PACKAGE LEAFLET: INFORMATION FOR THE USER

Pentacarinat® 300mg powder for solution for injection/infusion

Pentamidine isetionate

sanofi

Is this leaflet hard to see or read? Phone 0800 035 2525 for help

Read all of this leaflet carefully before taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or your pharmacist.

In this leaflet:

1. What Pentacarinat is and what it is used for

The name of your medicine is Pentacarinat 300mg powder for solution for injection/infusion (called Pentacarinat powder in this leaflet). Pentacarinat powder contains a medicine called pentamidine isetionate.
Pentacarinat powder can be used to:

- Treat or help prevent a lung infection called 'Pneumocystis carinii Pneumonia (PCP). It often happens in people with the HIV virus.
- Treat diseases of the skin or organs caused by parasites (Leishmania and Trypanosoma gambiense).

2. Before you have Pentacarinat Powder

Do not have this medicine if:
X You are allergic (hypersensitive) to pentamidine isetionate or any of the ingredients of this medicine (see Section 6: Further information).

Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of the lips, face, throat and tongue.
Do not have this medicine if the above applies to you.

Take special care with Pentacarinat powder
Check with your doctor or your pharmacist before having this medicine if:

- You have liver or kidney problems.
- You have high or low blood pressure.
- You have a slow heartbeat (bradycardia), an uneven heartbeat or any other heart problems.
- You have a high or low blood sugar level.
- You have a low white blood cell count - signs include an unexplained infection or fever.
- You have anaemia (look pale or feel tired).
- You have unusual bruising or your blood takes a long time to clot.
- You have asthma, other breathing problems, or had a collapsed lung (pneumothorax) in the past.
- You smoke.
- You have unusual salt levels in your blood, especially if you have low levels of potassium ('hypokalaemia') or magnesium ('hypomagnesaemia'). Blood tests will have shown this.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before having Pentacarinat 300mg.

Taking other medicines
If you have to go to a doctor, dentist or hospital for any reason, tell them that you are taking Pentacarinat powder. Also tell your doctor or pharmacist if you are taking or have recently taken any other medicine. This includes medicines you buy without a prescription, including herbal medicines. This is because Pentacarinat powder and some medicines can affect the way each other work.

In particular, tell your doctor if you are taking any of the following:

- Medicines for mood or thought problems called 'phenothiazines' (such as chlorpromazine and pericyazine).
- Medicines for depression called 'tricyclic antidepressants' (such as amitriptyline).
- Anti-histamines called terfenadine and astemizole - used for allergies.
- Antibiotics such as erythromycin or quinolones (includes ciprofloxacin).
- Halofantrine - used for malaria.
- Foscarnet - used for viral infections.

These medicines may cause an uneven heartbeat (seen on your ECG) called 'QT prolongation'. Pentacarinat 300mg can increase the chance of this happening.

Tests
Before you are given Pentacarinat powder, your doctor will check your blood pressure, heart and blood.

Pregnancy and breast-feeding
Talk to your doctor before taking this medicine if:

- You are pregnant, plan to get pregnant, or think you may be pregnant. Miscarriage has been reported during the first three months of pregnancy.
- You are breast-feeding or planning to breast-feed.

Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding.

Driving and using machines
You may feel dizzy, tired, light headedness or faint or have muscle spasms and twitches whilst taking Pentacarinat powder. If this happens, do not drive or use any tools or machines.

3. How Pentacarinat powder is given

How Pentacarinat powder is given

- Pentacarinat powder will usually be given to you by a doctor or nurse at a clinic or in a hospital.
- It will be given either by injection or by inhalation using a nebuliser.
- If you feel the effect of your medicine is too weak or too strong, do not change the dose yourself, but ask your doctor.

1) Having this medicine as an injection

- A doctor or nurse will mix Pentacarinat powder with water for injections. If given into a vein, they will dilute it further in another liquid.
- You must lie down when you are given a Pentacarinat powder injection.
- Your doctor will decide how much to give you. The dose depends on your weight.

Turn Over

The following information is intended for healthcare professionals only:

Practical information on preparation and administration of Pentacarinat 300mg powder for solution for injection/infusion (*see also Section 3*).

