

**DEFERAL® Vials 500 mg
(desferrioxamine mesilate)**

Patient Information Leaflet

What you need to know about Desferal

Your doctor has decided that you need this medicine to help treat your condition.

Please read this leaflet carefully before you start to take your medicine. It contains important information. Keep the leaflet in a safe place because you may want to read it again.

If you have any other questions, or if there is something you don't understand, please ask your doctor or pharmacist.

This medicine has been prescribed for you. Never give it to someone else. It may not be the right medicine for them even if their symptoms seem to be the same as 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 pharmacist.

This medicine will be called Desferal throughout this leaflet

In this leaflet:

1. What Desferal is and what it's used for
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1. What Desferal is and what it's used for

Desferal is an injection used to remove excess iron or aluminium from your blood.

Desferrioxamine mesilate, the active ingredient in Desferal, is a substance called a 'chelating' agent. This means that it binds to the iron and aluminium ions in the blood to form a complex which is then excreted from the body.

You may have too much iron or aluminium in your blood as a result of iron poisoning or as a side effect of blood transfusion or kidney dialysis. Certain illnesses can also have the same effect.

Desferal can also be used to test whether you have certain anaemias or diseases affecting the amount of iron in your blood.

2. What you need to know before you take Desferal

Some people MUST NOT take Desferal. Talk to your doctor if:

- you think you may be allergic to Desferal or desferrioxamine.

You should also ask yourself these questions before taking Desferal:

- Are you pregnant or planning to become pregnant? If you become pregnant while you are being treated with Desferal you must tell your doctor straight away.
- Are you breast feeding?
- Do you have any kidney problems or are you on dialysis?
- Do you have a heart condition?
- Do you have the blood condition thalassaemia?
- Is Desferal going to be given to a child under the age of 3 years? If it is, the doctor may want to monitor the child's growth regularly to make sure it is not being affected by the Desferal.

- Has your doctor told you that you have hyperparathyroidism (a condition resulting in excess calcium in the blood and problems with the bones)?
- Has your doctor told you that aluminium has affected your nerves? If so you may be given a dose of clonazepam before you are given Desferal.

If the answer to any of these questions is YES, tell your doctor or pharmacist because Desferal might not be the right medicine for you.

Are you taking other medicines?

Some medicines can interfere with your treatment. Tell your doctor if you are taking any of the following:

- prochlorperazine, a medicine used to control vertigo or nausea and vomiting, anxiety or schizophrenia
- erythropoietin (used to treat anaemia, particularly in people who are on dialysis)
- Vitamin C.

Always tell your doctor about all the medicines you are taking. *This means medicines you have bought yourself as well as medicines on prescription from your doctor.*

Will there be any problems with driving or using machinery?

Desferal can make you feel dizzy or drowsy. It can also affect your vision or hearing. You must not drive, operate machinery or do anything else which requires concentration until you know how your medicine affects you.

Other special warnings

- **Medical check-ups while you are using Desferal**

If you use Desferal for a long time or you have kidney problems and are on dialysis, your doctor may want to give you regular eye tests and hearing tests. This is because Desferal can affect your vision and your hearing. These tests are usually done every 3 months.

- **Children**

In children under the age of 3 years high doses of Desferal may affect growth. Regular checks on body weight and height are, therefore, recommended in children using Desferal. These checks are usually done every 3 months.

- **X-rays or scans**

The results may be affected by treatment with Desferal. Make sure that the doctor or nurse knows that you are being treated with Desferal if an X-ray or scan is suggested.

3. How to take Desferal

The doctor will have decided what dose of Desferal you need and when you should take it. The dose will be on the pharmacist's label. Check the label carefully. If you are not sure, ask your doctor or pharmacist.

A doctor or nurse may prepare your injection for you, or you may be taught how to do this yourself. The Desferal powder should be dissolved in the 'water for injection' that your pharmacist has given you.

