

**CENTER FOR DRUG  
EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER:**

**76-019**

**FINAL PRINTED LABELING**



## INDICATIONS AND USAGE

Deferoxamine mesylate for injection is indicated for the treatment of acute iron intoxication and of chronic iron overload due to transfusion-dependent anemias.

### Acute Iron Intoxication

Deferoxamine mesylate is an adjunct to, and not a substitute for, standard measures used in treating acute iron intoxication, which may include the following: induction of emesis with syrup of ipecac; 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

Deferoxamine mesylate can promote iron excretion in patients with secondary iron overload from multiple transfusions (as may occur in the treatment of some chronic anemias, including thalassemia). Long-term therapy with deferoxamine mesylate slows accumulation of hepatic iron and retards or eliminates progression of hepatic fibrosis.

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

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

### CONTRAINDICATIONS

Deferoxamine mesylate is contraindicated in patients with severe renal disease or anuria, since the drug and the iron chelate are excreted primarily by the kidney (See Warnings).

### WARNINGS

Ocular and auditory disturbances have been reported when deferoxamine mesylate was administered over prolonged periods of time, at high doses, or in patients with low ferritin levels. The ocular disturbances observed have been 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 abnormalities reported have been tinnitus and hearing loss including high frequency sensorineural hearing loss. In most cases, both ocular and auditory disturbances were reversible upon immediate cessation of treatment (see PRECAUTIONS/Information for Patients and ADVERSE REACTIONS/Special Senses).

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.

High doses of deferoxamine mesylate and concomitant low ferritin levels have also been associated with growth retardation. After reduction of deferoxamine mesylate dose, growth velocity may partially resume to pretreatment rates (see PRECAUTIONS/Pediatric Use).

Adult respiratory distress syndrome, also reported in children, has been described following treatment with excessively high intravenous doses of deferoxamine mesylate in patients with acute iron intoxication or thalassemia.

### PRECAUTIONS

#### General

Flushing of the skin, urticaria, hypotension, and shock have occurred in a few patients when deferoxamine mesylate was administered by rapid intravenous injection. THEREFORE, DEFEROXAMINE MESYLATE SHOULD BE GIVEN INTRAMUSCULARLY OR BY SLOW SUBCUTANEOUS OR INTRAVENOUS INFUSION.

Iron overload increases susceptibility of patients to *Yersinia enterocolitica* and *Yersinia pseudotuberculosis* infections. In some rare cases, treatment with deferoxamine mesylate has enhanced this susceptibility, resulting in generalized infections by providing this bacteria with a siderophore otherwise missing. In such cases, deferoxamine mesylate treatment should be discontinued until the infection is resolved.

In patients receiving deferoxamine mesylate, rare cases of mucormycosis, some with a fatal outcome, have been reported. If any of the suspected signs or symptoms occur, deferoxamine mesylate should be discontinued, mycological tests carried out and appropriate treatment instituted immediately.

In patients with severe chronic iron overload, impairment of cardiac function has been reported following concomitant treatment with deferoxamine mesylate and 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 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.

- Give vitamin C only if the patient is receiving deferoxamine mesylate 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.

- Clinical monitoring of cardiac function is advisable during such combined therapy.

In patients with aluminum-related encephalopathy, high doses of deferoxamine mesylate may exacerbate neurological dysfunction (seizures), probably owing to an acute increase in circulating aluminum. Deferoxamine mesylate may precipitate the onset of dialysis dementia. Treatment with deferoxamine mesylate in the presence of aluminum overload may result in decreased serum calcium and aggravation of hyperparathyroidism.

#### Drug Interactions

**Vitamin C:** 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 (see PRECAUTIONS). Vitamin C increases availability of iron for chelation. In general, 50 mg daily suffices for children under 10 years old and 100 mg daily for older children. Larger doses of vitamin C fail to produce any additional increase in excretion of iron complex.

**Prochlorperazine:** Concurrent treatment with deferoxamine mesylate and prochlorperazine, a phenothiazine derivative, may lead to temporary impairment of consciousness.

**Gallium-67:** Imaging results may be distorted because of the rapid urinary excretion of deferoxamine mesylate-bound gallium-67. Discontinuation of deferoxamine mesylate 48 hours prior to scintigraphy is advisable.

#### Information for Patients

Patients experiencing dizziness or other nervous system disturbances, or impairment of vision or hearing, should refrain from driving or operating potentially hazardous machines (see ADVERSE REACTIONS).

Patients should be informed that occasionally their urine may show a reddish discoloration.

#### Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in animals have not been performed with

deferoxamine mesylate.

Cytotoxicity may occur, since deferoxamine mesylate has been shown to inhibit DNA synthesis *in vitro*.

#### Pregnancy Category C

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

There are no adequate and well-controlled studies in pregnant women. Deferoxamine mesylate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

#### Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when deferoxamine mesylate is administered to a nursing woman.

#### Pediatric Use

Pediatric patients receiving deferoxamine mesylate should be monitored for body weight and growth every 3 months.

Safety and effectiveness in pediatric patients under the age of 3 years have not been established (see INDICATIONS AND USAGE, WARNINGS, PRECAUTIONS/Drug Interactions/Vitamin C, and ADVERSE REACTIONS).

### ADVERSE REACTIONS

The following adverse reactions have been observed, but there are not enough data to support an estimate of their frequency.

**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.

Rare infections with *Yersinia* and *Mucormycosis* have been reported in association with deferoxamine mesylate use (see PRECAUTIONS).

**Cardiovascular:** tachycardia, hypotension, shock.

**Digestive:** abdominal discomfort, diarrhea, nausea, vomiting.

**Hematologic:** blood dyscrasia (e.g., Cases of thrombocytopenia and/or leukopenia



Fliptop Vial

For single use only.

NDC 0074-2336-10

**Deteroxamine Mesylate**  
for Injection, USP

**500 mg**

**R** only

Reconstituted Exp.: See insert. Turbid solutions should not be used. Do not store above 25°C (77°F). Discard unused portion.

Exp/Lot

For S.C., I.M., or I.V. Use  
ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

RAO6333-5/01

**MAR 17 2004**

**APPROVAL**



**Deferoxamine Mesylate**  
**for Inj., USP**  
**500 mg/vial**

10/6-19C36/01 RAO636

Deferoxamine mesylate reconstituted with Sterile Water for Injection should be used immediately after reconstitution (commencement of treatment within 3 hours) for microbiological safety. When reconstituted under validated aseptic conditions (in a sterile laminar flow hood using aseptic technique), the product may be stored at room temperature for a maximum period of 24 hours before use. Do not refrigerate reconstituted solution. Turbid solutions should not be used.  
**Usual Dosage:** For full directions see package insert.  
 Keep this and all drugs out of the reach of children.  
**Do not store above 25°C (77°F).**

©Abbott 2001



(01) 1 030074 233610 6

Printed in USA

**Deferoxamine Mesylate**  
**for Injection, USP**  
**500 mg/vial**

**4 Flip-top Vials**  
**Deferoxamine Mesylate**  
**for Injection, USP**  
**500 mg/vial**  
**Rx only**

NDC 0074-2336-10  
 D110

Each vial contains deferoxamine mesylate USP, 500 mg in lyophilized form.  
 For subcutaneous, intramuscular or intravenous administration. For single use only. Discard unused portion.  
**ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA**

**Deferoxamine Mesylate**  
**for Injection, USP**  
**500 mg/vial**

**4WU 2.1 QVM**

**APPROVAL**