There is limited information available on the effects of this product on people who handle it.
It is therefore recommended that the following precautions are taken when the solution is administered by nebuliser:-

1. Dissolve the powder in water as described below: Use a vertical laminar flow cabinet if available.
2. When patients are using nebulisers always make sure that they are in a well ventilated room. This room should not be used for any other purpose whilst the procedure is in progress.
3. Only staff wearing adequate protective clothing (see 7 below) should be in the room when nebulisers are being used.
4. A nebuliser which is fitted with a filter to minimise loss of the drug to the atmosphere e.g. "Respirgard II", modified "Acorn System 22" or an equivalent device should be used.
5. Use a suitable exhaust tube which vents directly through a window to the external atmosphere if possible. Care should be taken to ensure that passers-by will not be exposed to the exhaust.
6. Make sure that the patient is wearing a well-fitting mask and the air flow to the nebuliser is turned off before the mask is removed.
7. Masks of nominal protection factor 10, goggles and gloves should be worn by all healthcare personnel administering nebulised pentamidine preparations. Once the system has been set up, staff should not stay in the room where pentamidine is being nebulised unless there is a particular clinical need.
8. Children, pregnant women and staff with a history of asthma should avoid coming into contact with nebulised pentamidine. Women of child-bearing potential should also avoid exposure to the drug unless they are taking adequate contraceptive precautions.
9. Staff should ensure that they are adequately vaccinated against tuberculosis.

If PENTACARINAT is used in the home, other members of the household should not be in the same room as the patient during nebulisation and the room should be adequately ventilated at the end of each administration. If other occupants remain in the room they may experience effects such as eye irritation, facial numbness or difficulty in breathing. They are also at risk of contracting other lung infections.

PRESENTATION

A sterile white powder supplied in single dose vials containing 300mg pentamidine isetionate.

DOSAGE AND ADMINISTRATION

Dosage by the inhalation route
For the prevention of recurring cases of PCP the dosage is 300mg pentamidine isetionate administered as a single inhalation every 4 weeks.

Dosage by the intravenous route
The following dosage regimens are recommended for adults, children and infants:

Treatment of PCP: Pentamidine isetionate 4 mg/kg bodyweight daily for at least 14 days, preferably by slow intravenous infusion.

Elderly: No specific dosage recommendations.

Dosage in renal failure (creatinine clearance <10ml/min): A modified dosage regimen is recommended - see data sheet for details.

Dosage in hepatic impairment: No information available.

Administration by inhalation
Solutions should be prepared as described below and then used immediately.

Prevention of recurring PCP: Dissolve the contents of one vial (300mg pentamidine isetionate) in 4-6ml of Water for Injections.
The freshly prepared solution should be administered by inhalation using a suitable nebuliser such as a "Respirgard II", modified "Acorn System 22" or an equivalent device. This should be fitted with either a portable compressor or piped oxygen at a flow rate of 6-10 litres/minute.
The optimal particle size for alveolar deposition is between 1 and 2 microns.
A suitable, well-fitted one-way system should be employed such that the nebuliser stores the aerosolised drug during exhalations and disperses exhaled pentamidine into a reservoir. A filter should be fitted to the exhaust line to reduce atmospheric pollution.
Also a suitable exhaust tube should be used which vents directly through a window to the external atmosphere if possible. Care should be taken to ensure that passers-by will not be exposed to the exhaust.

How much Pentacarinat is given
The usual dose of pentacarinat powder for adults, children and infants for the following illnesses is:

Lung Infection by PCP
- 4 mg for each kg of body weight, once each day for 14 days.
- If you have kidney problems, your doctor may give you this medicine less often.
- The dose is given by a slow infusion (drip) into a vein.

Infection of the skin by Leishmania
- 4 mg for each kg of your body weight, every other day for 3 doses.
- The dose is given by injection into your muscles or by a slow infusion (drip) into a vein.

Infection by Trypanosoma gambiense
Dose for adults, children and infants is:
- 4 mg for each kg of your body weight, once each day or for 7 days.
- The dose is given by injection into your muscles or by a slow infusion (drip) into a vein.

2) Having this medicine by inhalation
This medicine has been prescribed only for you.
- **It is dangerous for other people to be exposed to this medicine**
- This means that other people should not be in the same room when you are using the nebuliser.
  - The medicine is put in the nebuliser.
  - Air or oxygen is piped into the nebuliser.
  - This turns the medicine into a fine mist or spray.
  - This spray is then inhaled into your lungs.

