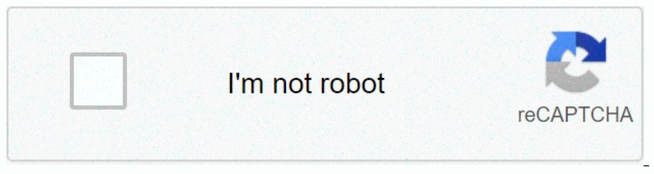

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Deferoxamine infusion guidelines

This information is intended for healthcare professionals Each vial contains desferrioxamine mesilate 500mg. A sterile, freeze-dried powder available in vials containing 500 mg of desferrioxamine messilate. Treatment of chronic iron overload, e.g., transfusion hemophage in patients receiving regular transfusions, e.g. major thalassemia - primary and secondary hemochromatosis in patients with concurrent disorders (e.g., severe anemia, hypoproteemia, kidney or heart failure) exclude phlebotomy. Treatment for acute iron poisoning. For the diagnosis of iron storage disease and some anemias. Aluminium overload - In patients on maintenance dialysis for end-stage renal failure where preventive measures (e.g. reverse osmosis) have failed and with proven bone disease and/or aluminum-related anemia, dialysis encephalopathy; and for the diagnosis of aluminum overload. Desferal can be administered relatively. For parenteral administration: The drug should preferably be used in the form of a 10% solution, for example 500 mg: by dissolving the contents of a 500mg vial into 5ml of water for injection. When administered subcutaneously, the needle should not be inserted too close to the derm. The 10% Desferal solution can be diluted with infusion solutions used regularly (salt solutions, glucose, dextrose or dextrose-saline), although they should not be used as a 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 relapsing peritonal dialysis (CCPD). Only light yellow Desferal solutions should be used. Opaque, cloudy or discoloured solutions must be discarded. Heparin is pharmaceutically incompatible with Desferal solutions. Treatment of acute iron poisoning Adults and children: Desferal may be administered parenterally. Desferal is a complement to the standard measures commonly used in the treatment of acute iron poisoning. It is important to initiate treatment as soon as possible. Desferal parenteral treatment should be considered in one of the following situations: - all symptomatic patients with more than minor transient symptoms (e.g. more than one episode of emesis or passage of a soft stool), patients with evidence of lethargy, significant abdominal pain, hypovolemia, or acidosis, patients with positive abdominal X-ray results demonstrating multiple radio-opacities (the vast majority of these patients will develop symptomatic iron poisoning), 300 to 350 micro g/dL regardless of total iron binding capacity (TIBC). It has also been suggested that a conservative approach without Desferal therapy or challenge should be considered when serum iron levels are in the range of 300 to 500 micro g/dL in asymptomatic patients, as well as in those with self-limited, non-bloody emesis or diarrhea without other symptoms. Lla Lla and the route of administration must be adapted to the severity of the 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 dose of 80 mg/kg within a 24-hour period. However, if the option of intravenous infusing is not available and the intramuscular route is used, the normal dose is 2 g for an adult and 1 g for a child, administered as a single intramuscular dose. The decision to discontinue dessferal therapy must be a clinical decision; however, it is believed that the above-suggested criteria represent appropriate requirements for the termination of Desferal. Chelation therapy should be continued until all the following criteria are met: - the patient must be free of signs and symptoms of systemic iron poisoning (e.g., no acidosis, no aggravating hepatoxicity), ideally, a corrected serum iron level should be normal or low (when the iron level falls below 100 microg/dL). Since laboratories cannot accurately measure serum iron concentrations in the presence of Desferal, it is acceptable to discontinue Desferal when all other criteria are met if the measured serum iron concentration is not high. Repeated abdominal radiographic testing should be performed in patients who initially demonstrated multiple radio-opacities to ensure that they disappeared before Desferal was discontinued because they serve as a marker for continuous iron absorption, If the patient initially developed wine-pink urine with desferal therapy, it seems reasonable that the urine color should return to normal before stopping Desferal (the absence of wine-pink urine is not sufficient in itself to indicate Desferal cessation). The effectiveness of the treatment depends on an adequate urine output so that the iron complex (ferrioxamine) is excreted from the body. Therefore, if oliguria or anuria develop, peritoneal dialysis or hemodialysis may become necessary to remove ferrioxamine. It should be noted that serum iron levels can increase sharply when iron is released from tissues. Theoretically 100 mg Desferal can chelate 8.5 mg of iron. Chronic iron overload The main goal of therapy in well-controlled patients is to maintain an iron balance and prevent hemosdeosis, while in overburdened patients a negative iron balance is desirable in order