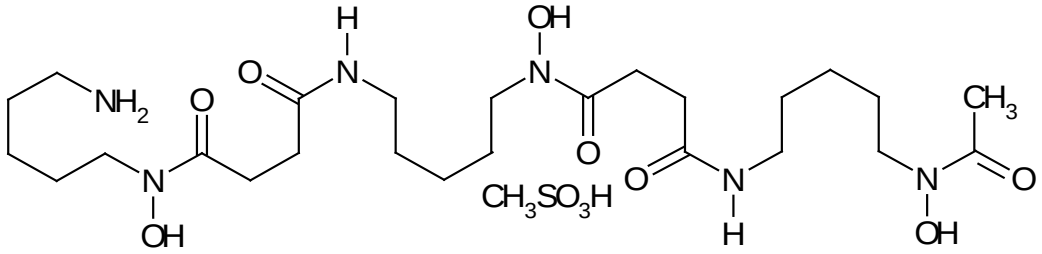
DESFERAL®

NAME OF THE DRUG

Active ingredient: Desferrioxamine mesylate
Structural formula:



DESCRIPTION

Chemical Name: Desferrioxamine N-[5-(3-[(5-aminopentyl)hydroxycarbamoyl] propionamido)--pentyl]-3-([5-(N-hydroxyacetamido) pentyl]-carbamoyl)-propionyl-hydroxamic acid methane sulphonate
Empirical formula: $C_{25}H_{48}N_6O_8.CH_3SO_3H$
CAS number: 138-14-7
Molecular weight: 656.8

Desferrioxamine mesylate is a white to cream-coloured, odourless or almost odourless powder with a bitter taste. Solubility: 1 to 5 (w/v) in water, insoluble in dehydrated alcohol, chloroform and ether. A 10% solution in water has a pH of 3.5 to 5.5.

PHARMACOLOGY

Pharmacodynamics

Desferal is a chelating agent which forms complexes predominantly with ferric iron and to a lesser degree with trivalent aluminium ions: the complex formation constants are 10^{31} and 10^{25}, respectively. The affinity of Desferal for divalent ions such as Fe^{2+}, Cu^{2+}, Zn^{2+}, Ca^{2+} is substantially lower (complex formation constants 10^{14} or below). Chelation occurs on a 1:1 molar basis, so that 1 gram desferrioxamine theoretically can bind 85 mg ferric iron.

Desferal chelates free iron and iron bound in ferritin and haemosiderin to form the complex, ferrioxamine. It does not chelate iron in transferrin, haemoglobin or other iron-containing proteins. Iron deposits in the lungs are not removed.

Desferal can facilitate excretion of 10 - 50 mg of iron per day from patients with iron overload (a transfusion of 500 mL whole blood adds 250 mg of iron to the body). The relationship between Desferal dose and the amount of iron excreted is non-linear, with reducing efficiency at higher doses.

Desferal reduces pathological iron deposits in the organs. Regular chelation with Desferal has been shown to improve life expectancy in patients with thalassaemia.

Desferal causes the release of histamine, which may be the basis for acute hypotensive episodes following rapid i.v. administration.

Desferal has some neurotoxic effects which may be due to its ability to chelate copper or zinc.

Desferal has a suppressant effect on lymphocytes.

In patients on haemodialysis who are not overloaded with iron, plasma concentrations of aluminium may rise in response to administration of Desferal.

Pharmacokinetics

Absorption and plasma concentrations:

Desferrioxamine methane sulfonate is rapidly absorbed by the intramuscular and subcutaneous route. Less than 10% is bound to serum proteins. In healthy subjects and in patients with transfusion induced iron overload, plasma concentrations of between 80 and 130 micromol/L were recorded 3 minutes after an intravenous injection of desferrioxamine (10 mg/kg), these concentrations falling one-half within 5 to 10 minutes, and thereafter declining more slowly. This rapid fall in concentration is due not only to distribution, metabolic transformation and excretion of the active substance, but also to formation of the iron complex ferrioxamine (which commences within a few minutes and proceeds to an extent which depends on the individual's iron status).

During continuous subcutaneous or intravenous infusion of desferrioxamine (100 mg/kg in 24 mL sterile water at a rate of 1 mL/hour), the plasma concentrations of desferrioxamine and ferrioxamine in healthy subjects rose, depending on each subject's individual iron status (serum concentration), to a plateau after 12 hours, or in some cases less, i.e. to maximum levels of 20 micromol/L for desferrioxamine and 2.75 micromol/L for ferrioxamine. The corresponding values in patients were 8.3 micromol/L for desferrioxamine and 12.9 micromol/L for ferrioxamine.

