

Package Leaflet: Information for the Healthcare Professional
Pentostam® Injection
 sodium stibogluconate
 equivalent to 100 mg pentavalent antimony in each ml.

DOSAGE AND ADMINISTRATION INFORMATION ONLY
 Please refer to the current Summary of Product Characteristics for Pentostam Injection, PL 00003/5105R for complete prescribing information.

Posology and method of administration

Route of administration

Filter immediately prior to administration
 Due to the presence of particulates (size range 20 to 300 microns) Pentostam solution should be drawn up through a filter immediately prior to administration. These particulates are insoluble complexes formed by an interaction between product preservative and the antioxidant in the rubber stopper. Filters of pore size 5 micron or less and membrane types polyvinylidene difluoride, polyethersulfone, polysulfone, nylon, surfactant-free cellulose acetate and mixed cellulose esters have been shown to be suitable. Where sterile filters are not available the risks and benefits of administering unfiltered Pentostam therapy should be assessed by the clinician on an individual basis.

Dosage recommendations

All dosage recommendations are based on the findings of the WHO Expert Committee on leishmaniasis which met in 2010. There are no special recommendations for different age groups.

- **Visceral leishmaniasis**
 20 mg pentavalent antimony (0.2 ml Pentostam) per kg body weight intramuscularly or intravenously daily for 30 days (or 28 days for L. infantum). Patients should be examined for evidence of relapse after 2 and 6 months and in Africa after 12 months.
- **Cutaneous leishmaniasis caused by Old World species:**
 For lesions requiring local therapy
 - 100 mg-500 mg intralesional pentavalent antimony (1-5 ml sodium stibogluconate injection) per session every 3-7 days for 1-5 sessions.
 For lesions requiring systemic therapy
 - 20 mg/kg pentavalent antimony (0.2 ml sodium stibogluconate injection) intramuscularly or intravenously for 10-20 days.
 Monotherapy with sodium stibogluconate is not recommended for the treatment of cutaneous leishmaniasis caused by *L. aethiops*. Please refer to WHO treatment recommendations for leishmaniasis.
- **Cutaneous leishmaniasis caused by New World species:**
 For lesions requiring local therapy
 - 100 mg-500 mg intralesional pentavalent antimony (1-5 ml sodium stibogluconate injection) per session every 3-7 days for 1-5 sessions.
 For lesions requiring systemic therapy
 - 20 mg/kg pentavalent antimony (0.2 ml sodium stibogluconate injection) intramuscularly or intravenously for 20 days.
 Monotherapy with sodium stibogluconate is not recommended for relapse treatment. Please refer to WHO treatment recommendations for leishmaniasis.

Muco-cutaneous leishmaniasis

- Patients should be treated with 20 mg pentavalent antimony (0.2 ml Pentostam) per kg body weight daily intramuscularly or intravenously for 30 days. Little data are available for the therapy of MCL due to *L. aethiops*.
- Diffuse cutaneous leishmaniasis in the New World and leishmaniasis recidivans
 For diffuse cutaneous leishmaniasis in the New World and leishmaniasis recidivans combination therapy should be considered. Please refer to WHO treatment recommendations for leishmaniasis.
- Use in the elderly
 There is little information on the effects of Pentostam on elderly individuals. If treatment of cutaneous leishmaniasis is necessary then local infiltration is preferred. The normal precautions should be strictly adhered to when treating older patients for visceral leishmaniasis.

Contra-indications

- Pentostam should not be given to any patient:
- with significantly impaired renal function
 - who has experienced a serious adverse reaction to a previous dose.

Package Leaflet: Information for the User

Pentostam® Injection
 sodium stibogluconate

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Pentostam is and what it is used for
2. What you need to know before you have Pentostam
3. How Pentostam is given
4. Possible side effects
5. How to store Pentostam
6. Contents of the pack and other information

1 What Pentostam is and what it is used for

The name of your injection is Pentostam. It contains a medicine called sodium stibogluconate. Pentostam kills parasites, which cause a disease called leishmaniasis. These parasites are spread by bites from sand flies.

There are 3 main ways in which leishmaniasis can show itself:

- by sores on your skin (cutaneous)
- by sores in your nose, mouth and throat (mucocutaneous)
- by affecting your internal organs like the liver (visceral).

