest that meglumine antimoniate is associated with a lethal effect on the embryo and/or a delay in development in juvenile animals, with doses approximately 100 times higher than the therapeutic dose in humans of 20 mg/kg, (see section 5.3.).

There are no clinical data available to date suggesting a potential teratogenic effect or fetotoxicity of meglumine antimonate in man.

However, administration of GLUCANTIME should not be used during pregnancy, except in life-threatening conditions where the potential benefit to the mother outweighs on potential harm to the fetus.

Feeding with milk

Whether or not meglumine antimoniate passes into breast milk is not known at this time. Consequently, breast-feeding is not recommended during treatment with GLUCANTIME.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Side effects

The following undesirable effects have been observed and reported during treatment with the frequencies following: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).

System classes organs	Side effects	Frequency
Metabolic and nutrition disorders	Anorexia	Frequent
Nervous disorders	Muscular weakness**	Rare
	Headaches	Very Common
Heart conditions	Arrhythmia (see section 4.4)	Rare
Respiratory, thoracic and mediastinal disease	Cough**	Frequency not known
	Dyspnea	Rare

Gastrointestinal disorders	Nausea**	Frequent
	Vomiting**	Frequent
	Abdominal pain	Frequent
	Pancreatitis	Frequency not known
Skin conditions and subcutaneous tissue	Hyperhidrosis **	Frequency not known
	Rash	Rare
Musculoskeletal conditions	Arthralgia	Very Common
	Myalgia	Very Common
Immune disorders	Hypersensitivity reactions (including anaphylactic shock and reactions type IV hypersensitivity) (see section 4.4)	Frequency not known
Kidney and urinary tract disease	Acute renal failure (see section 4.4)	Frequency not known
General disorders and site anomalies administration	Fever**	Frequency not known
	Chills**	Rare
	Malaise	Rare
	Face edema	Frequency not known
Tests	Modification of liver tests	Rare
	Increased liver enzymes	Frequency not known
	Modification of renal test	Frequency not known
	Electrocardiogram alterations, dose dependent and generally reversible	Rare
	T wave inversion*	Rare
	QT Prolongation*	Frequent

* most commonly, T wave inversion and QT interval prolongation precede the appearance of a serious arrhythmia.
** these effects may occur at the start of treatment.

Reporting of suspected adverse reactions

The reporting of suspected adverse reactions after authorization of the medicinal product is important. It allows continuous monitoring of the benefit/risk ratio of the medicinal product. Professionals report any suspected adverse reactions to the competent national authorities.

4.9. Overdose

If the total dose is too high, liver damage (severe jaundice), kidney damage (renal failure acute), cardiac (bradycardia, prolongation of the QT interval, flattening or inversion of the wave T), hematopoietic (anemia, agranulocytosis), neurological (polyneuritis).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antileishmanials, ATC code: P01CB01.

Meglumine antimonate has leishmanicidal activity.

5.2. Pharmacokinetic properties

More than 80% is excreted unchanged in the urine within 6 hours administration.

5.3. Preclinical safety data

Preclinical data available in the literature suggest that meglumine antimoniate, is associated with embryolethal effect and/or developmental delay in juvenile animals at high doses as described below:

- Administration of meglumine antimoniate to female rats for the duration of their gestation was embryotoxic and caused developmental delay in rats newborns when the doses administered were greater than or equal to 150 mg of antimonium pentavalent/kg body weight/day.
- It has also been described that a dose of 300 mg/kg/day of meglumine antimonate administered to pregnant rats reduced birth weight and the number of viable neonates among litters. Among the offspring, meglumine antimoniate did not have a significant impact on the development of reproductive functions.
- Administration for 10 days of meglumine antimonate (300 mg/kg/day) to female rats during the period of organogenesis resulted in a lethal effect on the embryos and resulted in increased incidence of variations in the development of the atlas bone.

6. PHARMACEUTICAL DATA

6.1. List of excipients

Potassium disulphite, anhydrous sodium sulphite, water for injections.

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medications.

6.3. Shelf-life

Before opening: 3 years.
After opening: the product must be used immediately.

6.4. Special precautions for storage

Before opening: no special precautions for storage.

6.5. Nature and contents of the outer packaging

5 ml in type I colorless glass bottle ampoule. Box of 5.

6.6. Special precautions for disposal and other handling

GLUCANTIME is a clear solution.
In rare cases, small particles may be present in the solution.

If particles are present, shake the ampoules well before use.
If the particles persist, do not use the ampoule.

7. MARKETING AUTHORIZATION HOLDER

SANOFI-AVENTIS FRANCE
82 AVENUE RASPAIL
94255 GENTILLY CEDEX
8. MARKETING AUTHORIZATION NUMBER(S)

- 6390041: 5 ml in ampoule (colorless glass). Box of 5.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Marketing Authorization date: November 1, 1994.
MA renewal date: November 2, 2019.

10. TEXT UPDATE DATE

September 2021 (Approved by ANSM on 03/12/2020)

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

13. PRESCRIPTION AND DELIVERY CONDITIONS

Medicinal product not subject to medical prescription.