DEFEROXAMINE - deferoxamine mesylate injection, powder, lyophilized, for solution
Fresenius Kabi USA, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DEFEROXAMINE MESYLATE FOR INJECTION safely and effectively. See full prescribing information for DEFEROXAMINE MESYLATE FOR INJECTION.

DEFEROXAMINE MESYLATE for Injection, for intramuscular, intravenous, or subcutaneous use
Initial U.S. Approval: 1968

INDICATIONS AND USAGE

Deferoxamine Mesylate for Injection is an iron-chelating agent indicated:

- As an adjunct to standard measures for the treatment of acute iron intoxication. (1.1)
- For the treatment of transfusional iron overload in patients with chronic anemia. (1.2)

Limitations of Use
Deferoxamine Mesylate for Injection is not indicated for the treatment of primary hemochromatosis (since phlebotomy is the method of choice for removing excess iron in this disorder).

DOSAGE AND ADMINISTRATION

Acute Iron Intoxication: (2.1)

- Intramuscular Administration: Use for patients not in shock. Initial dose is 1,000 mg. Depending upon the clinical response, subsequent doses of 500 mg may be administered every 4 hours to 12 hours. Maximum dose is 6,000 mg in 24 hours.
- Intravenous Administration: Only for patients in a state of cardiovascular collapse. Initial dose is 1,000 mg at a rate not to exceed 15 mg/kg/hr. Depending upon the clinical response, subsequent doses of 500 mg may be administered every 4 hours to 12 hours at a rate of up to 125 mg/hr. Maximum dose is 6,000 mg in 24 hours

Chronic Iron Overload: (2.2)

- Subcutaneous Infusion: Average daily dose is between 20 and 60 mg/kg. In patients with serum ferritin level below 2,000 ng/mL require about 25 mg/kg/day. Patients with serum ferritin level between 2,000 and 3,000 ng/mL require about 35 mg/kg/day. Patients with higher serum ferritin may require up to 55 mg/kg/day.
- Intravenous Administration: 20 mg/kg/day to 40 mg/kg/day for pediatric patients and 40 mg/kg/day to 50 mg/kg/day over 8 hours to 12 hours in adults for 5 days to 7 days per week. In pediatric patients and adults, maximum dose should not exceed 40 mg/kg/day and 60 mg/kg/day, respectively.
- Intramuscular Administration: 500 mg to maximum daily dose of 1,000 mg.

See Full Prescribing Information for instructions on preparation of Deferoxamine Mesylate for Injection for administration. (2.3)
Vitamin C (up to 200 mg) increases availability of iron for chelation and may be given as an adjuvant to iron chelation therapy. (2.4)

DOSAGE FORMS AND STRENGTHS

For injection: 500 mg and 2 g of deferoxamine mesylate is a white to off-white lyophilized powder in single-dose vial for reconstitution (3)

CONTRAINDICATIONS

- Known hypersensitivity to the active substance. (4)
- Patients with severe renal disease or anuria. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: More common with rapid intravenous infusion. Administer intramuscularly or by slow subcutaneous or intravenous infusion. (5.1) Auditory and Ocular Toxicity: Have been reported when administered over prolonged periods of time, at high doses, or in patients with low

ferritin levels. (5.2)
- Renal Toxicity: Cases of acute renal failure, renal tubular disorders and increase in serum creatinine have occurred. Monitor patients for changes in renal function. (5.3)
- Respiratory Toxicity: Acute respiratory distress syndrome has occurred. Risk increased with high intravenous doses. Recommended daily dose should not be exceeded. (5.4)
- Growth Suppression: Has occurred in pediatric patients treated with high doses and concomitant low ferritin levels. Dose reduction may partially resume growth velocity to pre-treatment rates. (5.5)
- Serious Infections: Cases of mucormycosis and Yersinia infections, some fatal, have occurred. Discontinue Deferoxamine Mesylate for Injection and initiate appropriate treatment immediately. (5.6)
- Cardiac Dysfunction with Concomitant Use of Vitamin C: Avoid coadministration in patients with cardiac failure. Delay Vitamin C for one month after start of Deferoxamine Mesylate for Injection. Avoid exceeding 200 mg daily in adults. Monitor cardiac function with combined treatment. (5.7)
- Risks of Deferoxamine Mesylate for Injection Treatment in Patients with Aluminum Overload: Risks include neurological dysfunction (including seizures), dialysis dementia, and aggravation of hyperparathyroidism. (5.8)
- Effects on Ability to Drive and Use Machines: May cause dizziness. (5.9)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use effective contraception (5.10, 8.1, 8.3)

ADVERSE REACTIONS

Most common adverse reactions are injection reactions (local and systemic), hypersensitivity reactions, infections with Yersinia and Mucormycosis, cardiovascular, gastrointestinal, hematologic, hepatic, musculoskeletal, urogenital, nervous, respiratory, ocular and hearing. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi, USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Concurrent treatment with prochlorperazine may lead to temporary impairment of consciousness. (7.1)
- Imaging results may be distorted due to rapid urinary excretion of Deferoxamine Mesylate for Injection bound gallium-67. Discontinue Deferoxamine Mesylate for Injection 48 hours prior to scintigraphy. (7.2)

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed (8.2)
- Geriatric Use: Increased risk of ocular disorders (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Acute Iron Intoxication

Deferoxamine Mesylate for Injection is indicated as an adjunct to standard measures for the treatment of acute iron intoxication.

1.2 Chronic Iron Overload

Deferoxamine Mesylate for Injection is indicated for the treatment of transfusional iron overload in patients with chronic anemia.