To stop further attacks of Pneumocystis carinii Pneumonia (PCP)
Dose for adults only is:
- Inhalation of the spray from 1 bottle every 4 weeks.

Or
- Inhalation of half a bottle every 2 weeks.

If you have more Pentacarinat powder than you should
If you have too much of this medicine, talk to doctor or go to a hospital straight away. Too much Pentacarinat powder can cause problems with your heart.

If you forget to visit your doctor to have your medicine
Contact your doctor straight away to arrange another appointment as soon as possible.

If you stop taking Pentacarinat powder
Do not stop having your medicine without talking to your doctor. You should not stop having Pentacarinat Powder just because you feel better. This is because the infection may come back again or get worse. If you have any further questions on the use of this product, ask your doctor or pharmacist.

4 Possible side effects

Like all medicines, Pentacarinat powder can cause side effects, although not everybody gets them. Your doctor will closely check for any possible side effects.

Stop having and speak to your doctor or nurse or go to a hospital straight away if you notice any of the following side effects - you may need urgent medical treatment:
- If you have an allergic reaction. The signs may include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- If you have severe skin reactions. Signs include blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals. Also flu-like symptoms and fever. This may be something called 'Stevens-Johnson syndrome'.
- Low blood pressure (hypotension). Signs include feeling dizzy, light-headed or fainting.
- Low blood sugar level (hypoglycaemia). Signs include feeling nervous, shaky or sweaty.
- Low numbers of white cells in your blood (leucopenia) - signs include an unexplained infection or fever.
- You bruise or bleed more easily than usual. This could be because of a blood disorder (thrombocytopenia).
- Kidney failure - changes in the way your kidneys are working. These would show up in the results of some blood or urine tests. You may also notice signs such as swollen ankles, passing less water (urine) than usual, low back pain.
- If you have low levels of calcium in your blood ('hypocalcaemia').
- Inflammation of the pancreas (pancreatitis). Signs include severe stomach pain - which may reach through to the back.
- Uneven or fast heart beat.

Tell your doctor straight away if you have any of the following side effects:
- Yellowing of the skin and eyes.
- Flushing or fainting.
- Feeling dizzy, tired or faint. This may be due to low blood pressure when standing up.
- Chest pain, cough, wheezing, shortness of breath or difficulty breathing.
- Feeling sick (nausea), being sick (vomiting) or stomach pain.
- Blood in your urine.
- Muscle spasm, muscle twitch or pins and needles.
- Pain, or a lump or abscess at the site where you were given the injection.
- Rash.
- Increased thirst or needing to go to the toilet more often.
- Change in the way things taste or a loss of appetite.
- Fever.
- Unexplained muscle pain, tenderness or weakness.
- Tingling or numbness in hands and feet.
- Reduced sensation or numbness around the mouth.
- Slow heartbeat.

Tell your doctor straight away if you notice any side effects not listed in this leaflet.

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

5 How to store Pentacarinat powder

Keep this medicine in a safe place where children cannot see or reach it. Store below 30°C, do not refrigerate. Once the powder has been mixed with liquid, store it in a fridge at 2-8°C. Use within 24 hours. Concentrated solution for inhalation or intramuscular routes: Use immediately. Do not use the medication after the expiry date which is stated on the carton and on the vial label after EXP. The expiry date refers to the last day of that month. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6 Further information

What Pentacarinat 300mg powder for solution for injection/infusion contains
- Each small glass bottle (vial) contains 300mg the active substance, Pentamidine isetionate (equivalent to 172.4 mg pentamidine base).

