Reference number(s)
4700-A

Standard Medicare Part B Management deferoxamine-Desferal

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Desferal	deferoxamine mesylate

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1,2]

Desferal and deferoxamine mesylate is indicated:

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

Compendial Uses[3,4,7]

- Aluminum toxicity in patients undergoing dialysis
- Iron toxicity in patients undergoing dialysis
- Malaria
- Porphyria
- Hereditary hemochromatosis

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All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

Transfusional iron overload in members with chronic anemia:

- Initial requests: Pretreatment serum ferritin level
- Continuation requests: Current serum ferritin level

Coverage Criteria

Transfusional Iron Overload in Chronic Anemia[1,2,5,6]

Authorization of 12 months may be granted for treatment of transfusional iron overload in members with chronic anemia when the pretreatment serum ferritin level is consistently greater than 1000 micrograms per liter (mcg/L).

Aluminum Toxicity in Members Undergoing Dialysis[3-5]

Authorization of 12 months may be granted for treatment of aluminum toxicity in members undergoing dialysis.

Iron Toxicity in Members Undergoing Dialysis[3]

Authorization of 12 months may be granted for treatment of iron toxicity in members undergoing dialysis.

Malaria[3]

Authorization of 30 days may be granted for treatment of malaria.

Porphyria[3]

Authorization of 12 months may be granted for treatment of porphyria when phlebotomy is contraindicated.

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Hereditary Hemochromatosis[4,7]

Authorization of 12 months may be granted for treatment of hereditary hemochromatosis when phlebotomy is not an option (e.g., poor venous access, poor candidate due to underlying medical disorders) or the member had an unsatisfactory response to phlebotomy.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Transfusional Iron Overload in Chronic Anemia

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat transfusional iron overload in members with chronic anemia.
- The member is receiving benefit from therapy. Benefit is defined as a decrease in serum ferritin levels as compared to pretreatment baseline.

Aluminum Toxicity in Members Undergoing Dialysis

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat aluminum toxicity in members undergoing dialysis.
- The member is receiving benefit from therapy. Benefit is defined as either of the following:
    - Decreased serum aluminum concentrations
    - Symptomatic improvement (e.g., neurological symptom improvement, decreased bone pain)

Iron Toxicity in Members Undergoing Dialysis

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat iron toxicity in members undergoing dialysis.
- The member is receiving benefit from therapy.

Porphyria

Authorization for 12 months may be granted when all of the following criteria are met:

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- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat porphyria.
- The member is receiving benefit from therapy (e.g., symptomatic improvement).

Hereditary Hemochromatosis

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat hereditary hemochromatosis.
- The member is experiencing benefit from therapy. Benefit is defined as a decrease in serum ferritin levels as compared to pretreatment baseline.

Malaria

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Desferal and generic deferoxamine.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service-Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- Guidelines for the management of transfusion dependent thalassaemia (TDT) 5th Edition, Thalassaemia International Federation
- Guidelines for the monitoring and management of iron overload in patients with haemoglobinopathies and rare anemias, British Society for Haematology
- American College of Gastroenterology (ACG) Clinical Guideline: Hereditary Hemochromatosis

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Desferal and generic deferoxamine are covered in addition to the following:

- Aluminum toxicity in patients undergoing dialysis
- Iron toxicity in patients undergoing dialysis
- Malaria
- Porphyria
- Hereditary hemochromatosis

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Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for requiring a pretreatment serum ferritin of at least 1000 mcg/L in patients with chronic iron overload due to transfusion-dependent anemias can be found in the guidelines from the Thalassemia International Federation. Long term control of serum ferritin has been linked to protection from heart disease and to improved survival if levels are consistently less than 2500 mcg/L and even better outcomes are noted at levels less than 1000 mcg/L. The guidelines from British Society for Haematology by Shah et al. also recommends initiating iron chelation therapy after 10 to 12 transfusions or when the serum ferritin exceeds 1000 mcg/L on two occasions in transfusion-dependent thalassemia patients.