1.3 Limitations of Use

Deferoxamine Mesylate for Injection is not indicated for the treatment of primary hemochromatosis (since phlebotomy is the method of choice for removing excess iron in this disorder).

2 DOSAGE AND ADMINISTRATION

The dosage (based on body weight in mg/kg/day), rates of administration, and mode of administration for both adults and pediatric patients are individually determined and adapted during the course of therapy based on the severity of the patient's iron overload. The minimum daily dose of Deferoxamine Mesylate for Injection is 20 mg/kg/day for both adults and pediatric patients. The maximum daily dose is 40 mg/kg/day for pediatric patients and 60 mg/kg/day for adults.

2.1 Recommended Dosage for Treatment of Acute Iron Intoxication for Adults and Pediatric Patients

Intramuscular (IM) Administration

Use for all patients not in shock.

The initial recommended dose of Deferoxamine Mesylate for Injection is 1,000 mg intramuscularly (IM) once. If needed based on the clinical response, administer subsequent doses of 500 mg every 4 hours to 12 hours. The maximum recommended daily dose is 6,000 mg in 24 hours.

Intravenous (IV) Administration

Administer Deferoxamine Mesylate for Injection intravenously (IV) to patients in a state of cardiovascular collapse and then only by slow infusion. As soon as the clinical condition of the patient permits, intravenous administration should be discontinued, and the drug should be administered intramuscularly.

The initial recommended IV dose of Deferoxamine Mesylate for Injection is 1,000 mg administered at an infusion rate of up to 15 mg/kg/hr. If needed based on the clinical response administer additional doses of 500 mg over 4 hours to 12 hours at a slower infusion rate of up to 125 mg/hr. The maximum recommended daily dose is 6,000 mg in 24 hours.

2.2 Recommended Dosage for Treatment of Chronic Iron Overload for Adults and Pediatric Patients

Subcutaneous Infusion Administration

The average daily dose of Deferoxamine Mesylate for Injection is usually between 20 and 60 mg/kg. In general patients with serum ferritin level below 2,000 ng/mL require about 25 mg/kg/day. Patients with serum ferritin level between 2,000 and 3,000 ng/mL require about 35 mg/kg/day. Patients with higher serum ferritin may require up to 55 mg/kg/day. It is not advisable 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 levels fall below 1,000 ng/mL, the risk of Deferoxamine Mesylate for Injection toxicity increases; it is important to monitor these patients particularly carefully and perhaps to consider lowering the total weekly dose. The doses specified here are the average daily doses. Since most patients use Deferoxamine Mesylate for Injection less than 7 days a week, the actual dose per infusion usually differs from the average daily dose; e.g. if an average daily dose of 40 mg/kg/day is required and the patient wears the pump 5 nights a week, each infusion should contain 56 mg/kg.

Slow subcutaneous infusion using a portable, light-weight infusion pump over a period of 8 to 12 hours is regarded as effective and especially convenient for ambulatory patients, but may also be given over a 24-hour period. Deferoxamine Mesylate for Injection should normally be used with the pump 5 to 7 times a week. Deferoxamine Mesylate for Injection is not formulated to support subcutaneous bolus injection.

Intravenous Administration

Deferoxamine Mesylate for Injection can be administered intravenously if needed in patients with intravenous access.

The recommended dose of Deferoxamine Mesylate for Injection in adults is 40 mg/kg/day to 50 mg/kg/day over 8 hours to 12 hours at a rate of up to 15 mg/kg/hour for 5 days to 7 days per week. Maximum dose is 60 mg/kg/day.

The recommended dose of Deferoxamine Mesylate for Injection in pediatric patients is 20 mg/kg/day to 40 mg/kg/day over 8 hours to 12 hours for 5 days to 7 days per week. The maximum recommended daily dose is 40 mg/kg/day until growth (body weight and linear growth) has ceased.

In case of missed doses, Deferoxamine Mesylate for Injection may be administered prior to or following same day blood transfusion (for example, 1 gram over 4 hours on the day of transfusion); however, the contribution of this mode of administration to iron balance is limited. Deferoxamine Mesylate for Injection should not be administered concurrently with the blood transfusion as this can lead to errors in interpreting side effects such as rash, anaphylaxis and hypotension.

Intramuscular Administration

If given intramuscularly, the recommended dose of Deferoxamine Mesylate for Injection is 500 mg to 1,000 mg per day. The maximum recommended daily dose is 1,000 mg per day.

2.3 Preparation

Reconstitute Deferoxamine Mesylate for Injection prior to administration. Deferoxamine Mesylate for Injection should be further diluted for intravenous infusion. Use appropriate aseptic technique.

Reconstitute each vial of Deferoxamine Mesylate for Injection with Sterile Water for Injection, USP per Table 1. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if visibly opaque particles, discoloration or foreign particles are observed. The reconstituted Deferoxamine Mesylate for Injection solution is an isotonic, clear and colorless to slightly-yellowish solution. Discard unused portion.

Table 1. Preparation of Deferoxamine Mesylate for Injection Prior to Administration

Vial Size	Route of Administration	Amount of Sterile Water for Injection, USP for Reconstitution	Concentration After Reconstitution
500 mg	Intramuscular	2 mL	213 mg/mL
500 mg	Intravenous*	5 mL	95 mg/mL**
500 mg	Subcutaneous	5 mL	95 mg/mL
2 grams	Intramuscular	8 mL	213 mg/mL
2 grams	Intravenous*	20 mL	95 mg/mL
2 grams	Subcutaneous	20 mL	95 mg/mL

*Intravenous route of administration requires further dilution with 150 mL of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP or Lactated Ringers Injection, USP

**Final concentration for intravenous administration is between 3 mg/mL to 3.5 mg/mL

If not used immediately, store at room temperature between 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F), for a maximum period of 24 hours. Do not refrigerate reconstituted solution.

