PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 05/04/2022

OVERVIEW

Oral iron chelator products are indicated for the **treatment of iron overload** for specific conditions.[1-4]

Deferasirox products are indicated for the following uses:[1,2]
- **Chronic iron overload due to blood transfusions**, 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 > 300 mcg/L.

Deferiprone tablets 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 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.

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.[6] 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.

Guidelines

- **Thalassemia Syndromes:** The Thalassemia International Federation published guidelines (2017) for transfusion-dependent thalassemia.[7] Initiation of an iron chelator generally starts after 10 to 12 infusions or when serum ferritin level is > 1,000 mcg/L. Recommendations do not prefer any iron chelator over the others; rather, the guidelines advise use based on patient characteristics and FDA-approved indications.

  The American Heart Association (AHA) published a consensus statement (2013) on cardiovascular function and treatment in 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 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 3.2022 – January 13, 2022) have recommendations for the management of iron overload.[9] The NCCN advises the use of deferasirox, deferiprone, or deferoxamine to decrease iron overload (aiming for target ferritin level < 1,000 mcg/mL) in specific patients with MDS or who are potential transplant candidates. 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 chelator products. 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 chelator products as well as the monitoring required for adverse events and long-term efficacy, initial approval requires oral iron chelator products 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 chelator products 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 **deferiprone products** is recommended in those who meet one of the following criteria:

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 criteria (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following criteria (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.
   - **B)** Patient is Currently Receiving a Deferiprone Product. Approve if the patient is benefiting from therapy, as confirmed by 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 criteria (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following criteria (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.

B) Patient is Currently Receiving a Deferiprone Product. Approve if the patient is benefiting from therapy, as confirmed by 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 criteria (A or B):
   A) Initial Therapy. Approve if the patient meets BOTH of the following criteria (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.
   B) Patient is Currently Receiving a Deferiprone Product. Approve if the patient is benefiting from therapy, as confirmed by the prescriber.
   Note: Examples of benefit from therapy include reduction in serum ferritin levels, stable disease, and reduced organ iron load.

II. Coverage of **deferasirox products** 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 criteria (A or B):
   A) Initial Therapy. Approve if the patient meets ALL of the following criteria (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.
   B) Patient is Currently Receiving a Deferasirox Product. Approve if the patient is benefiting from therapy, as confirmed by 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 criteria (A or B):
   A) Initial Therapy. Approve if the patient meets BOTH of the following criteria (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.
   B) Patient is Currently Receiving a Deferasirox Product. Approve if the patient is benefiting from therapy, as confirmed by 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 chelator products 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.

REFERENCES

1. Exjade® tablets for suspension [prescribing information]. East Hanover, NJ: Novartis; August 2021.
2. Jadenu® tablets and Jadenu® Sprinkle oral granules [prescribing information]. East Hanover, NJ: Novartis; February 2022.
3. Ferriprox® tablets [prescribing information]. Cary, NC: Chiesi; April 2021.
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. Palmer WC, Vishnu P, Sanchez W, et al. Diagnosis and Management of Genetic Iron Overload Disorders. *J Gen Intern Med.* 2018 Dec;33(12):2230-2236.
7. Cappellini MD, Cohen A, Porter, J, et al. A short guide for the management of transfusion dependent thalassaemia. 3rd Edition. Available at: https://thalassaemia.org.cy/wp-content/uploads/2017/10/Short-GUIDE-low-res.pdf. Accessed on April 25, 2022.
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 3.2022 – January 13, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed April 25, 2022.