Support for using Desferal or generic deferoxamine to treat aluminum toxicity in patients undergoing dialysis can be found in a study by Malluche et al. Intermittent long-term infusions of deferoxamine were effective in removing aluminum from bone in 7 patients undergoing long-term maintenance dialysis. Deferoxamine was given in doses of 14.25 mg/kg/hour (hr) intravenously (IV) 3 times weekly during the first 2 hours of dialysis in hemodialysis patients. In patients undergoing long-term ambulatory peritoneal dialysis, deferoxamine was given in doses of 85 mg/kg once weekly at rates of 14.25 mg/kg/hr IV. Symptomatic improvement was observed after 2 to 4 weeks of treatment corresponding to a reduction (or disappearance) of stainable bone aluminum and a decrease in the aluminum content of bone.

Additionally, in de la Serna et al., deferoxamine given in doses of 1 g IV following each dialysis session for 6 months was reported effective in improving hemoglobin levels and decreasing transfusion requirements in chronic hemodialysis patients with non-microcytic anemia, moderate aluminum overload, and normal or high iron scores. Improvement of anemia was related to a response in erythropoiesis, beginning after 2 to 3 months of treatment; the highest hemoglobin levels were achieved at 4 to 6 months of therapy. Improvement of erythropoiesis did not appear to be related to chelation of a heavy aluminum overload.

Support for using Desferal or generic deferoxamine to treat iron toxicity in patients undergoing dialysis can be found in a study by Lee et al. In an 8-month prospective study, low-dose deferoxamine decreased serum ferritin concentrations and increased hematocrit in 8 iron-overloaded hemodialysis patients, with no adverse side effects of deferoxamine treatment. Intravenous deferoxamine 500 mg in 100 mL normal saline was administered twice weekly during the last hour of hemodialysis. After 8 months, mean serum ferritin levels decreased significantly from 2102 to 1104 nanograms/milliliter, a 43.2% decrease (p less than 0.05). Mean hematocrit rose from 25.3 to 27 over the 8-month course (p less than 0.05). A decline was also noted in the mean required dose of recombinant human erythropoietin (from 106.5 mcg/kg/wk to 91.3 mcg/kg/wk). Deferoxamine was well tolerated, and no adverse events occurred.

Support for using Desferal or generic deferoxamine to treat malaria can be found in a study by Gordeuk et al. Deferoxamine was more beneficial than placebo in a study of 37 asymptomatic adult Zambians with Plasmodium falciparum counts between 88 to 3305/mcL (generally greater than 1000/mcL). In a double-blind manner, subjects were randomized to receive deferoxamine 100 mg/kg/day on days 0 to 3 as a continuous 72-hour subcutaneous infusion (n=16) or placebo (n=21). Mean parasite counts were significantly decreased with deferoxamine as compared with placebo. Subjects were questioned

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regarding several effects. While no adverse effects were reported, no formal audiologic or visual examinations were performed.

Additionally, Traore et al. found deferoxamine combined with chloroquine produced more rapid recovery from malaria than chloroquine alone in a small group of patients. Six patients with malaria received 0.5 g of deferoxamine intramuscularly (IM) every 12 hours for 3 days in addition to 25 mg/kg (total dose) of chloroquine. The patients who received deferoxamine in addition to chloroquine had a more rapid decrease in parasitemia than three patients who received only chloroquine.

Support for using Desferal or generic deferoxamine to treat porphyria can be found in two case reports (Taxay and Rasetti et al.). The two reports indicate that deferoxamine, in a dose of 500 mg administered IM, may have some beneficial effects in improving acute intermittent porphyria. However, the drug does not appear to alter the underlying body chemical abnormality. Phlebotomy remains the treatment of choice. Several published studies support the use of deferoxamine as an alternative for patients where phlebotomy is contraindicated (Stockenhuber et al., Rocchi et al., and Gibertini et al.).

Support for using Desferal or generic deferoxamine to treat hereditary hemochromatosis can be found in the guidelines for hereditary hemochromatosis published by the American College of Gastroenterology. The guideline recommends against chelation as first-line therapy given the effectiveness of phlebotomy, side effects of chelation, and the relatively small sample size of clinical trials supporting chelation. Chelation is to be reserved for patients who are intolerant or refractory to phlebotomy or when phlebotomy has potential for harm.

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