Pharmacy Policy Bulletin: J-0249 Chelating Agents – Commercial and Healthcare Reform	
Number: J-0249	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0249-010	**Original Date:** 11/06/2019
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Exjade (deferasirox) • Jadenu (deferasirox) • Ferriprox (deferiprone)

FDA-Approved Indication(s):	• Exjade (deferasirox) and Jadenu (deferasirox)
	  ○ Treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older
	  ○ Treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) and a serum ferritin greater than 300 mcg/L
	• Ferriprox (deferiprone)
	  ○ Treatment of patients with transfusional iron overload in adult and pediatric patients 8 years of age (tablets) and older or 3 years of age (oral solution) and older with thalassemia syndromes, sickle cell disease or other anemias.
	  ○

Background:	• The human body has no active mechanism for the excretion of iron.
	  ○ Deferasirox works in treating iron toxicity by binding trivalent (ferric) iron (for which it has a strong affinity), forming a stable complex which is eliminated via the kidneys. It is a tridentate ligand, two molecules of deferasirox are capable of binding to 1 atom of iron.
	  ○ Deferiprone has an affinity for ferric ion (iron III) and binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable over a wide range of pH values.
	• Transfusional Iron Overload
	  ○ A unit of transfused blood contains approximately 250 mg of iron. In patients who receive numerous transfusions including those with thalassemia major, sickle cell disease, myelodysplastic syndrome, aplastic anemia, hemolytic anemia, and refractory sideroblastic anemia,

the excess iron from the transfused erythrocytes gradually accumulates in various tissues, causing morbidity and mortality.
    - Thalassemia syndromes include alpha-thalassemia and beta-thalassemia.
- Non-Transfusion-Dependent Thalassemia (NTDT) Syndromes
    - NTDT is a term used to label patients who do not require such lifelong regular transfusions for survival, although they may require occasional or even frequent transfusions in certain clinical settings or for defined periods of time.
    - NTDT encompasses three clinically distinct forms: beta-thalassemia intermedia, hemoglobin E/beta-thalassemia (mild and moderate forms), and alpha-thalassemia intermedia (hemoglobin H disease).
- Serum ferritin and liver iron concentration (LIC) are two methods by which total iron concentrations in the body are measured. LIC is a more accurate measurement of total body iron stores. However, serum ferritin is measured via a simple blood test, whereas LIC is measured via liver biopsy or magnetic resonance imaging (MRI).
- The Thalassemia International Foundation Federation-published guidelines do not prefer any iron chelator over another.
- Prior authorization is utilized to ensure appropriate use. Step therapy contains criteria for prior utilization of products that are equally effective but less costly. Generic Jadenu tablets is the preferred generic step therapy.
    - Generic Exjade comes as oral dispersible tablets for suspension: 125 mg, 250 mg, 500 mg
    - Generic Jadenu comes as oral tablets and sprinkle granules: 90 mg, 180 mg, 360 mg
- Jadenu dosing is approximately 30% lower than Exjade dosing. Switching form one drug to the other can be done using the table below. Exjade or Jadenu should be rounded to the nearest whole tablet or nearest whole sachet content for granules.

	Exjade Tablets for Oral Suspension	**Jadenu Tablets or Sprinkle Granules**
Transfusion-Dependent Iron Overload		
Starting Dose	20 mg/kg/day	14 mg/kg/day
Titration Increments	5–10 mg/kg	3.5–7 mg/kg
Maximum Dose	40 mg/kg/day	28 mg/kg/day
Non-Transfusion-Dependent Thalassemia Syndromes		
Starting Dose	10 mg/kg/day	7 mg/kg/day
Titration Increments	5–10 mg/kg	3.5–7 mg/kg
Maximum Dose	20 mg/kg/day	14 mg/kg/day

- Prescribing Considerations:
    - Exjade and Jadenu
        - Jadenu is another oral formulation of Exjade tablets for oral suspension. While Exjade is a dispersible tablet that must be mixed in liquid and taken on an empty stomach, Jadenu is a tablet that be taken in a single step, with or without a light meal. Jadenu is also available as sprinkle granules.
        - The safety and efficacy of Exjade or Jadenu when administered with other iron chelation therapy have not been established.

	▪ Exjade and Jadenu have black box warnings for acute kidney injury, hepatic toxicity, and gastrointestinal hemorrhage. ○ Ferriprox ▪ Ferriprox has black box warnings for agranulocytosis and neutropenia. ▪ Liver enzymes should be monitored monthly when on Ferriprox. Ferriprox should be discontinued with persistent elevations. ▪ Ferriprox has not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or Diamond Blackfan anemia.

Approval Criteria

I. Initial Authorization

A. Chronic Iron Overload Due to Blood Transfusions

1. Exjade (deferasirox) or Jadenu (deferasirox)

When a benefit, coverage of Exjade (deferasirox) or Jadenu (deferasirox) may be approved when all of the following criteria are met **(a. through f.)**:

a. The member is 2 years of age or older.

b. The member has a diagnosis of chronic iron overload due to blood transfusions (ICD-10: E83.111).

c. The member has a transfusion history of ≥ 100 mL/kg of packed red blood cells (specifically, at least 20 units of packed red blood cells for a 40 kg person or more in individuals weighing more than 40 kg).

d. The member meets one (1) of the following criteria **(i. or ii.)**:

i. The member has a history of serum ferritin consistently > 1,000 mcg/L.

ii. The member has an LIC of ≥ 7 mg of iron per gram of liver dry weight (mg Fe/g dw).