2.4 Management of Vitamin C Deficiency

Patients with iron overload usually become vitamin C deficient, probably because iron oxidizes the vitamin. As an adjuvant to iron chelation therapy, vitamin C in doses up to 200 mg for adults may be given in divided doses, starting after an initial month of regular treatment with Deferoxamine Mesylate for Injection *[see Warnings and Precautions (5.7)]*. Vitamin C increases availability of iron for chelation. In general, 50 mg daily suffices for pediatric patients under 10 years old and 100 mg daily for older pediatric patients. Larger doses of vitamin C fail to produce any additional increase in excretion of iron complex.

3 DOSAGE FORMS AND STRENGTHS

For injection: 500 mg of deferoxamine mesylate (corresponding to 426.82 mg of deferoxamine as free base) is a white to off-white lyophilized powder in a single-dose vial for reconstitution.

For injection: 2 grams of deferoxamine mesylate (corresponding to 1.707 g of deferoxamine as free base) is a white to off-white lyophilized powder in a single-dose vial for reconstitution.

4 CONTRAINDICATIONS

Deferoxamine Mesylate for Injection is contraindicated in patients with:

- A history of a hypersensitivity reaction to deferoxamine or any of its inactive ingredients *[see Description (11)]*. Reactions have included anaphylaxis *[see*

Warnings and Precautions (5.1)].
- Severe renal disease or anuria since the drug and the iron chelate are excreted primarily by the kidney *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have occurred in Deferoxamine Mesylate for Injection-treated patients. Reactions have included flushing of the skin, urticaria, hypotension, and shock. These reactions typically occur when Deferoxamine Mesylate for Injection was administered by rapid intravenous injection. Therefore, administer Deferoxamine Mesylate for Injection intramuscularly or by slow subcutaneous or intravenous infusion.

5.2 Auditory and Ocular Toxicity

Ocular and auditory toxicities have been reported in Deferoxamine Mesylate for Injection-treated patients. The ocular toxicities observed have included blurring of vision; cataracts after prolonged administration in chronic iron overload; decreased visual acuity, including visual loss, visual defects, scotoma; impaired peripheral, color, and night vision; optic neuritis, cataracts, corneal opacities, and retinal pigmentary abnormalities. The auditory toxicities reported have been tinnitus and hearing loss, including high frequency sensorineural hearing loss. Risk factors for both ocular and auditory disturbances include prolonged treatment duration, higher doses, or low ferritin levels. In most cases, both ocular and auditory disturbances were reversible upon immediate cessation of treatment *[see Adverse Reactions (6)]*.

Visual acuity tests, slit-lamp examinations, funduscopy and audiometry are recommended periodically in patients treated for prolonged periods of time. Toxicity is more likely to be reversed if symptoms or test abnormalities are detected early.

5.3 Renal Toxicity

Renal toxicity, including increases in serum creatinine (possibly dose-related), acute renal failure and renal tubular disorders has occurred in Deferoxamine Mesylate for Injection-treated patients. Deferoxamine Mesylate for Injection is contraindicated in patients with severe renal disease *[see Contraindications (4)]*. Monitor serum creatinine to assess for changes in renal function.

5.4 Respiratory Toxicity

Acute respiratory distress syndrome has occurred in Deferoxamine Mesylate for Injection-treated patients following treatment with excessively high intravenous doses of Deferoxamine Mesylate for Injection in patients with acute iron intoxication or thalassemia. The recommended daily doses should therefore not be exceeded.

5.5 Growth Suppression

High doses of Deferoxamine Mesylate for Injection and concomitant low ferritin levels have also been associated with growth suppression in pediatric patients. After reduction of Deferoxamine Mesylate for Injection dose, growth velocity may partially resume to

pre-treatment rates. Monitor growth (weight and height) in pediatric patients treated with Deferoxamine Mesylate for Injection every 3 months.

5.6 Serious Infections

Yersinia Infections

Deferoxamine Mesylate for Injection may increase the risk of *Yersinia enterocolitica* and *Yersinia pseudotuberculosis* infections. Avoid starting Deferoxamine Mesylate for Injection treatment in patients with active Yersinia infections. Should Yersinia infection develop, interrupt Deferoxamine Mesylate for Injection treatment until the infection is resolved.

Mucormycosis

Cases of mucormycosis, some with a fatal outcome, have occurred in Deferoxamine Mesylate for Injection-treated patients. Signs or symptoms are specific to the site of infection. If mucormycosis is suspected, discontinue Deferoxamine Mesylate for Injection, conduct mycological testing, and treat immediately.

5.7 Cardiac Dysfunction with Concomitant Use of Vitamin C

Cardiac dysfunction has occurred in Deferoxamine Mesylate for Injection-treated patients with severe chronic iron overload following concomitant treatment with high doses of vitamin C (more than 500 mg daily in adults). The cardiac dysfunction was reversible when vitamin C was discontinued. The following precautions should be taken when vitamin C and Deferoxamine Mesylate for Injection are to be used concomitantly:

- Vitamin C supplements should not be given to patients with cardiac failure.
- Start supplemental vitamin C only after an initial month of regular treatment with Deferoxamine Mesylate for Injection.
- Give vitamin C only if the patient is receiving Deferoxamine Mesylate for Injection regularly, ideally soon after setting up the infusion pump.
- Do not exceed a daily vitamin C dose of 200 mg in adults, given in divided doses. In general, 50 mg daily suffices for pediatric patients under 10 years old and 100 mg for older pediatric patients.
- Clinical monitoring of cardiac function is advisable during such combined therapy.