Treatment with the solution should start within 3 hours of the vial being reconstituted. If the solution has been prepared under sterile conditions (for instance in a hospital), it may be stored at room temperature (25°C or below) for up to 24 hours before being used. Any unused Desferal injection should be thrown away.

Ways in which Desferal can be given

Desferal can be given in different ways, for example:

- By injection into a muscle. This is called being given intramuscularly.
- By injection into a vein. This is called being given intravenously. It should be given slowly over a period of time rather than all in one go. This is called a slow infusion.
- By injection under your skin. This is called being given subcutaneously. It may be given over a period of time using a special pump. This is called an infusion.
- By injection into the peritoneum (the membrane that lines the abdominal cavity and forms the outer coating of the abdominal organs). This is called intraperitoneal administration.

The dose that you need will depend on why you have to take Desferal. Your doctor will work out exactly how much Desferal you need. This is especially important if you have low serum ferritin levels or acute iron intoxication.

The usual doses and ways of taking Desferal are as follows:

- **Iron Poisoning Treatment**

To treat iron poisoning Desferal is usually given intravenously (injected into the vein). The recommended dose is 15 mg/kg body weight every hour. This may be reduced after 4 to 6 hours. The maximum recommended dose is 80 mg/kg body weight every 24 hours.

Desferal may also be given intramuscularly (injected into the muscle). The recommended dose if Desferal is given like this is 2 g for an adult or 1 g for a child. This is usually given in a single injection.

- **Iron Overload Treatment**

Your doctor will work out exactly how much Desferal you will need. This will depend on how much extra iron you have in your body. Desferal is usually given subcutaneously (a slow injection under the skin). It can sometimes be given intramuscularly (injected into the muscle) though. The dose is usually between 20 and 60 mg/kg body weight. It is usually given between 5 and 7 times a week, depending on how much extra iron you have got in your body. In children under 3 years of age the average daily dose is not usually more than 40 mg/kg.

- **Aluminium Overload Treatment**

Desferal is usually given by slow intravenous injection.

The exact dose of Desferal that you need will depend on how much extra aluminium you have in your body. Your doctor will do tests to work this out.

If you are on dialysis, the usual dose of Desferal is 5 mg/kg body weight. This is normally given once a week. When you are given your Desferal will depend on how much extra aluminium you have in your body. It will either be given during the last 60 minutes of your dialysis or 5 hours before your dialysis starts.

If you are on peritoneal dialysis (CAPD or CCPD), the usual dose of Desferal is, again, 5 mg/kg body weight. This is normally given once a week. Usually the Desferal is mixed with the fluid in your dialysis bag. However, it can also be given by any of the other ways listed above.

- **Testing to see if you have got too much iron in your body**

Desferal is usually given intramuscularly (injected into a muscle). The usual dose is 500 mg. After you have had your Desferal, your doctor or nurse will probably want you to collect urine samples for about 6 hours. They will then do tests on your urine to see how much iron is in it.

- **Testing to see if you have got too much aluminium in your body if you are on dialysis**

Your doctor or nurse will probably take a blood sample from you before you are given Desferal. This will be taken just before your dialysis. Tests will be done on the blood to see how much aluminium is in it.

The usual dose of Desferal is 5 mg/kg body weight. It is usually given by slow intravenous infusion (slow injection into a vein) during the last hour of dialysis.

Another blood test will probably be taken before your next session of haemodialysis to check how much aluminium is in your blood.

- **Use in older patients**

Desferal is used in older patients at the same doses as for other adults.

What if you have had too much Desferal? (Overdose)

If you think you have either been given or have taken too much Desferal tell your doctor or nurse straight away. If you think you have either been given it or have taken it too often, also tell your doctor or nurse straight away.

What if you miss a dose of Desferal?

If you miss one of your appointments, please let your doctor or nurse know immediately.

