PRIOR AUTHORIZATION POLICY

POLICY: Chelating Agents – Iron Chelators (Oral) Prior Authorization Policy
- Exjade® (deferasirox tablets for suspension – Novartis, generic)
- Jadenu® (deferasirox tablets – Novartis, generic)
- Jadenu® Sprinkle (deferasirox oral granules – Novartis, generic)
- Ferriprox® (deferiprone tablets and oral solution – Chiesi, generic [tablets only])

REVIEW DATE: 01/29/2025

OVERVIEW

Exjade, Jadenu (granules and tablets), and Ferriprox (granules and oral solution) are orally administered iron chelators used for the treatment of iron overload.[1-4] Exjade and Jadenu have the same chemical entity (deferasirox) in different formulations.[1,2] Note: deferoxamine is an intravenously administered iron chelator that is not targeted in this Policy.

Deferasirox (Exjade, Jadenu/Sprinkle; generics) is indicated for the following uses:[1,2]
- **Chronic iron overload due to blood transfusions** (transfusional hemosiderosis), in patients ≥ 2 years of age.
- **Chronic iron overload in non-transfusion-dependent thalassemia syndromes**, in patients ≥ 10 years of age with a liver iron concentration of at least 5 mg of iron per gram of liver dry weight and a serum ferritin level > 300 mcg/L.

Limitations of Use: The safety and efficacy of deferasirox when administered with other iron chelation therapy have not been established.[1,2]

Deferiprone tablets (Ferriprox tablets, generic) are indicated for the following uses:[3]
- **Transfusional iron overload with thalassemia syndromes**, in patients ≥ 8 years of age.
- **Transfusional iron overload with sickle cell disease or other anemias**, in patients ≥ 8 years of age.

Ferriprox (deferiprone) oral solution is indicated for the following uses:[4]
- **Transfusional iron overload with thalassemia syndromes**, in patients ≥ 3 years of age.
- **Transfusional iron overload with sickle cell disease or other anemias**, in patients ≥ 3 years of age.

Limitations of Use: Safety and effectiveness of deferiprone have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome (MDS) or in patients with Diamond Blackfan anemia.[3,4]

Table 1. Availability of Oral Iron Chelators.[1-4]

Disease Overview

Iron chelating therapy should be considered in all patients who require long-term blood transfusions.[5] Patients with sickle cell disease, myelodysplastic syndromes (MDS), thalassemia major, Diamond-Blackfan anemia, aplastic anemia, and other congenital and acquired forms of refractory anemia (e.g., hereditary hemochromatosis) may require regular blood transfusions and as a result, may require iron chelating therapy. This is because the body does not have an efficient mechanism to excrete iron. In patients requiring multiple blood transfusions, iron accumulates and is deposited into multiple organ

systems. The long-term consequences of chronic iron overload include multiple organ dysfunction (e.g., heart, liver) and/or organ failure. Iron chelation therapy is necessary to prevent organ failure and decrease mortality.

Other Uses with Supportive Evidence

Iron overload in thalassemia intermedia is mainly due to increased intestinal absorption of iron due to chronic anemia.[10] Transfusions play a minor role in iron overloading in these patients, but iron chelation therapy is indicated for thalassemia intermedia. A 5-year randomized, open-label, long-term trial was conducted in patients (n = 88) with thalassemia intermedia comparing Ferriprox with deferoxamine intravenous (IV) treatment. After 5 years, there were no statistically significant differences between Ferriprox and deferoxamine in the decrease in mean serum ferritin levels and overall survival. There are data available from other studies as well with Ferriprox use in iron-loaded non-transfusion dependent thalassemias.[11]