to deplete increased iron reserves and prevent the toxic effects of iron. Adults and children: Desferal therapy should be started after 10 to 20 blood transfusions, or where there is evidence of clinical monitoring that chronic iron overload is present (e.g. serum ferritin - 1000 ng/mL. The dose and method of administration should be individually adapted according to the degree of iron overload. The growth retardation may result from an iron overload or Doses. If chelation is started before 3 years of age, growth should be monitored carefully and the average daily dose should not exceed 40 mg/kg. (see section 4.4 Special Warnings and Precautions). Dose: The lowest effective dose should be used. The average daily dose is likely to be between 20 and 60 mg/kg/day. Patients with serum ferritin levels of 2000 ng/mL should need 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 used if the benefit to the patient outweighs the risk of adverse events. Patients with higher serum ferritin may need up to 55 mg/kg/day. It is not recommended to regularly exceed an average daily dose of 50 mg/kg/day, except when very intensive chelation is required in patients who have completed growth. If the ferritin values fall below 1000 ng/mL, the risk of desferal toxicity increases; it is important to monitor these patients particularly carefully and perhaps consider reducing the total weekly dose. To evaluate chelation therapy, 24-hour urinary iron excretion should initially be monitored daily. Starting with a dose of 500 mg per day, the dose should be increased until an iron excretion tray is reached. Once the appropriate dose has been established, urinary excretion rates can be assessed at intervals of a few weeks. Alternatively, the average daily dose can be adjusted for the level of ferritin to keep the therapeutic index below 0.025 (i.e. the average daily dose (mg/kg) of Desferal divided by serum ferritin level (micro g/L) should be less than 0.025). The therapeutic index is a valuable tool to protect the patient from excess chelation, but it is not a substitute for careful clinical monitoring. How to administer: The slow subcutaneous infusion using a light portable infusion pump over a period of 8 to 12 hours is effective and particularly convenient for walking 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. Desferal is not formulated to support the injection of subcutarated bolus. Because subcutaneous infusions are more effective, intramuscular injections are only given when subcutaneous infusions are not possible. Desferal's senior clinical studies did not include a sufficient number of subjects aged 65 and over to determine whether they respond differently to subjects Young. In general, the selection of doses for an elderly patient should be careful, usually from the lower end of the dosage range, reflecting the greater frequency of decrease in liver, kidney or heart function, and concomitant disease or other therapeutic drugs (see sections 4.4 Special Warnings and Precautions of Use and 4.8 Adverse Effects). Liver Deficiency No studies have been conducted in patients with liver impairment. Intravenous infusion during blood transfusion Le Le an intravenous line during blood transfusions allows for intravenous infusion, for example in patients who do not adhere to subcutaneous infusions and/or who do not tolerate. The Desferal solution should not be placed directly in the blood sac, but can be added to the blood line by means of an adaptor located near the venous injection site. The patient's pump should be used to administer Desferal as usual. Due to the limited amount of medication that can be administered by iv infusion during blood transfusion, the clinical benefit of this mode of administration is limited. Patients and nurses should be warned against accelerating infusion, as an intravenous Desferal bolus can lead to hot flashes, hypotension and circulatory collapse (see section 4.4 Special Warnings and Precautions). Continuous intravenous infusion is recommended for patients unable to continue subcutaneous infusions and for those with heart problems secondary to iron overload. Urinary 24-hour urinary iron excretion should be measured regularly where intensive chelation (c.v.) is required, and the dose adjusted accordingly. Implanted intravenous systems can be used during intensive chelation. Be careful when rinsing the line to avoid a sudden infusion of residual Desferal that may be present in the dead space of the line, as this can lead to hot flashes, hypotension and circulatory collapse (see section 4.4 Special Warnings and Precautions). Diagnosis of iron storage disease and certain anaemias The desferal test for iron overload is based on the principle that normal subjects do not excrete more than a fraction of one milligram of iron in their urine daily, and that a standard intramuscular injection of 500 mg of Desferal will not increase this more than 1 mg of iron (18 micro mol). In iron storage diseases, however, the increase can be well over 1.5 mg (27 micro mol). Keep in mind that the test does not give reliable results when kidney