4. Possible side effects

Most people who are prescribed Desferal will benefit from using it. As with all other medicines though, it can cause side effects in some people.

Do not be alarmed by this list of possible side effects. You may not experience any of them.

Your urine may turn a reddish-brown colour. This is because there is more iron in your urine. This is usually nothing to worry about, but if you are worried you should talk to your doctor or nurse.

Some side effects can be serious

Stop taking Desferal and tell your doctor straight away if you notice:

- Bronchospasm or tightness of chest with wheezing or coughing and difficulty in breathing.
- If you feel faint (you might have low blood pressure), have a rash, or experience itching, difficulty breathing or facial and throat swelling. These might be the result of an allergic reaction which is very rare (likely to affect fewer than 1 in 10,000 patients).
- If you notice severe decrease of urine output (sign of kidney problem) or experience convulsion (reported mainly in patients on dialysis). Those side effects were reported with unknown frequency.

Important information if you get an infection while you are taking Desferal

If you start to feel feverish with a sore throat or stomach pains, or general discomfort or develop shortness of breath while you are taking Desferal, you must seek medical advice immediately.

This is because people who have iron or aluminium overload are more vulnerable to certain types of infection. If you get an infection your doctor may want you to do some tests and give you some medicines to treat the infection. You may also have to stop using Desferal until any infections clear up.

It is **very common** (more than 10% of people) to develop pain, swelling, redness, a rash, itch or scabbing at the Desferal injection site. Less frequently blisters and a burning sensation might be experienced. Aching muscles or joints in the arms or legs is also very common.

The side effects listed below have also been reported.

Up to 1 in 10 people have experienced:

Headache, nausea (feeling sick) or fever

Itchy rash

Changes in their bones, slowing down of growth (especially in children under 3).

Up to 1 in 100 people have experienced:

Vomiting, stomach pains

Asthma

Problems with their ears such as tinnitus and deafness.

Up to 1 in 1,000 people have experienced:

Problems with their eyes such as blurred vision, impaired or loss of vision, not being able to see colours as well (colour blindness), not being able to see at night (night blindness), blind spots, changes in the retina, cataracts (cloudy lenses), cloudiness on the front of the eye (or cornea)

Low blood pressure (light headedness, dizziness, faintness). This can happen if Desferal is not given correctly.

Increased risk of getting certain infections.

Up to 1 in 10,000 people have experienced:

Skin rash covering most of the body

A serious condition which causes severe breathing problems called Acute Respiratory Distress Syndrome

Diarrhoea

Changes in the blood which can make you look pale or cause tiredness, headaches, nosebleeds, dizziness or being short of breath when exercising. You might also get more frequent viral infections (fever, chills, sore throat or mouth ulcers), or find that you bleed or bruise more easily than normal.

Stomach and gut infections.

Other effects such as dizziness, loss of feeling in their hands, feet, arms or legs, numbness or tingling (pins and needles).

In patients on dialysis: personality changes, headache, confusion, paralysis of part or all of the body, stiff neck, abnormal, speech and eye movements.

Frequency not known (cannot be estimated from the available data).

Muscle spasms

Abnormal liver or renal function test results

If any of the symptoms become troublesome, or if you notice anything else not mentioned here, please go and see your doctor or check with your pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 Desferal

The vials of Desferal powder before they are made up into the injection should not be stored above 25°C.

Each vial is for single use only.

Keep this medicine out of the sight and reach of children.

Do not use Desferal after the expiry date which is printed on the outside of the pack.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Content of the pack and other information

Desferal is available in clear glass vials containing 500 mg of desferrioxamine mesilate. This is a white or off-white powder.

Packs contain ten 500 mg vials.

Marketing Authorisation Holder and Manufacturer

Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ, United Kingdom.

This leaflet was revised in June 2020.

If you would like any more information, or would like the leaflet in a different format, please contact Medical Information at Novartis Pharmaceuticals UK Ltd, telephone number 01276 698370.

