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: 01/31/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Oral iron chelators are indicated for the **treatment of iron overload** for specific conditions.[1-4] Exjade and Jadenu have the same chemical entity (deferasirox) in different formulations.[1,2]

Deferasirox products (Exjade, Jadenu/Sprinkle; generics) are 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 products 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 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 products 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]

Exjade (deferasirox tablets for suspension)	**Ferriprox (deferiprone tablets and oral solution)**		**Jadenu/Sprinkle (deferasirox granules and tablets)**	
• 125 mg • 250 mg • 500 mg	**Tablets** • 500 mg • 1000 mg	**Solution** 100 mg/mL	**Granules** • 90 mg • 180 mg • 360 mg	**Tablets** • 90 mg • 180 mg • 360 mg

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 (2021) for transfusion-dependent thalassemia.[7] Initiation of an iron chelator generally starts after 10 to 20 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 combing chelator regimens as needed to control iron balance or distribution.

- 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 3.2023 – November 10, 2023) have recommendations for the management of iron overload.[9] NCCN advises consideration of deferasirox or deferoxamine (injectable iron chelator) 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.

RECOMMENDED

- **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)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

AUTHORIZATION CRITERIA

I. 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 (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.
   - **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 (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.
   - **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.

II. 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 (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.
   - **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 (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.
   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 (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.
   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.

CONDITIONS NOT COVERED

- **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)

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Exjade® tablets for suspension [prescribing information]. East Hanover, NJ: Novartis; August 2023.
2. Jadenu® tablets and Jadenu® Sprinkle oral granules [prescribing information]. East Hanover, NJ: Novartis; March 2023.
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. 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. 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 3.2023 – November 10, 2023). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 23, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/17/2023
Early Annual Revision	No criteria changes.	01/31/2024