5.8 Risks of Deferoxamine Mesylate for Injection Treatment in Patients with Aluminum Overload

Deferoxamine Mesylate for Injection may cause neurological dysfunction (including seizures) in patients with aluminum-related encephalopathy and receiving dialysis, possibly due to an acute increase in circulating aluminum *[see Adverse Reactions (6)]*.

Deferoxamine Mesylate for Injection may precipitate the onset of dialysis dementia.

Treatment with Deferoxamine Mesylate for Injection in the presence of aluminum overload may result in decreased serum calcium and aggravation of hyperparathyroidism.

5.9 Effects on Ability to Drive and Use Machines

Deferoxamine Mesylate for Injection may cause dizziness, which may impair the ability to

drive a car or operate machinery. Patients should not drive or operate machinery until they know how Deferoxamine Mesylate for Injection will affect their ability to engage in these activities.

5.10 Embryo-Fetal Toxicity

Based on findings in animals, Deferoxamine Mesylate for Injection can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of deferoxamine to pregnant mice and rabbits during the period of organogenesis caused adverse developmental outcomes including decreased fetal body weights and malformations at maternal doses less than those in patients at maximum recommended human dose (MRHD). Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Deferoxamine Mesylate for Injection and for one month after the last dose *[see Use in Specific Populations (8.1, 8.3), Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*
- Auditory and Ocular Toxicity *[see Warnings and Precautions (5.2)]*
- Renal Toxicity *[see Warnings and Precautions (5.3)]*
- Respiratory Toxicity *[see Warnings and Precautions (5.4)]*
- Growth Suppression *[see Warnings and Precautions (5.5)]*
- Serious Infections *[see Warnings and Precautions (5.6)]*
- Cardiac Dysfunction with Concomitant Use of Vitamin C *[see Warnings and Precautions (5.7)]*
- Risks of Deferoxamine Mesylate for Injection Treatment in Patients with Aluminum Overload *[see Warnings and Precautions (5.8)]*
- Effects on Ability to Drive and Use Machines *[see Warnings and Precautions (5.9)]*

6.1 Clinical Trials Experience

The following adverse reactions associated with the use of deferoxamine mesylate for injection were identified in clinical studies or postmarketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

At the Injection Site: Localized irritation, pain, burning, swelling, induration, infiltration, pruritus, erythema, wheal formation, eschar, crust, vesicles, local edema. Injection site reactions may be associated with systemic allergic reactions *([see Body as a Whole, below)]*

Hypersensitivity Reactions and Systemic Allergic Reactions: Generalized rash, urticaria, anaphylactic reaction with or without shock, angioedema

Body as a Whole: Local injection site reactions may be accompanied by systemic reactions like arthralgia, fever, headache, myalgia, nausea, vomiting, abdominal pain, or

asthma

Infections: Yersinia, mucormycosis

Cardiovascular: Tachycardia, hypotension, shock

Digestive: Abdominal discomfort, diarrhea, nausea, vomiting

Hematologic: Blood dyscrasia (thrombocytopenia, leukopenia)

Hepatic: Increased transaminases, hepatic dysfunction

Musculoskeletal: Muscle spasms. Growth retardation and bone changes (e.g., metaphyseal dysplasia)

Nervous System: Neurological disturbances, including dizziness, peripheral sensory, motor, or mixed neuropathy, paresthesias, seizures; exacerbation or precipitation of aluminum-related dialysis encephalopathy

Special Senses: High-frequency sensorineural hearing loss, tinnitus visual disturbances including acuity, blurred vision, loss of vision, dyschromatopsia, night blindness, visual field defects, scotoma, retinopathy (pigmentary degeneration), optic neuritis, and cataracts

Respiratory: Acute respiratory distress syndrome (with dyspnea, cyanosis, and/or interstitial infiltrates)

Skin: Generalized rash

Urogenital: Dysuria, acute renal failure, increased serum creatinine and renal tubular disorders

7 DRUG INTERACTIONS

7.1 Prochlorperazine

Concurrent treatment with Deferoxamine Mesylate for Injection and prochlorperazine, a phenothiazine derivative, may lead to temporary impairment of consciousness.

7.2 Gallium-67

Imaging results may be distorted because of the rapid urinary excretion of Deferoxamine Mesylate for Injection-bound gallium-67. Discontinue Deferoxamine Mesylate for Injection 48 hours prior to scintigraphy.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Deferoxamine Mesylate for Injection use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriages or adverse maternal or fetal outcomes.

In animal reproduction studies subcutaneous administration of deferoxamine to

pregnant animals (mice or rabbits) during organogenesis at doses approximately ≥0.2- (mice) and ≥0.7 (rabbits) times the maximum recommended human dose resulted in maternal toxicity and adverse developmental outcomes *(see Data)*. Advise pregnant women of the potential risk to a fetus. Consider the benefits and risks of Deferoxamine Mesylate for Injection for the mother and possible risks to the fetus when prescribing Deferoxamine Mesylate for Injection to a pregnant woman.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an embryo-fetal developmental study in mice, pregnant animals administered subcutaneous doses of deferoxamine at 180, and 540 mg/kg/day from gestation day 7 to gestation day 12 resulted in a dose dependent delay and irregularities of fetal skeletal maturation at doses ≥0.2 times the MRHD. At the highest dose of 540 mg/kg, in 1/23 fetuses had a unilateral lesion to the eye lens (approximately 0.5 times the MRHD).