GUIDELINES

- **Thalassemia Syndromes:**
  - The Thalassemia International Federation published guidelines (2021) for transfusion-dependent thalassemia.[7] Initiation of an iron chelator generally starts after 10 to 20 red blood cell (RBC) infusions or when serum ferritin level is > 1,000 mcg/L. Recommendations advise use based on patient characteristics and FDA-approved indications, and also advocate for switching, rotating, and combining chelator regimens as needed to control iron balance or distribution.
  - The Thalassemia International Federation guidelines for the management of non-transfusion dependent thalassemia (2023) recommend iron chelation therapy with deferasirox in patients ≥ 10 years of age with liver iron concentration ≥ 5 mg of iron per gram of liver dry weight, serum ferritin level ≥ 800 ng/mL, and other scenarios.[6]
  - The American Heart Association (AHA) published a consensus statement (2013) on cardiovascular function and treatment in patients with β-thalassemia major.[8] Deferasirox, deferiprone, and deferoxamine (injectable iron chelator) are recommended chelating treatments. The AHA advises the use of Ferriprox monotherapy in patients with cardiac siderosis, patients with reduced left ventricular ejection fraction (LVEF), or asymptomatic left ventricular dysfunction. Exjade and Jadenu monotherapy can be used in patients with detectable cardiac iron levels and normal cardiac function. However, Exjade and Jadenu are not recommended as first-choice treatment for cardiac siderosis with cardiac iron (T2*) < 6 ms or in patients with reduced LVEF.
- **MDS:** The National Comprehensive Cancer Network (NCCN) guidelines for MDS (version 2.2025 – January 17, 2025) have recommendations for the management of iron overload.[9] NCCN advises consideration of deferasirox orally or deferoxamine (injectable iron chelator) for iron chelation to decrease iron overload (aiming for target ferritin level < 1,000 mcg/mL) in patients who have received >20 to 30 RBC transfusions, particularly for patients with lower-risk MDS or who are potential transplant candidates (with low to intermediate-1 MDS). The guidelines note that deferiprone is available; however, controversy remains regarding the use of this agent for MDS due to the Boxed Warning for agranulocytosis.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of oral iron chelators. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with oral iron chelators as well as the monitoring required for adverse events

and long-term efficacy, initial approval requires oral iron chelators to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of oral iron chelators as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of **deferasirox** is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Iron Overload, Chronic – Transfusion-Related.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is receiving blood transfusions at regular intervals for a chronic condition; AND
       Note: Examples of chronic conditions include thalassemia syndromes, myelodysplastic syndrome, chronic anemia, and sickle cell disease.
     - **ii.** Prior to starting chelating therapy, serum ferritin level was > 1,000 mcg/L **[documentation required]**; AND
     - **iii.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving deferasirox. Approve if the patient is benefiting from therapy, according to the prescriber.
     Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

2. **Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Prior to starting chelating therapy, serum ferritin level was > 300 mcg/L **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving deferasirox. Approve if the patient is benefiting from therapy, according to the prescriber.
     Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

FDA-Approved Indications

1. **Iron Overload, Chronic – Transfusion-Related Due to Thalassemia Syndromes.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Prior to starting chelating therapy, serum ferritin level was > 1,000 mcg/L **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving deferiprone. Approve if the patient is benefiting from therapy, according to the prescriber.
     Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

2. **Iron Overload, Chronic – Transfusion-Related Due to Sickle Cell Disease or Other Anemias.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Prior to starting chelating therapy, serum ferritin level was > 1,000 mcg/L **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving deferiprone. Approve if the patient is benefiting from therapy, according to the prescriber.
     Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

Other Uses with Supportive Evidence

3. **Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Prior to starting chelating therapy, serum ferritin level was > 300 mcg/L **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with a hematologist; OR
   - **B)** Patient is Currently Receiving deferiprone. Approve if the patient is benefiting from therapy, according to the prescriber.
     Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of oral iron chelators is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

1. Exjade® tablets for suspension [prescribing information]. East Hanover, NJ: Novartis; July 2024.
2. Jadenu® tablets and Jadenu® Sprinkle oral granules [prescribing information]. East Hanover, NJ: Novartis; July 2024.
3. Ferriprox® tablets [prescribing information]. Cary, NC: Chiesi; July 2023.
4. Ferriprox® oral solution [prescribing information]. Cary, NC: Chiesi; November 2021.
5. Brittenham GM. Iron-chelating therapy for transfusional iron overload. *N Engl J Med.* 2011;364:146-156.
6. Taher AT, Musallam KM, Cappellini MD. *Guidelines for the Management of Non-Transfusion-Dependent β-Thalassaemia*. 3rd ed. Nicosia (Cyprus): Thalassemia International Federation; 2023.
7. Farmakis D, Porter J, Taher A, et al. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. *Hemasphere*. 2022;6(8):e732. Published 2022 Jul 29.
8. Pennell DJ, Udelson JE, Arai AE, et al. Cardiovascular function and treatment in β-thalassemia major. A consensus statement from the American Heart Association. *Circulation.* 2013;128:281-308.
9. The NCCN Myelodysplastic Syndrome Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 27, 2025.
10. Calvaruso G, Vitrano A, Di Maggio R, et al. Deferiprone versus deferoxamine in thalassemia intermedia: results from a 5-year long-term Italian multicenter randomized clinical trial. *Am J Hematol*. 2015;90:634-638.
11. Kontoghiorghe CN, Kontoghiorghes GJ. Efficacy and safety of iron-chelation therapy with deferoxamine, deferiprone, and deferasirox for the treatment of iron-loaded patients with non-transfusion-dependent thalassemia syndromes. *Drug Des Devel Ther*. 2016;10:465-481.