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Information for the healthcare professional

Special Precautions for Storage

Vial: Do not store above 25 °C.

Reconstituted solution: Single use only.

The product should be used immediately after reconstitution (commencement of treatment within 3 hours). When prepared under validated aseptic conditions the reconstituted solution may be stored for a maximum of 24 hours at room temperature (25°C or below) before administration. If not used immediately, in-use storage times and conditions prior to administration are the responsibility of the user. Unused solution should be discarded.

Therapeutic Indications

Treatment for chronic iron overload.

Treatment for acute iron poisoning.

For the diagnosis of iron storage disease and certain anaemias.

Aluminium overload - In patients on maintenance dialysis for end stage renal failure where preventative measures (e.g. reverse osmosis) have failed and with proven aluminium-related bone disease and/or anaemia, dialysis encephalopathy; and for diagnosis of aluminium overload.

Posology and Method of Administration

Desferal may be administered parenterally.

For parenteral administration:

The drug should preferably be employed in the form of a 10% solution, e.g. 500 mg: by dissolving the contents of one 500mg vial in 5ml of water for injection. When administered subcutaneously the needle should not be inserted too close to the dermis. The 10% Desferal solution can be diluted with routinely employed infusion solutions (saline, glucose, dextrose or dextrose-saline), although these should not be used as solvent for the dry substance. Dissolved Desferal can also be added to dialysis fluid and given intraperitoneally to patients on continuous ambulatory peritoneal dialysis (CAPD) or continuous cyclic peritoneal dialysis (CCPD).

Only clear pale yellow Desferal solutions should be used. Opaque, cloudy or discoloured solutions should be discarded. Heparin is pharmaceutically incompatible with Desferal solutions.

Treatment of acute iron poisoning

Dosage:

The continuous intravenous administration of Desferal is the preferred route and the recommended rate for infusion is 15 mg/kg per hour and should be reduced as soon as the situation permits, usually after 4 to 6 hours so that the total intravenous dose does not exceed a recommended 80 mg/kg in any 24 hour period.

However, if the option to infuse intravenously is not available and if the intramuscular route is used the normal dosage is 2 g for an adult and 1 g for a child, administered as a single intramuscular dose.

Chronic Iron Overload

Dose:

The lowest effective dose should be used. The average daily dose will probably lie between 20 and 60 mg/kg/day. Patients with serum ferritin levels of < 2000 ng/mL should require about 25 mg/kg/day, and those with levels between 2000 and 3000 ng/mL about 35 mg/kg/day. Higher doses should only be employed if the benefit for the patient outweighs the risk of unwanted effects.

Patients with higher serum ferritin may require up to 55 mg/kg/day. It is inadvisable to regularly exceed an average daily dose of 50 mg/kg/day except when very intensive chelation is needed in patients who have completed growth. If ferritin values fall below 1000 ng/mL, the risk of Desferal toxicity increases; it is important to monitor these patients particularly carefully and perhaps to consider lowering the total weekly dose.

To assess the chelation therapy, 24 hour urinary iron excretion should initially be monitored daily. Starting with a dose of 500 mg daily the dose should be raised until a plateau of iron excretion is reached. Once the appropriate dose has been established, urinary iron excretion rates can be assessed at intervals of a few weeks.

Mode of administration:

Slow subcutaneous infusion using a portable, light-weight, infusion pump over a period of 8-12 hours is effective and particularly convenient for ambulant patients. It may be possible to achieve a further increase in iron excretion by infusing the same daily dose over a 24 hour period. Desferal should normally be used with the pump 5-7 times a week.

Since the subcutaneous infusions are more effective, intramuscular injections are given only when subcutaneous infusions are not feasible.

Desferal can be administered by intravenous infusion during blood transfusion.