e. If the request is for brand Jadenu tablets, the member has experienced therapeutic failure or intolerance to generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

f. If the request is for brand Exjade or Jadenu Sprinkles, the member has experienced therapeutic failure or intolerance to the plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

2. Ferriprox (deferiprone)

When a benefit, coverage of Ferriprox (deferiprone) may be approved when all of the following criteria are met **(a. through f.)**:

a. The member meets one (1) of the following criteria **(i. or ii.)**:

i. If the request is for Ferriprox tablets, the member is 8 years of age or older.

ii. If the request is for Ferriprox oral solution, the member is 3 years of age or older.

b. The member has a diagnosis of transfusional iron overload due to thalassemia syndromes, sickle cell disease, or other anemias. (ICD-10: E83.111).

c. The member has a transfusion history of ≥ 100 mL/kg of packed red blood cells (specifically, at least 20 units of packed red blood cells for a 40 kg person or more in individuals weighing more than 40 kg).

d. The member meets one (1) of the following criteria **(i. or ii.)**:

i. The member has a history of serum ferritin consistently > 1,000 mcg/L.

ii. The member has an LIC of ≥ 7 mg Fe/g dw.

e. If the request is for brand Ferriprox, the member has experienced therapeutic failure or intolerance to plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

f. If the request is for brand Ferriprox, the member has experienced therapeutic failure or intolerance to generic deferiprone tablets.

B. Chronic Iron Overload in Non-Transfusion-Dependent Thalassemia (NTDT) Syndromes

1. Exjade (deferasirox) or Jadenu (deferasirox)

When a benefit, coverage of Exjade (deferasirox) or Jadenu (deferasirox) may be approved when all of the following criteria are met **(a. through f.)**:

a. The member is 10 years of age or older.

b. The member has a diagnosis of chronic iron overload due to NTDT. (ICD-10: D56.0, D56.1, D56.5).

c. The member has an LIC of ≥5 mg Fe/g dw.

d. The member has a serum ferritin > 300 mcg/L.

e. If the request is for brand name Jadenu tablets, the member has experienced therapeutic failure or intolerance to generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

f. If the request is for brand Exjade or Jadenu sprinkles (deferasirox), the member has experienced therapeutic failure or intolerance to plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

II. Reauthorization

A. Chronic Iron Overload Due to Blood Transfusions

1. Exjade (deferasirox) or Jadenu (deferasirox)

When a benefit, reauthorization of Exjade (deferasirox) or Jadenu (deferasirox) may be approved when all of the following criteria are met **(a. through e.)**:

a. The prescriber attests that the member has experienced positive clinical response to therapy.

b. The member continues to require regular blood transfusions.

c. The member meets one (1) of the following criteria **(i. or ii)**:

i. The member has a serum ferritin level ≥ 500 mcg/L.

ii. The member has an LIC of ≥ 3 mg Fe/g dw.

d. If the request is for brand Jadenu tablets, the member has experienced therapeutic failure or intolerance to generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

e. If the request is for brand Exjade or Jadenu Sprinkles, the member has experienced therapeutic failure or intolerance to the plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

2. Ferriprox (deferiprone)

When a benefit, coverage of Ferriprox (deferiprone) may be approved when all of the following criteria are met **(a. through e.)**:

a. The prescriber attests that the member has experienced positive clinical response to therapy.

b. The member continues to require regular blood transfusions.

c. The member meets one (1) of the following criteria **(i. or ii)**:

i. The member has a serum ferritin level ≥ 500 mcg/L.

ii. The member has an LIC of ≥ 3 mg Fe/g dw.

d. If the request is for brand Ferriprox, the member has experienced therapeutic failure or intolerance to plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

e. If the request is for brand Ferriprox, the member has experienced therapeutic failure or intolerance to generic deferiprone tablets.

B. Chronic Iron Overload in Non-Transfusion-Dependent Thalassemia (NTDT) Syndromes

1. **Exjade (deferasirox) or Jadenu (deferasirox)**
   When a benefit, reauthorization of Exjade (deferasirox) or Jadenu (deferasirox) may be approved when all of the following criteria are met **(a. through d.)**:
   - **a.** The prescriber attests that the member has experienced positive clinical response to therapy.
   - **b.** The member has a liver iron concentration of ≥ 3 mg Fe/g dw.
   - **c.** If the request is for brand name Jadenu tablets, the member has experienced therapeutic failure or intolerance to generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.
   - **d.** If the request is for brand Exjade or Jadenu sprinkles (deferasirox), the member has experienced therapeutic failure or intolerance to plan-preferred, generic deferasirox tablets. Therapeutic failure or intolerance to generic deferasirox granules is not accepted as meeting this criterion.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Exjade [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
2. Jadenu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
3. Ferriprox tablets [package insert]. Ontario, Canada: Apotex Inc; March 2025.
4. Ferriprox oral solution [package insert]. Ontario, Canada: Apotex Inc.; March 2025.
5. Ajebo G, Mangaonkar AA, Ahmad I, et al. Correlation of serum ferritin levels with liver iron concentration by MRI measurement in sickle cell patients with transfusional iron overload. *Blood.* 2018; 132(1); 4926.
6. Chou ST, Alsawas M, Fasano RM. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. *Blood Adv*. 2020;4(2):327-355.
7. Thalassaemia International Federation. A short guide for the management of transfusion dependent thalassaemia (TDT) 2nd edition 2022. Available at: https://thalassaemia.org.cy/wp-content/uploads/2022/08/TDT-GUIDE-2022-FOR-web.pdf. Accessed May 2, 2025.