In the embryo-fetal developmental studies in rabbits, pregnant animals administered subcutaneous doses of deferoxamine either 200 mg/kg or 200, 300, and 540 mg/kg from gestation day 6 to gestation day 14 resulted in maternal toxicity and embryo-fetal developmental effects at 0.7 times the MRHD). Maternal toxicity included reduced fetal body weights and embryo-fetal effects included malformations of spina bifida, and increased incidence of abnormally ossified ribs and vertebrae.

No maternal toxicity or embryo-fetal effects were observed in rats at deferoxamine doses tested (up to 0.9 times the MRHD).

8.2 Lactation

There are no data on the presence of deferoxamine or its metabolite in either human or animal milk, the effects on the breastfed child, or the effects on milk production. It is not known whether deferoxamine is excreted in human milk. Because of the potential for serious adverse reactions in the breastfed child, advise patients not to breastfeed during treatment with Deferoxamine Mesylate for Injection, and for one week after the last dose.

8.3 Females and Males of Reproductive Potential

Based on animal data, Deferoxamine Mesylate for Injection can cause malformations at doses less than the human dose *[see Use in Specific Populations (8.1)].*

Contraception

Females

Deferoxamine Mesylate for Injection can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)].* Advise female patients of reproductive potential to use effective contraception during treatment with Deferoxamine Mesylate for Injection and for one month after the last dose.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients 3 years of age and older have been established for the treatment of acute iron intoxication and for the treatment of transfusional iron overload in patients with chronic anemia. Safety and effectiveness in pediatric patients under the age of 3 years have not been established.

Iron mobilization with Deferoxamine Mesylate for Injection is relatively poor in patients under the age of 3 years with relatively little iron overload. Deferoxamine Mesylate for Injection is not recommended for use. The drug should ordinarily not be given to these patients unless significant iron mobilization (e.g., 1 mg or more of iron per day) can be demonstrated.

High doses of Deferoxamine Mesylate for Injection and concomitant low ferritin levels have been associated with growth suppression in pediatric patients. Monitor weight and height in pediatric patients receiving Deferoxamine Mesylate for Injection every 3 months *[see Warnings and Precautions (5.5), Adverse Reactions (6.1)].*

8.5 Geriatric Use

Clinical Studies of Deferoxamine Mesylate for Injection did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from the younger subjects. Postmarketing reports suggest a possible trend for an increased risk of eye disorders in the geriatric population, specifically the occurrence of color blindness, maculopathy, and scotoma.

However, it is unclear if these eye disorders were dose related. Although the number of reports was very small, certain elderly patients may be predisposed to eye disorders when taking Deferoxamine Mesylate for Injection. Postmarketing reports also suggest that there may be an increased risk of deafness and hearing loss in the geriatric population *[see Adverse Reactions (6)]*. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Renal Impairment

Deferoxamine Mesylate for Injection is contraindicated in patients with severe renal disease *[see Contraindications (4)]*.

For patients with renal impairment, dose selection should usually start at the low end of the dosing range.

Deferoxamine can cause increases in serum creatinine (possibly dose-related), acute renal failure and renal tubular disorders *[(see Warnings and Precautions (5.3)]*. Monitor patients for changes in renal function.

8.7 Hepatic Impairment

For patients with hepatic impairment, dose selection should usually start at the low end of the dosing range.

10 OVERDOSAGE

Acute Toxicity

Intravenous LD_{50}s (mg/kg): mice, 287; rats, 329.

Inadvertent administration of an overdose or inadvertent intravenous bolus administration/rapid intravenous infusion may be associated with hypotension, tachycardia and gastrointestinal disturbances; acute but transient loss of vision, aphasia, agitation, headache, nausea, pallor, CNS depression, including coma, bradycardia and acute renal failure have been reported.

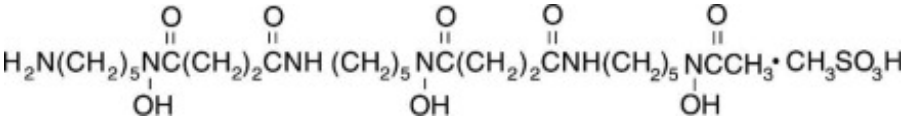
Acute respiratory distress syndrome has been reported following treatment with excessively high intravenous doses of Deferoxamine Mesylate for Injection in patients with acute iron intoxication and in patients with thalassemia.

There is no specific antidote for Deferoxamine Mesylate for Injection overdose. In case of overdose, discontinue Deferoxamine Mesylate for Injection and provide symptomatic supportive care.

Deferoxamine Mesylate for Injection is readily dialyzable.

11 DESCRIPTION

Deferoxamine Mesylate for Injection, USP is an iron-chelating agent, available in vials for injection via intramuscular, subcutaneous, and intravenous administration. Deferoxamine Mesylate for Injection, USP is supplied as vials containing 500 mg and 2 g of deferoxamine mesylate USP (corresponding to 426.82 mg and 1.707 g of deferoxamine as free base) in sterile, lyophilized form. Deferoxamine mesylate is *N*- [5-[3-[(5-aminopentyl)hydroxycarbamoyl]propionamido]pentyl]-3-[[5-(*N*-hydroxyacetamido)pentyl]carbamoyl]propionohydroxamic acid monomethanesul-fonate (salt), and its structural formula is:



Deferoxamine mesylate is a white to almost white powder. It is freely soluble in water and slightly soluble in methanol. Its molecular weight is 656.79 g/mol.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Deferoxamine Mesylate for Injection chelates iron by forming a stable complex that prevents the iron from entering into further chemical reactions. It readily chelates iron from ferritin and hemosiderin but not readily from transferrin; it does not combine with the iron from cytochromes and hemoglobin.

Deferoxamine Mesylate for Injection does not cause any demonstrable increase in the excretion of electrolytes or trace metals. Theoretically, 100 parts by weight of Deferoxamine Mesylate for Injection is capable of binding approximately 8.5 parts by

weight of ferric iron.

