



## Drug Coverage Policy

Effective Date ..... 4/1/2026  
Coverage Policy Number .....IP0271  
Policy Title.....Iron Chelators (Oral)

### Chelating Agents - Iron Chelators (Oral)

- Exjade® (deferasirox tablets for suspension – Novartis, generic)
- Ferriprox® (deferiprone tablets\_– Chiesi, generic)
- Ferriprox® Oral Solution (deferiprone oral solution – Chiesi)
- Jadenu® (deferasirox tablets – Novartis, generic)
- Jadenu® Sprinkle (deferasirox oral granules – Novartis, generic)

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#### **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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see “Coding Information” below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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.

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## OVERVIEW

Exjade, Jadenu (granules and tablets), and Ferriprox (granules and oral solution), orally administered iron chelators, are used for the treatment of iron overload.<sup>1-4</sup> Exjade and Jadenu products have the same chemical entity (deferasirox) in different formulations.<sup>1,2</sup>

Note: deferoxamine, an injectable iron chelator, is not targeted in this Policy.

**Deferasirox** (Exjade, Jadenu/Sprinkle; generics) is indicated for the following uses:<sup>1,2</sup>

- **Chronic iron overload due to blood transfusions** (transfusional hemosiderosis), in patients  $\geq$  2 years of age.
- **Chronic iron overload in non-transfusion-dependent thalassemia syndromes**, in patients  $\geq$  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.<sup>1,2</sup>

**Deferiprone** tablets (Ferriprox tablets, generic) are indicated for the following uses:<sup>3</sup>

- **Transfusional iron overload with thalassemia syndromes**, in patients  $\geq$  8 years of age.
- **Transfusional iron overload with sickle cell disease or other anemias**, in patients  $\geq$  8 years of age.

**Ferriprox Oral Solution** (deferiprone oral solution) is indicated for the following uses:<sup>4</sup>

- **Transfusional iron overload with thalassemia syndromes**, in patients  $\geq$  3 years of age.
- **Transfusional iron overload with sickle cell disease or other anemias**, in patients  $\geq$  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.<sup>3,4</sup>

**Table 1. Availability of Oral Iron Chelators.**<sup>1-4</sup>

Exjade (deferasirox tablets for suspension)	Ferriprox (deferiprone tablets and oral solution)		Jadenu/Sprinkle (deferasirox granules and tablets)	
	Tablets	Solution	Granules	Tablets
<ul style="list-style-type: none"><li>• 125 mg</li><li>• 250 mg</li><li>• 500 mg</li></ul>	<ul style="list-style-type: none"><li>• 500 mg</li><li>• 1000 mg</li></ul>	100 mg/mL	<ul style="list-style-type: none"><li>• 90 mg</li><li>• 180 mg</li><li>• 360 mg</li></ul>	<ul style="list-style-type: none"><li>• 90 mg</li><li>• 180 mg</li><li>• 360 mg</li></ul>

## Disease Overview

Iron chelating therapy should be considered in all patients who require long-term blood transfusions.<sup>5</sup> 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.<sup>10</sup> 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.<sup>11</sup>

### **Guidelines**

- **Thalassemia Syndromes:**

- The Thalassemia International Federation published guidelines (2025) for transfusion-dependent  $\beta$ -thalassemia.<sup>7</sup> 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  $\beta$ -thalassemia (2023) recommend iron chelation therapy with deferasirox in patients  $\geq$  10 years of age with liver iron concentration  $\geq$  5 mg of iron per gram of liver dry weight, serum ferritin level  $\geq$  800 ng/mL, and other scenarios.<sup>6</sup>
- The American Heart Association (AHA) published a consensus statement (2013) on cardiovascular function and treatment in patients with  $\beta$ -thalassemia major.<sup>8</sup> 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 2.2026 – December 15, 2025) have recommendations for the management of iron overload.<sup>9</sup> 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.

### **Safety**

Deferasirox products have a boxed warning regarding possible renal failure, hepatic failure, and gastrointestinal hemorrhage.<sup>1,2</sup> Deferiprone products have a boxed warning regarding the risk of neutropenia and fatal agranulocytosis.<sup>3,4</sup>

## Coverage Policy

### POLICY STATEMENT

Prior Authorization is required for 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.

**Oral iron chelating agents are considered medically necessary when ONE of the following are met:**

**I. Deferasirox products are considered medically necessary when ONE of the following are met:**

#### 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, iii, and iv):
    - 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; AND
    - iii.** The medication is prescribed by or in consultation with a hematologist; AND
    - iv.** Preferred product criteria is met for the products listed in the below table(s)
  - 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 ALL of the following (i, ii, and iii):
    - i.** Prior to starting chelating therapy, serum ferritin level was > 300 mcg/L; AND
    - ii.** The medication is prescribed by or in consultation with a hematologist; AND
    - iii.** Preferred product criteria is met for the products listed in the below table(s)
  - 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.

**II. Deferiprone products are considered medically necessary when ONE of the following are met:**

#### 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 ALL of the following (i, ii, and iii):
- i.** Prior to starting chelating therapy, serum ferritin level was > 1,000 mcg/L; AND
  - ii.** The medication is prescribed by or in consultation with a hematologist; AND
  - iii.** Preferred product criteria is met for the products listed in the below table(s)

- 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 ALL of the following (i, ii, and iii):
- i.** Prior to starting chelating therapy, serum ferritin level was > 1,000 mcg/L; AND
  - ii.** The medication is prescribed by or in consultation with a hematologist; AND
  - iii.** Preferred product criteria is met for the products listed in the below table(s)

- 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 ALL of the following (i, ii, and iii):
- i.** Prior to starting chelating therapy, serum ferritin level was > 300 mcg/L; AND
  - ii.** The medication is prescribed by or in consultation with a hematologist; AND
  - iii.** Preferred product criteria is met for the products listed in the below table(s)

- 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.