Elimination:

The ferrioxamine complex is completely excreted. Urinary ferrioxamine reflects iron derived from plasma turnover and faecal ferrioxamine reflects iron derived from intrahepatic iron chelation.

The 48 hour urinary excretion averaged 118 micromol in the healthy subjects and 836 micromol in the patients. In patients with haemochromatosis, the increase in iron excretion occurring in response to desferrioxamine was approximately as high in the faeces as in the urine.

Within 12 hours after desferrioxamine had been administered to 20 volunteers, 33.1% of the dose was excreted in the urine (the bulk of it in the first 3 hours) in the form of desferrioxamine and ferrioxamine, and the remainder in the form of metabolites; the corresponding figure in a patient with haemochromatosis was 60.5% of the dose.

The urine may appear a red wine colour ("vin rose") if the iron-desferrioxamine complex, ferrioxamine, is present. This appearance is dependent on urine pH; therefore, it is not a sensitive test of chelatable iron in the circulation.

INDICATIONS

Desferal is indicated for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anaemias.

Acute Iron Intoxication
Desferal is an adjunct to, and not a substitute for, standard measures used in treating acute iron intoxication, which may include the following: gastric lavage; suction and maintenance of a clear airway; control of shock with intravenous fluids, blood, oxygen and vasopressors; and correction of acidosis.

Chronic Iron Overload
Desferal can promote iron excretion in patients with iron overload secondary to multiple transfusions (as may occur in the treatment of some chronic anaemias, including thalassaemia). Long-term therapy with Desferal slows accumulation of hepatic iron and retards or eliminates progression of hepatic fibrosis.

Iron mobilisation with Desferal is relatively poor in patients under the age of 3 years with relatively little iron overload. The drug should not normally be given to such patients unless significant iron mobilisation (e.g. 1 mg or more of iron per day) can be demonstrated.

Desferal is not indicated for the treatment of primary haemochromatosis, since phlebotomy is the method of choice for removing excess iron in this disorder.

CONTRAINDICATIONS

- Known hypersensitivity to the active substance, except where desensitisation proves possible.
- Absence of excess iron stores.

PRECAUTIONS

Susceptibility to infections:

Patients suffering from iron overload are particularly susceptible to infections, and it has been reported that infections (including septicaemia), especially with *Yersinia enterocolitica* and *Yersinia pseudotuberculosis*, may be promoted by Desferal. If a patient under treatment with Desferal develops fever accompanied by acute enteritis/enterocolitis, diffuse abdominal pain, or pharyngitis, the treatment should be withdrawn temporarily, appropriate bacteriological tests performed and suitable antibiotic therapy instituted at once. After the infection has cleared, treatment with Desferal can be resumed.

In patients receiving Desferal, there have been very rare reports of severe fungal infections (e.g. cases of mucormycosis, some with fatal outcome, or infection with Pneumocystis carinii or Rhizopus). Whilst a causal relationship with the drug has not been firmly established, the known suppressant effect of Desferal on lymphocytes may have been a contributing factor. If any of the suspected signs or symptoms occur, Desferal should be discontinued, mycological tests carried out and appropriate treatment instituted immediately. Mucormycosis may also develop in patients who are not receiving Desferal, indicating that other factors (such as dialysis, diabetes mellitus, disturbances of acid-base balance, haematological malignancies, immunosuppressive drugs or a compromised immune system) may also play a role in the development of this infection.

Disturbances of vision and hearing:

During prolonged treatment with Desferal, particularly where the doses used were higher than those recommended, disturbances of vision and hearing have been observed. High doses of Desferal especially in patients with low ferritin plasma levels, may lead to disturbances of vision and hearing. 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. The risk of these side effects is reduced when low-dose therapy is employed.

By keeping the ratio of the mean daily dose (mg/kg) of Desferal divided by the serum ferritin level (micrograms/L) below 0.025, the risk of audiometric abnormalities may be reduced in patients with thalassaemia.