function is normal. Desferal is given as an intramuscular injection of 500 mg. The urine is then collected for a period of 6 hours and its iron content determined. The 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) may be considered pathological. Treatment of aluminum overload in patients with end-stage renal failure Patients should receive desferal if: - they have symptoms or evidence of organ deficiency due to aluminum overload - are asymptomatic, but their serum aluminum levels are consistently above 60 ng/mL and associated with a positive desferal test (see below), especially if a bone biopsy provides evidence of aluminum-related bone disease. Desferal's iron and aluminum complexes are dialable. In patients with kidney failure, their elimination will be increased by dialysis. Adults and children: Patients with maintenance hemodialysis or hemofilter: 5 mg/kg mg/kg A week. Patients with post-desferrioxamine test serum aluminum 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 free drug loss in dialysate). Patients with a post-desferrioxamine test serum aluminum value greater than 300 ng/ml: Desferal should be administered by slow infusion i.v. 5 hours before dialysis session. Four weeks after completion of a three-month course of Desferal treatment a Desferal infusion test should be performed, followed by a second trial 1 month later. Serum aluminum increases of less than 50ng/mL over the baseline measured in 2 successive infusion trials indicate that Desferal treatment is not necessary. Patients on CAPD or CCPD: 5 mg/kg once a week before the final exchange of the day. It is recommended that the invasive pathway be used in these patients. However, Desferal can also be administered by slow infusion i.v. or s.c. Diagnosis of aluminum overload in patients with end-stage kidney failure A Desferal infusion test is recommended in patients with serum aluminum levels associated with serum ferritin levels - 100 ng/mL. Just before the start of the hemodialysis session, a blood sample is taken to determine the base level of the aluminum serum. During the last 60 minutes of the hemodialysis session, a dose of 5 mg/kg is administered as a slow intravenous infusion. At the beginning of the next hemodialysis session (i.e. 44 hours after the aforementioned Desferal infusion), the second blood sample is taken to determine once again the aluminum level of the serum. An increase in serum aluminum above the baseline of more than 150 ng/mL suggests an aluminum overload. It should be noted that a negative test does not completely rule out the possibility of aluminum overload. Theoretically 100 mg Desferal can bind 4.1 mg Al. Use in the elderly No special dosing regimen is required, but concomitant kidney failure must be taken into account. Hypersensitivity to desferrioxamine mesilate unless patients can be desensitized. Desferal kidney failure should be used with caution in patients with kidney failure as the metal complexes are excreted via the kidneys. In these patients, dialysis will increase the elimination of chelated iron and aluminum. Isolated cases of acute kidney failure have been reported (see also section 4.8 Adverse effects). Consideration should be given to monitoring changes in kidney function (e.g., increased serum creatinine). Neurological disorders only Desferal can exacerbate neurological impairment in patients with aluminum-related encephalopathy. This deterioration (manifest in the form of convulsions) is probably related to an acute increase in cerebral aluminum secondary to high circulation levels. Pre-treatment with clonazepam has been shown to provide protection against such a deficiency. In addition, the treatment of aluminum overload can lead to a decrease in serum calcium and Rapid intravenous infusion Treatment with intravenous desferals should only be given in the form of slow infusions. Rapid intravenous infusion can lead to hypotension and shock (e.g., flushing, tachycardia, circulatory collapse and hives). Desferal's instructions for using and handling should not be administered in concentrations and/or doses higher than recommended, as local irritation at the administration site may occur more frequently. Infections Patients with 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/enterocolite, Desferal therapy should be discontinued, and appropriate treatment with antibiotics should be instituted. Desferal treatment can be resumed once the infection has disappeared. In patients, receiving Desferal for aluminum and/or iron overload, there have been rare reports of mucormycosis (a severe fungal infection), some with fatal findings. If characteristic signs or symptoms occur, desferal treatment should be discontinued, mycological testing performed and appropriate treatment immediately instituted. Mucormycosis has been reported to occur in dialysis patients not receiving Desferal, so no causal link with drug use has been established. Visual and Auditory Impairment Disturbances of vision and hearing were reported during prolonged Desferal therapy. In particular, this occurred in patients on higher than recommended