12.3 Pharmacokinetics

Deferoxamine Mesylate for Injection is metabolized principally by plasma enzymes, but the pathways have not yet been defined. The chelate is readily soluble in water and passes easily through the kidney, giving the urine a characteristic reddish color. Some is also excreted in the feces via the bile.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in animals have not been performed with Deferoxamine Mesylate for Injection. Cytotoxicity may occur, since Deferoxamine Mesylate for Injection has been shown to inhibit DNA synthesis *in vitro*.

Deferoxamine Mesylate for Injection was not mutagenic when tested in an in vitro bacterial reverse mutation (Ames) and was not genotoxic in an in vivo micronucleus assay in rats.

Animal studies to assess fertility effects have not been conducted.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Deferoxamine Mesylate for Injection, USP is supplied in single-dose vials containing 500 mg and 2 g of deferoxamine mesylate (corresponding to 426.82 mg and 1.707 g of deferoxamine as free base) as a sterile, white to off-white lyophilized powder.

Product No.	**NDC No.**	**Strength**	**Vial size**
509710	63323-597-10	500 mg per vial	10 mL vial packaged individually.
509930	63323-599-30	2 grams per vial	30 mL vial packaged individually.

Storage and Handling

STORE AT: 20ºC to **25**°C (**68**ºF to **77**°F) [see USP Controlled Room Temperature].

The container closure is not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Caution patients about the potential allergic reactions associated with rapid intravenous administration of Deferoxamine Mesylate for Injection and the need for monitoring allergic reactions during treatment *[see Warnings and Precautions (5.1)]*.

Caution patients about the potential auditory and ocular toxicities due to prolonged use of Deferoxamine Mesylate for Injection, conduct auditory testing and ophthalmic testing at regular intervals. Advise patients to contact their healthcare provider if they develop

visual or auditory changes during treatment *[see Warnings and Precautions (5.2)]*.

Caution patients about the potential for kidney toxicity when taking Deferoxamine Mesylate for Injection and the need for kidney function test to monitor for increase in serum creatinine *[see Warnings and Precautions (5.3)]*.

Inform patients that if they have difficulty in breathing during treatment, they should inform the health care provider as this is a symptom of acute respiratory distress syndrome which can occur with excessively high intravenous doses of Deferoxamine Mesylate for Injection *[see Warnings and Precautions (5.4)]*.

Caution pediatric patients and their caregivers that child treated with Deferoxamine Mesylate for Injection could have slower than normal growth and the need to monitor for body weight and height every 3 months *[see Warnings and Precautions (5.5)]*.

Caution patients about the increased risk of bacterial infections (*Yersinia enterocolitica and Yersinia pseudotuberculosis*) with Deferoxamine Mesylate for Injection treatment and the need for treatment discontinuation until the infection is resolved *[see Warnings and Precautions (5.6)]*.

Caution patients about the potential risk of fungal infections (M*ucormycosis*) when receiving Deferoxamine Mesylate for Injection treatment and the need for treatment discontinuation, mycological tests and required treatment for treating the infection *[see Warnings and Precautions (5.6)]*.

Caution patients about the potential impairment of cardiac function when taking Deferoxamine Mesylate for Injection concomitantly with high doses of Vitamin C (more than 500 mg daily in adults). Inform adult patients not to exceed a daily Vitamin C dose of 200 mg given in divided doses. Inform pediatric patients under 10 years of age and older pediatric patients or their care takers not to exceed a daily Vitamin C of 50 mg and 100 mg, respectively. *[see Dosage and Administration (2.4) and Warnings and Precautions (5.7)]*.

Inform patients with cardiac failure not to take Vitamin C supplements when on treatment with Deferoxamine Mesylate for Injection *[see Dosage and Administration (2.4) and Warnings and Precautions (5.7)]*.

Caution patients with aluminum-related encephalopathy and receiving dialysis about potential neurological dysfunction *[see Warnings and Precautions (5.8)]*.

Cautions patients that treatment with Deferoxamine Mesylate for Injection in the presence of aluminum overload may result in decreased serum calcium and aggravation of hyperparathyroidism *[see Warnings and Precautions (5.8)]*.

Inform patients that they should refrain from driving or operating potentially hazardous machines if they experience dizziness or other nervous system disturbances, or impairment of vision or hearing *[see Warnings and Precautions (5.9)]*.

Advise patients to inform the healthcare provider if they have received prochlorperazine prior to Deferoxamine Mesylate for Injection treatment as this may lead to temporary impairment of consciousness *[see Drug Interactions (7.1)]*.

Inform patients that if they are going for any imaging tests while receiving Gallium-67 and Deferoxamine Mesylate for Injection concomitantly it can result in reports with distorted images *[see Drug Interactions (7.2)]*.

Inform patients that their urine may occasionally show a reddish discoloration.

Embryo-fetal Toxicity:

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.10), Use in Specific Populations (8.1, 8.3)].*

Advise females of reproductive potential to use effective contraceptive during treatment with Deferoxamine Mesylate for Injection and for one month after the last dose *[see Use in Specific Populations (8.3)].*

Lactation

Advise patients to avoid breastfeeding while taking Deferoxamine Mesylate for Injection and for one week after the final dose *[see Use in Specific Populations (8.2)]*.