2 What you need to know before you have Pentostam

You should not have Pentostam if you:

- are allergic to sodium stibogluconate or any of the other ingredients of this medicine (listed in section 6)
- have serious kidney disease.

Do not have Pentostam if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before having Pentostam.

Warnings and precautions

Take special care with Pentostam if you have:

- liver problems
- heart problems, an unusual heart rhythm or beat
- been treated for leishmaniasis disease before
- sores in your nose, mouth or throat.

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before you have Pentostam.

Your doctor or nurse will normally check your heart rhythm and beat before and during your Pentostam treatment. The doctor or nurse will use an electrocardiogram (ECG) to check how well your heart works.

If you are having blood tests to check for changes to the blood, pancreas or liver function, let your doctor, pharmacist or nurse know that you are on Pentostam. This is because Pentostam can affect the results of these types of tests.

Other medicines and Pentostam

Please tell your doctor, pharmacist or nurse if you are taking, have recently taken or might use any other medicines, including medicines obtained without a prescription.

Your doctor, pharmacist or nurse will take special care if you have medicines for an unusual heart rhythm or beat (anti-arrhythmics), like amiodarone and sotalol. This is because Pentostam can change your heart rhythm and increase the effects of these medicines.

If your doctor recommends that you take amphotericin B they may wish to delay starting this treatment and check your electrolyte levels before use. This is because amphotericin B given shortly after Pentostam can cause abnormal heartbeats.

Pregnancy and breast-feeding

Talk to your doctor, pharmacist or nurse before having this medicine if you are pregnant, planning to get pregnant or breast-feeding. If you are, you should not have Pentostam.

3 How Pentostam is given

You will never give yourself this medicine. A qualified person, like a doctor or a nurse, will give you this medicine.

Pentostam can be given as an injection into a vein (intravenous) or a muscle (intramuscular). Your doctor will decide which one is best for you.

The dose and how long you will have this treatment

- The dose that you will have is different for each type of leishmaniasis. Your doctor will decide the dose and how long your treatment will last.
- Treatment is usually one injection daily for 30 days.

It is recommended that you return to your doctor after 2 months and again after 6 months so that your condition can be assessed.

If more Pentostam is given to you than recommended

If you think you have been given too much Pentostam, tell your doctor immediately.

- You may get the following symptoms:
- feeling sick (nausea), being sick (vomiting), severe diarrhoea
 - your skin or the whites of your eyes may turn yellow (jaundice)

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Colour Standard Reference Number: Not applicable		
Technical Reference No(s): JMF293 <small>(do NOT include the technical reference doc(s) version no(s))</small>		
Printing Process: Not available		
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Special warnings and precautions for use

Intravenous injection should be filtered immediately before use (see Posology and method of administration). Administer very slowly over 5 minutes to reduce the risk of local thrombosis. In the unlikely event of coughing, vomiting or substernal pain occurring, administration should be discontinued immediately. In such cases, extreme care should be taken if Pentostam is re-administered by this route.

Successful treatment of mucocutaneous leishmaniasis may induce severe inflammation around the lesion. In cases of pharyngeal or tracheal involvement, this may be life-threatening. Under such circumstances, corticosteroids may be used.

Very rarely, anaphylactic shock may develop during treatment for which adrenaline injection and appropriate supportive measures should be given immediately.

Prolongation of the QTc interval has been observed in some patients taking sodium stibogluconate and appears to be dose-related. There have also been reports of fatal cardiac arrhythmias in patients receiving higher dose antimonial therapy for visceral leishmaniasis. Therefore, ECG monitoring is recommended before and during therapy with sodium stibogluconate. Where ECG monitoring is not available, the risks and benefits of sodium stibogluconate therapy should be assessed on an individual basis.

If clinically significant prolongation of QTc interval occurs, sodium stibogluconate should be discontinued. Electrocardiographic changes, notably alterations in T-wave amplitude may be expected in the majority of patients given sodium stibogluconate, these appear to be reversible on cessation of therapy and are not of serious significance.

Sodium stibogluconate should be used with caution in patients with cardiovascular disease, a history of ventricular arrhythmias or other risk factors known to predispose towards QT prolongation: for example, those with congenital QTc prolongation or taking concomitant drugs known to significantly prolong the QT interval (e.g. class III anti-arrhythmics such as sotalol and amiodarone).