Ophthalmological (e.g. slit lamp examination of the lens) tests and audiometry should be carried out before starting treatment with Desferal, as well as at regular intervals of about 3 months during the treatment, particularly if ferritin levels are low. If disturbances of vision or hearing occur, treatment with Desferal should be discontinued immediately in order to increase the chances that these disturbances will prove reversible. Later resumption of treatment with Desferal at a reduced dosage should be done under close ophthalmological or audiological control, and with due regard to the benefit-risk ratio.

Acute respiratory distress syndrome:
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. The recommended daily dose should, therefore, not be exceeded.

Use in patients with renal failure:
Caution is indicated in patients with severe renal failure as approximately 50% or more of the ferrioxamine formed is excreted via the kidneys. The iron complex is dialysable and, in patients with renal failure, its elimination will be increased by dialysis.

Isolated cases of acute renal failure have been reported (see “ADVERSE REACTIONS”). Monitoring patients for changes in renal function (eg increased serum creatinine) should be considered.

Growth impairment in children:
In children receiving Desferal, growth is impaired and bone changes (e.g. metaphyseal dysplasia, spinal abnormalities) may occur. The risk is greater in patients under the age of 3 years. Growth impairment may be due to both iron overload and Desferal treatment. Weight and height should be monitored every 3 months. The Desferal dose should be kept to the minimum necessary to control iron overload (see "DOSAGE AND ADMINISTRATION"). Even at low doses, predicted adult height is not attained.

Effects on ability to drive and use machinery:
Patients experiencing dizziness or other central nervous system disturbances, or impairment of vision or hearing should refrain from driving a vehicle or operating machinery (see "ADVERSE REACTIONS").

Precautions with administration of Desferal:
Desferal should not be given in doses higher than recommended. The drug should not be given at concentrations higher than 10% as this increases the risk of local reactions.

Intravenous administration of Desferal should be undertaken only by means of slow infusions. Rapid intravenous injection may lead to severe hypotension and shock (e.g. flushing, tachycardia, urticaria and circulatory collapse). Rates of infusion should not exceed 15 mg/kg/hr.

When given by intramuscular injection, it may be necessary to administer the dose at more than one site in order to allow sufficient dilution and distribution of the injection volume, and to minimise pain on injection (see “DOSAGE AND ADMINISTRATION”).

For subcutaneous infusion, the needle should not be inserted too close to the dermis. Desferal is not formulated to support subcutaneous bolus injection.

Urine discolouration:
Excretion of the iron complex may cause reddish-brown discolouration of the urine.

Mutagenicity, carcinogenicity and reproductive studies:
No evidence of mutagenic potential has been observed in vitro. Long-term carcinogenicity studies in animals have not been performed with Desferal.

Delayed ossification in mice and skeletal anomalies in rabbits were observed after Desferal was administered in daily doses up to 4.5 times the maximum human daily dose. No adverse effects were observed in similar studies in rats.

Use in Pregnancy (Category 'B3')
There is a limited amount of data on the use of desferrioxamine in pregnant patients. The risk to the fetus/mother is unknown. Since Desferal has proved teratogenic in animal experiments, it should only be employed during pregnancy - especially in the first 3 months - if its use is of vital necessity.

Use in Lactation
It is not known whether or not the active substance of Desferal passes into breast milk. Because many drugs are excreted in human milk and because of the potential for serious adverse drug reactions in breast-fed newborns/infants, a decision should be made whether to abstain from breastfeeding or to abstain from using the medicinal product. In each case the benefits for the mother must be weighed against the risks for the child.

Interactions with Other Drugs
In patients with iron-storage disease and heavy iron overload, concomitant oral treatment with Vitamin C (up to 200 mg daily) may enhance excretion of the iron complex formed in response to Desferal. Larger doses of Vitamin C fail to produce any additional increase in excretion of the iron complex.

Patients with iron overload usually become Vitamin C deficient, probably because iron oxidises the vitamin. 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. Bilateral cataracts have also been described in a patient on long-term combined therapy with Desferal and Vitamin C.

The following precautions should be taken when Desferal and Vitamin C are to be used concomitantly:

- Vitamin C supplements should not be given to patients with cardiac failure.
- Treatment with Vitamin C should only be given to patients who are receiving regular treatment with Desferal.

- Vitamin C should be started only after an initial month of regular treatment with Desferal and it should only be given on days when Desferal is received, ideally soon after setting up the pump.
- The daily dose of Vitamin C for adults should not exceed 200 mg, given in divided doses. In general, 50 mg Vitamin C per day suffices for children under 10 years of age and 100 mg per day suffices for older children.
- Monitoring of cardiac function is indicated during such combined therapy.