Lake Zurich, IL 60047

www.fresenius-kabi.com/us

451101F

PACKAGE LABEL - PRINCIPAL DISPLAY - Deferoxamine Mesylate 500 mg per vial Vial Label

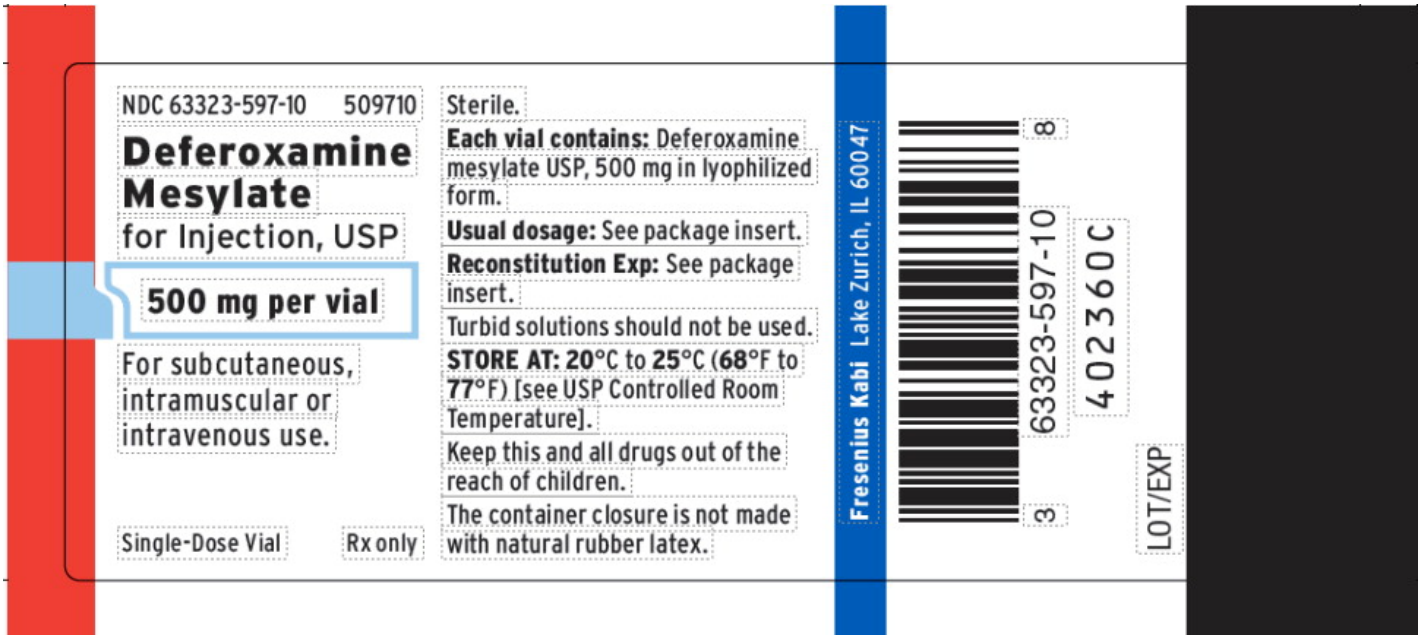
NDC 63323-597-10 509710

Deferoxamine Mesylate for Injection, USP

500 mg per vial

For subcutaneous, intramuscular or intravenous use.

Rx only



PACKAGE LABEL - PRINCIPAL DISPLAY - Deferoxamine Mesylate 500 mg per vial Carton Panel

NDC 63323-597-10 509710

Deferoxamine Mesylate for Injection, USP

500 mg per vial

For subcutaneous, intramuscular or intravenous use.

Rx only

Single-Dose Vial

62947C

PACKAGE LABEL - PRINCIPAL DISPLAY - Deferoxamine Mesylate 2 grams per vial Vial Label

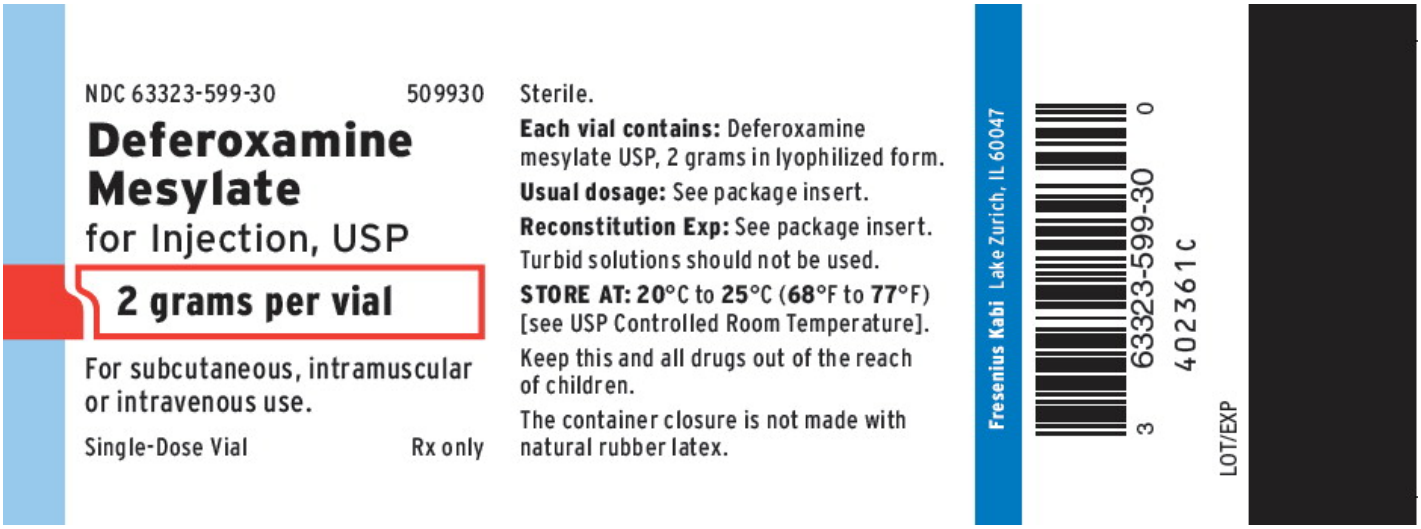
NDC 63323-599-30 509930

Deferoxamine Mesylate for Injection, USP

2 grams per vial

For subcutaneous, intramuscular or intravenous use.