The Desferal solution should not be put directly into the blood bag but may be added to the blood line by means of a "Y" adaptor located near to the venous site of injection. The patient's pump should be used to administer Desferal as usual. Patients and nurses should be warned against accelerating the infusion, as an intravenous bolus of Desferal may lead to flushing, hypotension and acute collapse (see section 4.4 **Special warnings and special precautions for use**).

Continuous intravenous infusion is recommended for patients incapable of continuing subcutaneous infusions and in those who have cardiac problems secondary to iron overload. 24 hour urinary iron excretion should be measured regularly where intensive chelation (i.v.) is required, and the dose adjusted accordingly. Implanted intravenous systems can be used when intensive chelation is carried out.

Care should be taken when flushing the line to avoid the sudden infusion of residual Desferal which may be present in the dead space of the line, as this may lead to flushing; hypotension and acute collapse (see section 4.4 **Special warnings and special precautions for use**).

Diagnosis of iron storage disease and certain anaemias

Desferal is administered as 500 mg intramuscular injection. Urine is then collected for a period of 6 hours and its iron content determined.

Excretion of 1-1.5 mg (18-27 micro mol) of iron during this 6-hour period is suggestive of iron overload; values greater than 1.5 mg (27 micro mol) can be regarded as pathological.

Treatment for aluminium overload in patients with end stage renal failure

Adults and children:

Patients on maintenance haemodialysis or haemofiltration: 5 mg/kg once a week. Patients with post-desferrioxamine test serum aluminium levels up to 300 ng/mL: Desferal should be given as a slow i.v. infusion during the last 60 minutes of a dialysis session (to reduce loss of free drug in the dialysate). Patients with a post-desferrioxamine test serum aluminium value above 300 ng/ml: Desferal should be administered by slow i.v. infusion 5 hours prior to the dialysis session.

Four weeks after the completion of a three month course of Desferal treatment a Desferal infusion test should be performed, followed by a second test 1 month later. Serum aluminium increases of less than 50ng/mL above baseline measured in 2 successive infusion tests indicate that further Desferal treatment is not necessary.

Patients on CAPD or CCPD:

5 mg/kg once a week prior to the final exchange of the day. It is recommended that the intraperitoneal route be used in these patients. However, Desferal can also be given i.m., by slow infusion i.v. or s.c.

Diagnosis of aluminium overload in patients with end stage renal failure

A Desferal infusion test is recommended in patients with serum aluminium levels > 60ng/mL associated with serum ferritin levels >100 ng/mL.

Just before starting the haemodialysis session, a blood sample is taken to determine the baseline level serum aluminium level.

During the last 60 minutes of the haemodialysis session a 5 mg/kg dose is given as a slow intravenous infusion.

At the start of the next haemodialysis session (i.e. 44 hours after the aforementioned Desferal infusion) the second blood sample is taken to determine the serum aluminium level once more.

Use in the elderly

No special dosage regime is necessary but concurrent renal insufficiency should be taken into account.

Contraindications

Hypersensitivity to desferrioxamine mesilate unless the patients can be desensitised.

Special Warnings and Precautions and Interactions

Desferal should be used with caution in patients with renal impairment since the metal complexes are excreted via the kidneys. In these patients, dialysis will increase the elimination of chelated iron and aluminium.

Used alone Desferal may exacerbate neurological impairment in patients with aluminium-related encephalopathy. This deterioration (manifest as seizures) is probably related to an acute increase in brain aluminium secondary to elevated circulating levels. Pretreatment with clonazepam has been shown to afford protection against such impairment. Also, treatment of aluminium overload may result in decreased serum calcium and aggravation of hyperparathyroidism.

Treatment with Desferal by the intravenous route should only be administered in the form of slow infusions. Rapid intravenous infusion may lead to hypotension and shock (e.g. flushing, tachycardia, collapse and urticaria).