Concurrent administration of Desferal with a single dose of prochlorperazine, a phenothiazine derivative, may lead to severe temporary impairment of consciousness.

The neuro-ophthalmic toxicity of Desferal may be potentiated by concurrent use of prochlorperazine or methyldopa.

Gallium-67 imaging results may be distorted because of the rapid urinary excretion of Desferal-bound gallium-67. Discontinuation of Desferal 48 hours prior to scintigraphy is advisable.

ADVERSE REACTIONS

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: 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 including isolated reports: “unknown” (when not possible to reliably estimate the frequency of the adverse reactions reported from post-marketing experience because reports are from a population of uncertain size). Within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.

General disorders and administration site conditions:
Very common: pain, swelling, infiltration, erythema, pruritus and eschar/crust at the injection site. See special remarks. Common: pyrexia
Uncommon: vesicles, oedema and burning at the injection site

Musculoskeletal and connective tissue disorders:
Very common: arthralgia/myalgia
Common: growth retardation and bone disorder (e.g. metaphyseal dysplasia) in patients given doses of Desferal above 60 mg/kg, especially those who begin iron chelation in the first 3 years of life (see “PRECAUTIONS”).
Unknown: Muscle spasms

Eye disorders:
Rare: (except if high doses are given) loss of vision, scotoma, retinal degeneration, optic neuritis, cataracts, decreased visual acuity, blurred vision, night blindness, visual field defects, chromatopsia (impairment of colour vision), corneal opacities

Ear and labyrinth disorders:
Uncommon (if doses are kept within guidelines): deafness neurosensory, tinnitus

Loss of vision and hearing may be irreversible (see "PRECAUTIONS").

Immune system disorders:
Very rare: anaphylactic shock, anaphylactoid reaction, angioneurotic oedema, allergic skin reactions

Skin and subcutaneous tissue disorders:
Common: urticaria
Very rare: dermatitis medicamentosa, generalised rash

Respiratory, thoracic and mediastinal disorders:
Uncommon: asthma
Very rare: acute respiratory distress, lung infiltration (see "PRECAUTIONS")

Nervous system disorders:
Common: headache
Very rare: neurological disturbances including dizziness, precipitation or exacerbation of aluminium-related dialysis encephalopathy (e.g. grand mal seizures, hallucinations, paranoid delusions, dialysis dementia), neuropathy peripheral, paraesthesia
Unknown: Convulsion
Convulsions has been mainly reported in dialysed patients with aluminium overload

Gastrointestinal disorders:
Common: nausea
Uncommon: vomiting, abdominal pain
Very rare: diarrhoea

Renal and urinary disorders:
Very rare: Renal impairment (including a rise in serum creatinine)
Unknown: Acute renal failure, renal tubular disorder, blood creatinine increased (see "PRECAUTIONS" and "OVERDOSAGE")

Vascular disorders:
Rare: Hypotension, tachycardia and shock may occur if the recommended precautions for the administration of Desferal are not followed (see "PRECAUTIONS")

Blood and lymphatic system disorders:
Very rare: blood disorders (e.g. thrombocytopenia, leukopenia, eosinophilia)

Infections and infestations:
Rare: Mucormycosis (see "PRECAUTIONS")
Very rare: Gastroenteritis Yersinia, unusual infections (e.g. with Pneumocystis carinii, Yersinia or Rhizopus (see "PRECAUTIONS").

Other:
Impaired hepatic function, cardiac arrhythmias, leg cramps, transient depression of serum calcium, transient bone pain, aggravation of pyelonephritis, inhibition of DNA synthesis in T and B lymphocytes, reversible aphasia with visual loss and bradycardia; hyperparathyroid bone disease in a few patients treated for aluminium toxicity.

Some of the signs or symptoms mentioned above may also be manifestations of iron overload.

Rare cases of increased transaminases have been reported in patients who have been treated with Desferal, however a causality with the drug is not established.

Special Remarks
At the injection site pain, swelling, infiltration, erythema, pruritus and eschar/crust are very common, while vesicles, local oedema and burning are uncommon. Local manifestations may be accompanied by systemic reactions such as arthralgia/myalgia (very common), headache (common), urticaria (common), nausea (common), pyrexia (common), vomiting (uncommon), abdominal pain (uncommon) or asthma (uncommon).

Excretion of the iron complex may cause reddish-brown discoloration of the urine.