As there appears to be a dose relationship in the development of ECG abnormalities, prior exposure to antimonial therapy should be considered when assessing a patient's suitability for initiating or continuing therapy with sodium stibogluconate.

Patients who have recently received other antimonial drugs should be monitored closely for signs of antimony intoxication such as bradycardia and cardiac arrhythmias during administration of sodium stibogluconate.

There have been some reports of cardiac arrhythmias and sudden death when amphotericin B deoxycholate is administered soon after sodium stibogluconate for retreatment of visceral leishmaniasis. Electrolyte imbalances should be corrected prior to administration of amphotericin B deoxycholate, and patients appropriately monitored.

Intercurrent infections, such as pneumonia, should be sought and treated concomitantly.

High concentrations of antimony are found in the livers of animals after repeated dosage with pentavalent antimony. Pentostam should therefore be used with caution in patients with hepatic disease. However, some abnormalities of liver function may be expected in cases of visceral leishmaniasis. In such patients the benefit of pentavalent antimony treatment outweighs the risk. Pentostam may induce mild elevation of hepatic enzymes in serum which later return to normal.

Fertility, pregnancy and lactation

Although no effects on the foetus have been reported, Pentostam should be withheld during pregnancy unless the potential benefits to the patient outweigh the possible risk to the foetus. Children should not be breast-fed by mothers receiving Pentostam.

Storage, use and handling

Special precautions for storage

- Store below 25°C.
- Do not freeze.
- Protect from light.
- Not be used more than 1 month after removing the first dose.

Instructions for disposal and other handling

Pentostam solution should be filtered immediately prior to use (see Posology and method of administration).

Leaflet date: February 2014

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- your urine may become darker or your stools may become paler.

Your doctor may give you another medicine to help your recovery.

If you have any further questions about how this product is given, ask your doctor, pharmacist or nurse.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very rarely, a sudden and severe allergic reaction to Pentostam can occur. If you get any of the following symptoms tell your doctor, pharmacist or nurse immediately:

- Rash, itching or hives on the skin.
- Swelling of the face, lips, tongue or other parts of the body.
- Shortness of breath, wheezing or trouble breathing.

Some patients can get pneumonia. If you get any of the following tell your doctor, pharmacist or nurse as soon as possible:

- Fever and chills.
- Cough with phlegm or blood.

The pneumonia may be caused by Pentostam or the leishmaniasis disease itself.

Other side effects include:

- Common (may affect up to 1 in 10 patients)
 - Feeling sick (nausea), being sick (vomiting), diarrhoea or stomach pain.
 - General feeling of tiredness, drowsiness or lack of energy.
 - Muscle pain.
 - Joint pains.
 - Headache.
 - Weight loss or lack of appetite.

Rare (may affect up to 1 in 1,000 patients)

- Your skin or the whites of your eyes may turn yellow.
- High temperature, sweating and flushing of your face.
- Bleeding from your nose or gum.
- Dizziness or a spinning feeling, also called vertigo.
- Rash or worsening of your sores.
- Chest pain.

The following side effects may occur but the frequency with which these may occur is not known:

- Pain where you had the injection. If you have the injections into your vein (intravenous) you may feel brief pain along the vein or get a blood clot in the vein due to the injection (thrombosis).
- Coughing straight after you have the injection.
- Severe stomach pain, which may spread to the back (associated with the inflammation of the pancreas), often with feeling sick (nausea) and being sick (vomiting).

- Short term changes in blood chemistry. Please also see section 2.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Pentostam

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is printed on the carton and the bottle label. This expiry date (Exp.) refers to the last day of that month.
- Store below 25°C and do not freeze.
- Pentostam should be stored in the carton to protect from light.

6 Contents of the pack and other information

What Pentostam contains

- The active substance is sodium stibogluconate.
- The other ingredients are chlorocresol, glucono-delta-lactone and Water for Injections.

What Pentostam looks like and contents of the pack

Each carton contains an amber glass bottle containing 100 ml of solution.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
The Wellcome Foundation Ltd,
Stockley Park West, Uxbridge,
Middlesex UB11 1BT

Manufacturer: Glaxo Wellcome Operations,
Barnard Castle, Durham DL12 8DT

Other formats

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product name Pentostam Injection
Reference number 00003/5105R

This is a service provided by the Royal National Institute of Blind People.

Leaflet date: February 2014

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