therapy or in patients with low serum ferritin levels. Patients with kidney failure who receive maintenance dialysis and have low levels of ferritin may be particularly prone to adverse reactions, with visual symptoms reported after simple doses of Desferal. Therefore, ophthalmological and audiological tests should be performed both before the establishment of therapy with Desferal and at 3-month intervals during treatment especially if ferritin levels are low. By keeping the ratio of the average daily dose (mg/kg of Desferal) divided by serum ferritin (micro g/L) below 0.025, the risk of audiometric abnormalities may be reduced in patients with thalassemia. A detailed ophthalmological assessment is recommended (visual field measurements, fundoscopy and color vision tests using pseudoisochromatic plates and Farnsworth D-15 color tests, slit lamp study, potential evoked visual studies). If trouble vision or hearing occur, treatment with Desferal must be stopped. Such disturbances are usually reversible. If desferal therapy is later re-instituted at a lower dose, close monitoring of ophthalmological/hearing function should be carried out with due consideration of the risk-benefit ratio. Pediatrics: Growth Delay The use of unduly high doses of Desferal in patients with low levels of ferritin or or (3 years at the start of treatment) was also associated with stunted growth; dose reduction was observed to restore growth rates to pre-treatment levels in some cases. Three monthly checks on body weight and height are recommended for children. Growth retardation if associated with excessive doses of Desferal should be distinguished from the growth retardation of iron overload. Delayed growth in 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 the reduction in dose may result in a return of growth speed, however, the expected adult height is not reached. Acute Respiratory Distress Syndrome Acute Respiratory Distress syndrome was described after treatment with excessively high doses of 100 i.v. Desferal in patients with acute iron poisoning, as well as in thalhamic patients (see section 4.8 Adverse Effects). The recommended daily doses should not be exceeded. It should be noted that desferrioxamine will affect aluminum levels and may require some dosage adjustment of erythropoietin if co-prescribed. Oral administration of vitamin C (up to a maximum of 200 mg per day, given in divided doses) can be used to improve the excretion of the iron complex in response to Desferal; higher doses of vitamin C do not produce an additional effect. Monitoring of cardiac function is indicated during such combined therapy. Vitamin C should be administered only if the patient receives Desferal regularly and should not be administered in 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 (over 500 mg per day) of cardiac function was encountered; this proved reversible when vitamin C was removed. Vitamin C supplements should therefore not be given to patients with heart failure. Desferal should not be used in combination with prochlorperazine (a derivative of phenothiazine) since prolonged unconsciousness may result. Gallium67 imaging results may be deformed due to rapid urinary excretion of the desferal-related radiolabel. Stopping Desferal 48 hours before the scan is advised. Women of childbearing age In women with reproductive potential, each case, the benefits to the mother must be assessed against the risks to the child. Pregnancy There is a limited amount of data on the use of desferrioxamine in pregnant patients. Studies of animals (rabbits) have shown a reproductive teratogenicity (see section 5.3 Preclinical Safety Data). The risk to the fetus/mother is unknown. Desferals should only be used during pregnancy if the expected benefits to the mother outweigh the potential

risk to the fetus. Breastfeeding It is not known if Desferal is excreted in breast milk. Because many drugs are excreted in human milk, and because of the possibility of serious serious adverse drugs In breastfed infants, it is necessary to decide whether to abstain from breastfeeding or refrain from using the drug, given the importance of the medication to the mother. Patients who experience CNS effects such as dizziness or visual or hearing impairment should be cautioned against driving or using machines. Adverse events (Table 1) are classified as frequency, the most common first, according to the following convention: very common (≥ 1/10); (≥ 1/100 to 1/10); rare (≥ 1/1,000 to ≤ 1/100); rare (≥ 1/10,000 to ≤ 1/1,000); very rare (≤ 1/10,000) including isolated reports; (cannot be estimated from available data). Some signs and symptoms reported as side effects may also be manifestations of the underlying disease (iron and/or aluminum overload). Table 1 Rare Infections and Infestations: Mucormycosis Infections Have Been Reported (see 4.4 Special Warnings and Precautions). Very rare: Yersinia gastroenteritis infections have been reported (see 4.4 Special Warnings and Precautions). Very rare blood and lymphatic system disorders: blood disorders, including thrombocytopenia Unknown: leukopenia