Desferal should not be administered s.c. in concentrations and/or doses higher than those recommended as local irritation at the site of administration may occur more frequently. Patients suffering from iron overload are particularly susceptible to infection. There have been reports of Desferal promoting some infections such as *Yersinia enterocolitica* and *Y. pseudotuberculosis*. If patients develop fever with pharyngitis, diffuse abdominal pain or enteritis/enterocolitis, Desferal therapy should be stopped, and appropriate treatment with antibiotics should be instituted. Desferal therapy may be resumed once the infection has cleared.

In patients, receiving Desferal for aluminium and/or iron overload there have been rare reports of mucormycosis (a severe fungal infection), some with fatal outcome. If any characteristic signs or symptoms occur Desferal treatment should be discontinued, mycological tests carried out and appropriate treatment immediately instituted. Mucormycosis has been reported to occur in dialysis patients not receiving Desferal, thus no causal link with the use of the drug has been established.

Disturbances of vision and hearing have been reported during prolonged Desferal therapy. In particular, this has occurred in patients on higher than recommended therapy or in patients with low serum ferritin levels. Patients with renal failure who are receiving maintenance dialysis and have low ferritin levels may be particularly prone to adverse reactions, visual symptoms having been reported after single doses of Desferal. Therefore, ophthalmological

and audiological tests should be carried out both prior to the institution of long-term therapy with Desferal and at 3-monthly intervals during treatment. By keeping the ratio of the mean daily dose (mg/kg of Desferal) divided by the serum ferritin (micro g/L) below 0.025 the risk of audiometric abnormalities may be reduced in thalassaemia patients. A detailed ophthalmological assessment is recommended (visual field measurements, fundoscopy, and colour vision testing using pseudoisochromatic plates and the Farnsworth D-15 colour test, slit lamp investigation, visual evoked potential studies).

If disturbances of vision or hearing do occur, treatment with Desferal should be stopped. Such disturbances are usually reversible. If Desferal therapy is re-instituted later at a lower dosage, close monitoring of ophthalmological/auditory function should be carried out with due regard to the risk-benefit ratio.

The use of inappropriately high doses of Desferal in patients with low ferritin levels or young children (<3 years at commencement of treatment) has also been associated with growth retardation; dose reduction has been found to restore the growth rate to pretreatment levels in some cases. Three monthly checks on body weight and height are recommended in children. Growth retardation if associated with excessive doses of Desferal must be distinguished from growth retardation from iron overload. Growth retardation from Desferal use is rare if the dose is kept below 40 mg/kg; if growth retardation has been associated with doses above this value, then reduction of the dose may result in return in growth velocity, however, predicted adult height is not attained.

Acute respiratory distress syndrome has been described following treatment with excessively high i.v. doses of Desferal in patients with acute iron intoxication, and also in thalassaemic patients (see section 4.8 Undesirable effects). The recommended daily doses should therefore not be exceeded.

It should be noted that desferrioxamine will affect aluminium levels and may necessitate some dosage adjustment of erythropoietin if co-prescribed.

Interactions with other Medicaments and other forms of Interaction

Oral administration of vitamin C (up to a maximum of 200 mg daily, given in divided doses) may serve to enhance excretion of the iron complex in response to Desferal; larger doses of vitamin C fail to produce an additional effect. Monitoring of cardiac function is indicated during such combined therapy. Vitamin C should be given only if the patient is receiving Desferal regularly and should not be administered within the first month of Desferal therapy. In patients with severe chronic iron-storage disease undergoing combined treatment with Desferal and high doses of vitamin C (more than 500 mg daily) impairment of cardiac function has been encountered; this proved reversible when the vitamin C was withdrawn. Vitamin C supplements should not, therefore, be given to patients with cardiac failure.

Desferal should not be used in combination with prochlorperazine (a phenothiazine derivative) since prolonged unconsciousness may result.

Gallium⁶⁷ imaging results may be distorted because of the rapid urinary excretion of Desferal-bound radiolabel. Discontinuation of Desferal 48 hours prior to scintigraphy is advised.