DOSAGE AND ADMINISTRATION

The presence of iron overload, preferably quantified, should be established before initiating therapy with Desferal.

Treatment for Chronic Iron Overload
Commencement of therapy:
The main aim of chelation therapy in iron overload in young patients is to achieve an iron balance and to prevent haemosiderosis, while in older patients a negative iron balance is desirable in order to reduce slowly the increased iron stores and to prevent the toxic effects of iron. It is recommended that therapy with Desferal be started after the first 10 - 20 blood transfusions or when the serum ferritin level has reached 1000 microgram/L.

In children, the earliest age at which therapy with Desferal should be undertaken is 2 to 3 years (see “PRECAUTIONS”).

Dosage:
The lowest effective dose should be used.

In most patients average daily doses of 20 to 60 mg/kg body weight are adequate. Patients with a serum ferritin level of less than 2000 microgram/L require about 25 mg/kg/day. Patients with a serum ferritin level between 2000 and 3000 microgram/L require about 35 mg/kg/day. Patients with higher serum ferritin levels 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 are no longer growing. If ferritin values fall below 1000 microgram/L, the risk of Desferal toxicity increases. Therefore, it is important to monitor these patients particularly carefully and to consider lowering the total weekly dose.

Note that the doses recommended represent the average daily dose. Since most patients receive the drug on less than 7 days per week, the actual dose per infusion usually differs from the average daily dose (e.g. if an average daily dose of 40 mg/kg is required and the patient receives the drug on 5 days per week, each infusion should contain 56 mg/kg).

To assess the chelation therapy, individual iron balance can be calculated based upon the amount of iron excreted in the urine. Negative iron balance is considered to be achieved when the total amount of iron excreted in the urine, plus a further 50% (which corresponds roughly to the mean iron excretion in the stools), exceeds the total iron received from blood transfusions (each 100 mL of pure red blood cells contains 116 mg of iron). The expected rate of excretion of iron lies in the range of 10 to 20 mg/day. To assess the response to chelation therapy, 24-hour urinary iron excretion should be monitored daily initially and the response to increasing doses of Desferal established. The lowest effective dose of Desferal resulting in a negative iron balance should be used. Once the appropriate dosage has been established, urinary iron excretion rates should be assessed at intervals of a few weeks.

Alternatively, the mean daily dose may be adjusted according to the ferritin value to keep the therapeutic index less than 0.025 (i.e. mean daily dose of Desferal in mg/kg divided by the serum ferritin level in microgram/L is below 0.025) [see “PRECAUTIONS”]. The therapeutic index is a valuable tool in protecting the patient from excess chelation, but it is not a substitute for careful clinical monitoring.

Hepatic impairment
No studies have been performed in patients with hepatic impairment.

Methods of administration:

Subcutaneous infusion:

Slow subcutaneous infusion over 8 - 12 hours using a portable infusion pump is the recommended route of administration. In some patients it is possible to achieve a further increase in iron excretion by infusing the same daily dose over a 24 hour period. Heavily iron-loaded patients should use the pump 5 to 7 times a week as protection against iron toxicity. However, if the iron load is low, infusions may be given 3 to 5 times a week.

Continuous intravenous infusion:

Continuous intravenous infusion of Desferal is indicated in patients who are incapable of continuing subcutaneous infusions and in those who have cardiac problems secondary to iron overload. An implanted intravenous delivery system can be used for continuous intravenous infusion at home. The rate of infusion should not exceed 15 mg/kg/hour. Care should be taken when flushing the intravenous 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 circulatory collapse (see "PRECAUTIONS - Administration of Desferal").

Intravenous infusion during blood transfusion:

The availability of an intravenous line during blood transfusions makes it possible to administer an intravenous infusion of Desferal on these occasions. However, because of the limited time available, this method cannot replace regular subcutaneous infusion. 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 the venous site of injection. The patient’s pump should be used to administer Desferal as usual. Patients and staff should be warned against accelerating the infusion since an intravenous bolus of Desferal may lead to circulatory collapse (see “PRECAUTIONS- Administration of Desferal”).

Intramuscular administration:

Desferal may be injected intramuscularly though this method is less effective than subcutaneous infusion. It may be necessary to administer an intramuscular dose at more than one site in order to allow sufficient dilution and distribution of the injection volume, and to minimise pain on injection.