What Pentacarinat powder looks like and content of the pack
Pentacarinat powder is a white or almost white plug of lyophilised powder contained in a glass vial. Pentacarinat powder is supplied in cartons containing 5 glass vials. Each vial contains a single dose of Pentacarinat powder for solution for injection/infusion.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder
Sanofi, 410 Thames Valley Park Drive, Reading,
Berkshire, RG6 1PT, UK
Tel: 0800 035 2525
Email: uk-medicalinformation@sanofi.com
Manufacturer
Sanofi S.r.l., Via Valcanello 4, 03012 - Anagni (FR), ITALY

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This leaflet was last revised in 10/2020

Administration by the intravenous route
In order to reduce the incidence of sudden, severe hypotension, PENTACARINAT should be administered parenterally only by slow intravenous infusion with the patient lying down. Bolus intravenous injections should be avoided if possible and should never be given rapidly. PENTACARINAT must be reconstituted only with Water for Injections. The reconstituted solution may be further diluted for intravenous infusion using either Glucose Intravenous Infusion 5% w/v or 0·9% (Normal) Sodium Chloride Injection. It must not be mixed or diluted with any other injection solutions.
For slow intravenous infusion the contents of one vial (300mg pentamidine isetionate) should be dissolved in a known volume (3-5ml) of Water for Injections. The dose calculated for an individual patient may then be diluted further in 50-250ml of Glucose Intravenous Infusion 5% w/v or 0·9% (Normal) Sodium Chloride Injection. The resulting solution containing pentamidine isetionate should be infused over a period of at least 60 minutes with the patient remaining supine under close medical supervision.

PRECAUTIONS

PENTACARINAT should be used with particular caution in patients with hepatic and/or renal dysfunction, hypertension or hypotension, hyperglycaemia or hypoglycaemia, leucopenia, thrombocytopenia or anaemia.
Fatalities due to severe hypotension, hypoglycaemia, acute pancreatitis and cardiac arrhythmias have been reported in patients treated with pentamidine isetionate, by both the intramuscular and intravenous routes. Baseline blood pressure should be established and patients should receive the drug lying down. Blood pressure should be closely monitored during administration and at regular intervals until treatment is concluded.
Therefore patients receiving PENTACARINAT by inhalation should be closely monitored for the development of severe adverse reactions.
Bronchospasm has been reported to occur following the use of the nebulizer. This has been particularly noted in patients who have a history of smoking or asthma. This can be controlled by prior use of bronchodilators.
Pentamidine isetionate may prolong the QT interval. Cardiac arrhythmias indicative of QT prolongation, such as Torsades de Pointes, have been reported in isolated cases with administration of pentamidine isetionate. Therefore, pentamidine isetionate should be used with care in patients with conditions known to increase the proarrhythmic risk, including patients with long QT syndrome, cardiac disease (e.g. coronary heart disease heart failure), a history of ventricular arrhythmias, uncorrected hypokalaemia and or hypomagnesaemia, bradycardia (<50 bpm), or during concomitant administration of pentamidine isetionate with QT prolonging agents.
Particular caution is necessary if the QTc exceeds 500 msec whilst receiving pentamidine isetionate therapy, continuous cardiac monitoring should be considered in this case.
Should the QTc- interval exceed 550 msec then an alternative regimen should be considered.

Laboratory monitoring: The following tests should be carried out before, during and after treatment by the i.v. route:
(I) Blood urea nitrogen and serum creatinine daily during therapy.
(II) Complete blood and platelet counts daily during therapy.
(III) Fasting blood glucose measurements daily during therapy, and at regular intervals after completion of therapy. Hyperglycaemia and diabetes mellitus, with or without preceding hypoglycaemia have occurred up to several months after cessation of therapy.
(IV) Liver function tests (LFTs) including serum bilirubin, alkaline phosphatase, aspartate aminotransferase (AST/SGOT) and alanine aminotransferase (ALT/SGPT). If baseline measurements are normal and remain so during therapy, test weekly thereafter.
When there is baseline elevation in LFTs and/or LFTs increase during therapy, continue monitoring weekly unless the patient is on other hepatotoxic agents, when monitoring every 3-5 days is appropriate.
(V) Serum calcium, test weekly.
(VI) Urine analysis and serum electrolytes daily during therapy.
(VII) Electrocardiograms at regular intervals.

PHARMACEUTICAL PRECAUTIONS

This product should be reconstituted in a fume cupboard.
Store the dry product below 30°C.
Store dilute reconstituted solutions between 2-8°C and discard all unused portions within 24 hours of preparation.
Concentrated solutions for administration by the inhalation route should be used immediately.
After reconstitution with Water for Injections, PENTACARINAT should not be mixed with any injection solution other than Glucose Intravenous Infusion 5% w/v and 0·9% (Normal) Sodium Chloride Injection.