Immune system disorders Very rare: anaphylactic shock, anaphylactic reactions, angionerotic edema. Very rare nervous system disorders: neurological disorders, including dizziness, precipitation or exacerbation of aluminum-related dialysis encephalopathy, peripheral neuropathy, paresthesia (see 4.4 Special Warnings and Precautions). Unknown: convulsion. Rare eye disorders: vision loss, scotoma, retinal degeneration, optic neuritis, cataracts (decreased visual acuity), blurred vision, night blindness, visual field defects, chromatopsia (color vision impairment), corneal opacities, (see 4.4. Special warnings and precautions of use). Eye problems are rare unless high doses are given. Rare ear and maze disorders: sensorineural deafness, tinnitus (see 4.4. Special warnings and precautions of use). Compliance with dose guidelines helps minimize the risk of auditory side effects. Rare vascular disorders: hypotension, tachycardia and shock if administrative precautions are not followed (see 4.2 Posology and method of administration and 4.4 Special Warnings and precautions). Respiratory, chest and mediastinal disorders Very rare: pulmonary infiltration of acute respiratory distress (see 4.4 Special Warnings and Precautions). Very rare gastrointestinal disorders: diarrhea. Skin and subcutaneous tissue disorders Very rare: generalized rash. Disorders and connective tissues Frequent: growth retardation and bone disorders (e.g. metaphysical dysplasia) are common in chelated patients who have received doses of 60 mg/kg, especially those who begin iron chelation in the first three years of life. If doses are maintained at 40 mg/kg or less, the risk is significantly reduced (see 4.4 Special Warnings and Precautions). Unknown: Unknown: Spasms. Kidney and urinary disorders Unknown: acute kidney failure, renal tubular disorder, increased blood creatinine (see 4.4 Special Warnings and Precautions of Use and Section 4.9 Overdose). Special Notes Pain, swelling, infiltration, rash, pruritus and eschar/crust are very common at the injection site; vesicles, local edema and combustion are rare reactions. Local manifestations may be accompanied by systemic reactions such as arthralgia/myalgia (very common), headache (common), hives (common), nausea (common), pyrexia (common), vomiting (rare), or abdominal pain (rare) or asthma (rare). Excretion of the iron complex can cause reddish-brown discoloration of the urine. The convulsion has been mainly reported in dialysis patients with aluminum overload. Patients treated for chronic aluminum overload The aluminum overload of desferal chelation can lead to hypocalcemia and worsening of hyperparathyroidism (see Section 4.4 Special Warnings and Precautions). Reporting Suspicious Side Effects Report Suspicious Side Effects After Drug Authorization Is Important. It allows continuous monitoring of the benefit/risk balance of the drug. Health care professionals are asked to report any suspicious adverse events through the yellow card program at: www.mhra.gov.uk/yellowcard. Desferal is usually administered relatively and acute poisoning is unlikely to occur. Signs and symptoms: tachycardia, hypotension and gastrointestinal symptoms have sometimes occurred in patients who have received an overdose of Desferal. Accidental administration of Desferal through i.v. may be associated with acute but transient loss of vision, aphasia, agitation, headache, nausea, bradycardia, hypotension and acute kidney failure (see Section 4.8 Adverse Effects). Acute respiratory distress syndrome has been described after treatment with excessively high doses of 1000 i.v. of Desferal in patients with acute iron poisoning, as well as in thalassemia patients (see also section 4.4 Special Warnings and Precautions of Use). Treatment: there is no antidote specific to Desferal, but the signs and symptoms can be eliminated by reducing the dosage and Desferal is dialable. Appropriate supportive therapy should be instituted. Chélatation agent (ATC code: V03AC01) Desferal is a chélatation agent for trivalent iron and aluminum ions; chelates (ferrioxamine and aluminoxamine) are stable and non-toxic. Neither chelate undergoes intestinal absorption, and any systemic formed at the parenteral administration is quickly excreted by the kidneys without deleterious effects. Desferal takes iron either free or related to ferritin and hemosiderine. Similarly, it mobilizes and chelates the aluminum linked to the fabrics. It does not remove iron from hephine containing substances, including hemoglobin and transferrin. Since ferrioxamine and aluminoxamine are completely excreted, Desferal Desferal iron and aluminum in urine and faeces, reducing pathological deposits of iron or aluminum in organs and tissues. Absorption Desferrioxamine is quickly absorbed after intramuscular bolus injection or slow subcutaneous infusion, but is only poorly absorbed by the gastrointestinal tract in the presence of intact mucous membrane. During peritoneal dialysis, desferrioxamine is absorbed if administered in dialysis fluid. Distribution In healthy volunteers, maximum plasma concentrations