DESFEROXAMINE

Class: Antidote; Chelating Agent

Indications: Adjunct in the treatment of acute iron intoxication; treatment of chronic iron overload secondary to multiple transfusions.

Available dosage form in the hospital:

- DESFEROXAMINE 500MG VIAL

Dosage:

-Acute iron toxicity: Note: The I.V. route is used when severe toxicity is evidenced by cardiovascular collapse or systemic symptoms (coma, shock, metabolic acidosis, or gastrointestinal bleeding) or potentially severe intoxications (peak serum iron level >500 mcg/dL) (Perrone, 2011). When severe symptoms are not present, the I.M. route may be used (per the manufacturer).

-I.M., I.V.: Initial: 1000 mg, may be followed by 500 mg every 4 hours for 2 doses; subsequent doses of 500 mg have been administered every 4-12 hours based on clinical response (maximum recommended dose: 6000 mg/day [per manufacturer])

-*Canadian labeling:*

-I.M.: Initial: 90 mg/kg/dose (maximum/dose: 2000 mg) followed by 45 mg/kg every 4-12 hours as needed (maximum: 6000 mg/24 hours)

-I.V.: 15 mg/kg/hour up to a maximum of 80 mg/kg/dose or maximum of 6000 mg/24 hours

-Chronic iron overload:

- I.M.: 500-1000 mg/day (maximum: 1000 mg/day)
- I.V.: 40-50 mg/kg/day (maximum: 60 mg/kg/day) over 8-12 hours for 5-7 days per week
- SubQ: 1000-2000 mg/day or 20-40 mg/kg/day over 8-24 hours
- Unlabeled dosing: I.V., SubQ: 25-50 mg/kg over 8-10 hours 5-7 days per week.
- *Canadian labeling:* I.V., SubQ: 1000-4000 mg/day (20-60 mg/kg/day) over ~12 hours (may further increase iron excretion with infusion at the same dose over 24 hours). SubQ infusions are administered 4-7 days per week based on the degree of iron overload.

-Diagnosis of aluminum-induced toxicity with CKD (unlabeled u; K/DOQI guidelines, 2003se): I.V.: Test dose: 5 mg/kg during the last hour of dialysis if serum aluminum levels are 60-200 mcg/L, or clinical signs/symptoms of toxicity, or aluminum exposure prior to parathyroid surgery. Measure aluminum just prior to deferoxamine; remeasure 2 days later (test is positive if serum aluminum is ≥50 mcg/L). Do not use if aluminum serum levels are >200 mcg/L.

-*Canadian labeling:* **Note:** Measure serum aluminum levels prior to and after administration of deferoxamine. I.V.: Test dose: 5 mg/kg/dose (infusion rate not to exceed 15 mg/kg/hour) following hemodialysis (preferred) or during the last hour of dialysis if serum aluminum levels are >60 mcg/L in association with serum ferritin levels >100 mcg/L; continuous rise in serum aluminum over the next 24-48 hours suggests overload. Remeasure serum aluminum levels prior to next hemodialysis, test is considered positive if serum aluminum levels increase >150 mcg/L above baseline.

-Treatment of aluminum toxicity with CKD: (unlabeled use; K/DOQI guidelines, 2003):I.V.:

Administer after diagnostic deferoxamine test dose. **Note:** The risk for deferoxamine-associated neurotoxicity is increased if aluminum serum levels are >200 mcg/L; withhold deferoxamine and administer intensive dialysis until <200 mcg/L.

- Aluminum rise ≥300 mcg/L: 5 mg/kg once a week 5 hours before dialysis for 4 months
- Aluminum rise <300 mcg/L: 5 mg/kg once a week during the last hour of dialysis for 2 months

-*Canadian labeling:* Treatment should be considered for symptomatic patients with serum aluminum levels >60 mcg/L and a positive deferoxamine test dose.

- Hemodialysis: I.V.: 5 mg/kg/dose (infusion rate not to exceed 15 mg/kg/hour) once weekly for 3 months following hemodialysis (preferred) or during the last hour of dialysis administered. Withhold treatment for 1 month then perform deferoxamine test. Further treatment is not recommended if 2 consecutive tests (performed 1 month apart) yield an increase in serum aluminum levels <75 mcg/L.
- Continuous ambulatory or cyclic peritoneal dialysis: Intraperitoneal (preferred), I.M., SubQ infusion (slow), or I.V. infusion (slow): 5 mg/kg/dose once weekly prior to final daily exchange

Geriatric

Refer to adult dosing. May initiate at the lower end of the dosing range.

Renal Impairment:

-Severe renal disease or anuria: Use is contraindicated in the manufacturer's U.S. labeling.

*The following adjustments have been used by some clinicians (Aronoff, 2007): Adults:

- Clcr >50 mL/minute: No adjustment required
- Clcr 10-50 mL/minute, CRRT: Administer 25% to 50% of normal dose
- Clcr<10 mL/minute, hemodialysis, peritoneal dialysis: Avoid use

Hepatic Impairment:

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Common side effect:

Cardiovascular: Flushing, hypotension, shock, tachycardia
Central nervous system: Dizziness, encephalopathy (aluminum toxicity/dialysis-related), fever, headache, seizure
Dermatologic: Angioedema, rash, urticaria
Endocrine & metabolic: Growth retardation (children), hyperparathyroidism (aggravated), hypocalcemia
Gastrointestinal: Abdominal discomfort, abdominal pain, diarrhea, nausea, vomiting
Genitourinary: Dysuria, urine discoloration (reddish color)
Hematologic: Leukopenia, thrombocytopenia
Hepatic: Hepatic dysfunction, transaminases increased
Local: Injection site: Burning, crust, edema, erythema, eschar, induration, infiltration, irritation, pain, pruritus, swelling, vesicles, wheal formation
Neuromuscular & skeletal: Arthralgia, metaphyseal dysplasia (children <3 years; dose related), muscle spasms, myalgia, neuropathy (peripheral, sensory, motor, or mixed), paresthesia
Ocular: Blurred vision, cataract, corneal opacities, dyschromatopsia, loss of vision, night blindness, optic neuritis, peripheral vision impaired, retinal pigment abnormalities, scotoma, visual acuity decreased, visual field defects
Otic: Hearing loss, tinnitus
Renal: Acute renal failure, renal tubular disorders, serum creatinine increased
Respiratory: Acute respiratory distress syndrome (dyspnea, cyanosis, and/or interstitial infiltrates), asthma
Miscellaneous: Anaphylaxis (with or without shock), hypersensitivity reaction, infections (Yersinia, mucormycosis)

Pregnancy Risk Factor: C.