**Employer Plans:**

<b>Product</b>	<b>Criteria</b>
<b>Exjade</b> (deferasirox) tablet for suspension	Patient has tried <b>deferasirox tablet for suspension</b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Ferriprox</b> (deferiprone) 1000 mg tablets two times per day	Patient meets ONE of the following (1 <u>or</u> 2): 1. Patient has tried deferiprone tablets (generic Ferriprox tablets) [may require prior authorization] 2. Dose prescribed cannot be attained with deferiprone tablets
<b>Ferriprox</b> (deferiprone) 500 mg and 1000 mg	Patient has tried <b>deferiprone 500 mg or 1000 mg tablet</b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product

<b>Product</b>	<b>Criteria</b>
tablets three times per day	which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Ferriprox Solution</b> (deferiprone) oral solution	Patient meets ONE of the following (1, 2, <u>or</u> 3): <ol style="list-style-type: none"> <li>1. Patient has tried deferiprone tablets (generic Ferriprox tablets) [may require prior authorization]</li> <li>2. Dose prescribed cannot be attained with deferiprone tablets</li> <li>3. Patient cannot swallow or has difficulty swallowing tablets.</li> </ol>
<b>Jadenu</b> (deferasirox) tablet	Patient has tried <b><u>deferasirox tablet</u></b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Jadenu Sprinkle</b> (deferasirox) oral granules	Patient has tried <b><u>deferasirox granule packet</u></b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]

#### Individual and Family Plans:

<b>Product</b>	<b>Criteria</b>
<b>Exjade</b> (deferasirox) tablet for suspension	Patient has tried <b><u>deferasirox tablet for suspension</u></b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, which would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Ferriprox</b> (deferiprone) 1000 mg tablets two times per day	Patients meets ONE of the following (1 <u>or</u> 2): <ol style="list-style-type: none"> <li>1. Patient has tried deferiprone tablets (generic Ferriprox tablets) [may require prior authorization]</li> <li>2. Dose prescribed cannot be attained with deferiprone tablets</li> </ol>
<b>Ferriprox</b> (500 mg & 1000 mg) deferiprone tablets three times per day	Patient has tried <b><u>deferiprone 500 mg or 1000 mg tablet</u></b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Ferriprox Solution</b> (deferiprone) oral solution	Patient meets ONE of the following (1, 2, <u>or</u> 3): <ol style="list-style-type: none"> <li>1. Patient has tried deferiprone tablets (generic Ferriprox tablets) [may require prior authorization]</li> <li>2. Dose prescribed cannot be attained with deferiprone tablets</li> <li>3. Patient cannot swallow or has difficulty swallowing tablets.</li> </ol>

Product	Criteria
<b>Jadenu</b> (deferasirox) tablet	Patient has tried <b>deferasirox tablet</b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]
<b>Jadenu Sprinkle</b> (deferasirox) oral granules	Patient has tried <b>deferasirox granule packet</b> (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]

### Conditions Not Covered

**Oral iron chelating agents for any other use is considered not medically necessary. Criteria will be updated as new published data are available.**

### References

1. Exjade® tablets for suspension [prescribing information]. East Hanover, NJ: Novartis; July 2024.
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3. Ferriprox® tablets [prescribing information]. Cary, NC: Chiesi; March 2025.
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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  $\beta$ -Thalassaemia*. 3rd ed. Nicosia (Cyprus): Thalassaemia International Federation; 2023.
7. Taher AT, Farmakis D, Porter JB, Cappellini MD, Musallam KM, eds. *Guidelines for the Management of Transfusion-Dependent  $\beta$ -Thalassaemia (TDT)*. 5th ed. Nicosia, Cyprus: Thalassaemia International Federation; 2025.
8. Pennell DJ, Udelson JE, Arai AE, et al. Cardiovascular function and treatment in  $\beta$ -thalassaemia 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 2.2026 – December 15, 2025). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 8, 2025.
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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 thalassaemia syndromes. *Drug Des Devel Ther.* 2016;10:465-481.

### Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p><b>Iron Overload, Chronic – Transfusion-Related (Deferasirox):</b> Removed age</p> <p><b>Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes (Deferasirox):</b> Removed age</p> <p><b>Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes:</b> Removed prior to starting chelating therapy, Liver iron (Fe) concentration (LIC) level greater than or equal to 5 mg Fe per gram of dry weight</p> <p><b>Ferriprox Solution</b> for Employer and Individual and Family Plans: <b>Added</b> as a requirement option: “Dose prescribed cannot be attained with deferiprone tablet” and “patient who cannot swallow or have difficulty swallowing tablets”</p>	5/1/2024
Annual Revision	<p><b>Patients Currently Receiving an Oral Chelator:</b> The verbiage “Approve if the patient is benefiting from therapy, according to the prescriber.” was updated to “Approve if the patient is benefiting from therapy, according to the prescriber.”</p> <p><b>Removed</b> deferiprone 500 mg and 1000 mg (three times daily) preferred product criteria (for Individual and Family Plans only).</p> <p><b>Updated</b> Ferriprox 1000 mg tablets (two times daily) and solution preferred product criteria.</p> <p><b>Updated</b> Ferriprox 500 mg and 1000 mg (three times daily) preferred product criteria.</p>	5/1/2025
Annual Revision	<p><b>Employer Plans and Individual and Family Plans Preferred Product Tables:</b> <b>Added</b> “[e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber,” to Exjade, Ferriprox (500 mg and 1000 mg three times a day) Jadenu, Jadenu Sprinkles criteria. <b>Added</b> “may require prior authorization” to all products</p>	4/1/2026

The policy effective date is in force until updated or retired.

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