Single-Dose Vial
Rx only



PACKAGE LABEL - PRINCIPAL DISPLAY - Deferoxamine Mesylate 2 grams per vial Carton Panel

NDC 63323-599-30 509930

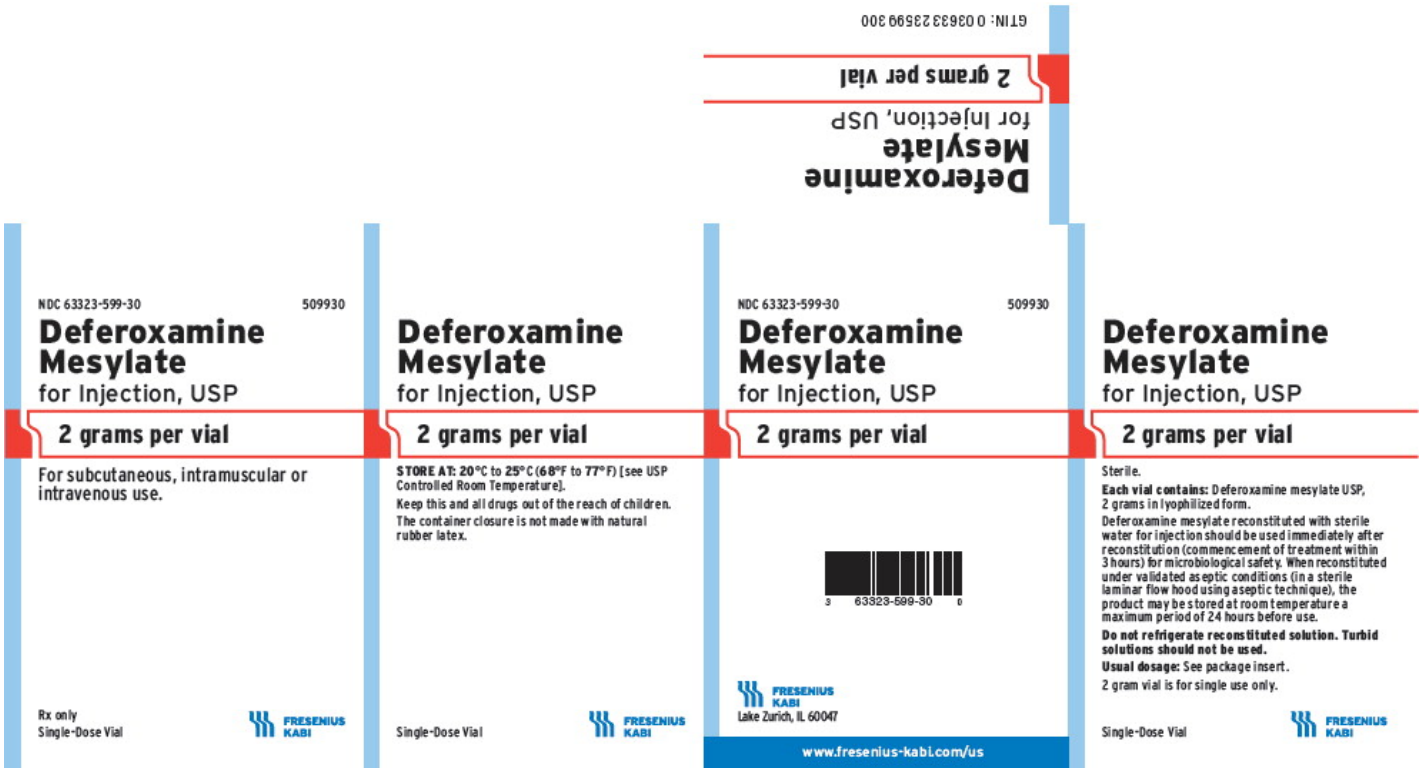
Deferoxamine Mesylate for Injection, USP

2 grams per vial

For subcutaneous, intramuscular or intravenous use.

Rx only

Single-Dose Vial



DEFEROXAMINE

deferoxamine mesylate injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63323-599
Route of Administration	INTRAVENOUS, INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEFEROXAMINE MESYLATE (UNII: V9TKO7EO6K) (DEFEROXAMINE - UNII:J06Y7MXW4D)	DEFEROXAMINE MESYLATE	95 mg in 1 mL

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:63323-599-30	1 in 1 BOX	12/15/2009	
1		21.1 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA078718	12/15/2009	

DEFEROXAMINE

deferoxamine mesylate injection, powder, lyophilized, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63323-597
Route of Administration	INTRAVENOUS, INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DEFEROXAMINE MESYLATE (UNII: V9TKO7EO6K) (DEFEROXAMINE - UNII:J06Y7MXW4D)	DEFEROXAMINE MESYLATE	95 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:63323-597-10	1 in 1 BOX	12/15/2009	
1		5.3 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA078718	12/15/2009	

Labeler - Fresenius Kabi USA, LLC (608775388)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi USA, LLC		840771732	ANALYSIS(63323-597, 63323-599) , MANUFACTURE(63323-597, 63323-599)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi USA, LLC		023648251	ANALYSIS(63323-597, 63323-599) , MANUFACTURE(63323-597, 63323-599)