of desferrioxamine (15.5 micro mol/L (87 micro g/mL)) were measured 30 minutes after an intramuscular injection of 10 mg/kg of desferrioxamine. One hour after injection, the maximum concentration of ferrioxamine was 3.7 micro mol/L (2.3 micro g/mL). Less than 10% of desferrioxamine is linked to serum proteins in vitro. Biotransformation Four metaboites of desferrioxamine were isolated from the urine of patients with iron overload. The following biotransformation reactions were found to occur with desferrioxamine: transamination and oxidation producing an acid metabolite, beta-oxidation also producing an acid metabolite, decroxylation and N-hydroxylation producing neutral metabolites. Elimination Desferrioxamine and ferrioxamine biphasic elimination after intramuscular injection in healthy volunteers; for desferrioxamine the apparent half-life of distribution is 1 hour, and for ferrioxamine 2.4 hours. The apparent terminal half-life is 6 hours for both. Within six hours of injection, 22% of the dose appears in the urine as desferrioxamine and 1% in ferrioxamine. Characteristics in patients with hemochromatosis, advanced plasma levels of 7.0 micro mol/L (3.9 micro g/mL) were measured for desferrioxamine, and 15.7 micro mol/L (9.6 micro g/mL) for ferrioxamine, 1 hour after intramuscular injection of 10 mg/kg of desferrioxamine. These patients eliminated desferrioxamine and ferrioxamine with half-lifes of 5.6 and 4.6 hours respectively. Six hours after injection 17% of the dose was excreted in the urine as desferrioxamine and 12% as ferrioxamine. In patients diagnosed with kidney failure who received 40 mg/kg of desferrioxamine infused i.v. within 1 hour, plasma concentration at the end of the infusion was 152 micro mol/L (85.2 micro g/mL) when the infusion was given between dialysis sessions. Plasma concentrations of desferrioxamine were between 13% and 27% lower when the infusion was administered during dialysis. In all cases, ferrioxamine concentrations were about 7.0 micro mol/L (4.3 micro g/mL) with concomitant aluminoxamine levels of 2-3 micro mol/litre (1.2-1.8 microg/mL). After that was discontinued, plasma concentrations of desferrioxamine decreased rapidly with a half-life of 20 minutes. A smaller fraction of the dose was eliminated with a longer half-life of 14 hours. Plasma concentrations of aluminoxamine continued to increase for 48 hours after infusion and reached values of approximately 7 micro mol/L (4 micro g/mL). g/mL). dialysis the plasma concentration of aluminoxamine fell to 2.2 micro mol/L (1.3 micro g/mL), indicating that the aluminoxamine complex is dialysable. In patients with 50mg/24h continuous intravenous infusion of 50mg/kg/24h thalassemia desferrioxamine resulted in regular plasma desferrioxamine state levels of 7.4 micro mol/L. Elimination of plasma desferrioxamine was biphasic with an average distribution half-life of 0.28 hours and an apparent terminal half-life of 3.0 hours. Total plasma clearance was 0.5 L/h/kg and distribution volume at a stable condition was estimated at 1.35 L/kg. Exposure to the main iron bonding metabolite was about 54% of that of desferrioxamine in terms of AUC. The apparent monoexponential half-life of metabolite elimination was 1.3 hours. Clinical studies Desferrioxamine was used as a comparator in a randomized, one-year clinical trial studying the use of another iron kelp (deferasirox) in patients with beta-thalassemia and transfusional hemosidosis. A total of 290 patients were treated with subcutaneous desferrioxamine at start doses of 20 to 60 mg/kg for 5 days per week. The study showed a dose-dependent effect of desferrioxamine on serum ferritin levels, liver iron concentration and iron excretion rate. Desferrioxamine was also used as a comparator in a second one-year randomized trial of deferasirox use in patients with sickle cell disease and transfusion hemosideosis. A total of 63 patients were treated with subcutaneous desferrioxamine at starting doses of 20 to 60 mg/kg at least 5 days per week. At the end of the study, the average change in liver iron concentration (LIC) was -0.7 mg of Fe/g dry weight. There is no relevant preclinical data for the prescriber in addition to those already included in other sections of the Product Characteristics Summary. Flask: Don't store above 25oC Reconstituted solution: Single use only. From a microbiological point of view, the product should be used immediately after reconstruction (start of treatment within 3 hours). When the reconstruction is carried out under validated aseptic conditions, the reconstituted solution can be stored for up to 24 hours at room temperature (25oC or less) before administration. If not used immediately, storage times in use and conditions before administration are the user's responsibility. The unused solution must be discarded. Each bottle contains a virtually white white lyophilisate provided in a clear glass bottle in a pack size of 10 (500 mg). Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks White City Place, 195 Wood Lane, London, W12 7FQ United Kingdom 31 October 1997 / 12 December 2000 23 July 2020