Acute Iron Poisoning

Commencement of therapy:

Desferal is an adjunct to standard measures generally used in treating acute iron poisoning. These may include gastric lavage, control of shock, and correction of acidosis. Desferal should not be administered orally after an oral overdose of iron, as this may result in increased iron absorption.

The decision to commence Desferal is dependent on the presence of symptoms and signs of iron toxicity and the serum iron concentration. Measurement of transferrin saturation may be

useful in determining the likelihood of acute toxicity. If a patient does not develop symptoms or signs within 6 hours of iron ingestion, then iron toxicity is unlikely.

Serum iron usually peaks 4 - 6 hours after overdosage (later for delayed-release formulations). In the case of slow-release or enteric-coated tablets, serum iron measurement should be repeated at 6 - 8 hours, since absorption may be erratic.

Desferal is indicated if:

- There are significant symptoms or signs of iron toxicity (e.g. lethargy, gastrointestinal bleeding, hypotension, metabolic acidosis, abdominal radiopacities) or
- Serum iron concentration is > 90 micromol/L within 8 hours of ingestion.

Dosage:
The dosage of Desferal should take into account the total amount of iron ingested, the severity of symptoms and the serum iron concentration. The maximum recommended dose is 80 mg/kg/day.

Administer Desferal by continuous intravenous infusion at a maximum rate of infusion of 15 mg/kg/hour. Reduce the rate of infusion as soon as the situation permits, usually after 4 - 6 hours. The usual duration of treatment is 24 hours.

Patients with renal failure:
Desferal elimination is prolonged as much as 8-fold in patients with renal failure. Therefore, infusion rates should be reduced accordingly.

The effectiveness of Desferal is dependent on an adequate urine output in order to ensure that the iron complex, ferrioxamine, is excreted from the body. If oliguria or anuria develop, peritoneal dialysis or haemodialysis may be necessary to remove ferrioxamine. In patients on maintenance haemodialysis or haemofiltration, Desferal doses of 1 - 4 grams per week have proven effective. Administration of Desferal may precipitate aluminium toxicity in patients on dialysis.

Cessation of chelation therapy:
Chelation therapy should be continued until all of the following criteria are satisfied:

- The patient is free of symptoms and signs of iron poisoning.
- The measured serum iron concentration is not elevated. Note that laboratories cannot measure serum iron concentrations accurately in the presence of Desferal.
- No radiopacities are present on abdominal x-ray, if a previous x-ray showed radiopacities.
- The patient's urine colour is normal, if it had been a red wine colour ("vin rose").

Instructions for Use
When administered parenterally, the drug should be prepared as a 10% solution in water for injections. 5 mL water for injection is injected into the vial containing 500 mg Desferal

powder, and the vial shaken well. For Desferal 2 g, an approximately 10% solution is prepared by adding 20 mL of water for injection into the vial and shaking well. Only clear and colourless to slightly yellowish solutions should be used. Opaque or cloudy solutions should be discarded. The 10% Desferal solution can be further diluted with routinely employed infusion solutions (sodium chloride, glucose, Ringer's solution).

Dissolved Desferal can also be added to the dialysis fluid and given intraperitoneally to patients on CAPD or CCPD.

To reduce microbiological hazard, use as soon as practicable after reconstitution/preparation. If storage is necessary, hold at 2-8°C for not more than 24 hours.

Incompatibilities:

- Heparin injectable solution may cause cloudiness or precipitation when mixed with Desferal solution.
- Physiological saline (0.9%) should not be used as a solvent for the dry substance since it produces a hypertonic solution, but it can be employed, after reconstitution with water for injections, for further dilution.

OVERDOSAGE

Signs and symptoms:

Inadvertent administration of an overdose or intravenous bolus administration /rapid intravenous infusion may be associated with tachycardia, hypotension, and gastrointestinal symptoms. Acute renal failure has also been reported. In one well-documented case, a 6 year-old child accidentally received an i.v. infusion in excess of 200 mg/kg/24 h for an unknown period, and experienced acute transient loss of vision, aphasia, agitation, headache, nausea, bradycardia and hypotension. The signs and symptoms reverted to normal within 8 hours after discontinuation of Desferal and infusion of fluids.

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 thalassemic patients.

Treatment:

There is no specific antidote. Signs and symptoms of overdosage may be eliminated by reducing the dosage. Desferal is dialysable.

PRESENTATION

Vials 500 mg (dry substance), box of 10.
Vials 2 g (dry substance) box of 1.

SPONSOR

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