MEDICAL MUTUAL®

# Drug Policy

| Policy: | Iron Chelators (Oral)<br><br>Ferriprox (deferiprone tablets and oral solution)<br>Deferasirox tablets, granules and capsules | Annual Review Date:<br>06/20/2024<br><br>Last Revised Date:<br>06/20/2024 |
|---|---|---|

## OVERVIEW

Exjade, Jadenu (granules and tablets), and Ferriprox are orally administered iron chelators used for the treatment of iron overload. Exjade and Jadenu have the same chemical entity (deferasirox) in different formulations.

Exjade and Jadenu (granules and tablets) have the following FDA-approved indications:

- Treatment of chronic iron overload due to blood transfusions (transfusion iron overload) in patients ≥ 2 years of age. Exjade/Jadenu therapy should be considered when a patient has evidence of chronic transfusional iron overload (e.g., at least 20 units of packed red blood cells for a 40 kg person or more) and a serum ferritin consistently > 1,000 mcg/L.
- Exjade and Jadenu are also indicated for the treatment of chronic iron overload in patients ≥ 10 years of age 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 > 300 mcg/L. This indication is based on achievement of an LIC < 5 mg Fe/g dw. An improvement in survival or disease-related symptoms has not been established.

Ferriprox is indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. Ferriprox approval was based on a reduction in serum ferritin levels. There are no controlled trials demonstrating a direct treatment benefit, such as an improvement in disease-related symptoms, functioning, or increased survival. Safety and effectiveness of Ferriprox for the treatment of transfusional iron overload in patients with other chronic anemias have not been established.

## POLICY STATEMENT

This policy involves the use of Exjade, Jadenu (granules or tablets), and Ferriprox. Prior authorization is recommended for pharmacy benefit coverage of Exjade, Jadenu, and Ferriprox. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Exjade, Jadenu, and Ferriprox as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Exjade, Jadenu, and Ferriprox be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

**RECOMMENDED AUTHORIZATION CRITERIA**

**I.** Coverage of **deferiprone (brand or generic)** is recommended in those who meet the following criteria:

**FDA-Approved Indications**

1. **Iron Overload, Chronic – Transfusion-Related Due to Thalassemia Syndromes.** Approve deferiprone for 1 year if the patient meets the following criteria (A or B):
   - **A)** Initial Therapy. Approve if the patient meets all of the following criteria :
     - **i.** Prior to starting chelating therapy, the serum ferritin level was > 1000 micrograms/liter [mcg/L] **[documentation required]**; AND
     - **ii.** Deferiprone is prescribed by or in consultation with a hematologist.
     - **iii.** If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):
       - a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
       - b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
       - c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.
   - **B)** Patients Currently Receiving deferiprone . Approve for 1 year if the patient meets the following (i AND ii)
     - **i.** The patient is benefiting from deferiprone therapy (e.g., reduction in the serum ferritin levels, stable disease, reduced organ iron load), as confirmed by the prescribing physician.
     - **ii.** If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):
       - a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
       - b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
       - c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.

2. **Iron Overload, Chronic – Transfusion – Related Due to Sickle Cell Disease or Other Anemias.** Approve deferiprone for 1 year if the patient meets the following criteria (A or B).
   - **A)** Initial Therapy. Approve deferiprone for 1 year if the patient meets all the following criteria (i and ii):
     - **i.** Prior to starting chelating therapy, the patient's serum ferritin level was > 1,000 micrograms/liter (mcg/L) **[documentation required]**; AND
     - **ii.** Deferiprone is prescribed by or in consultation with a hematologist; AND
     - **iii.** If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):

a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.

**B)** Patients Currently Receiving deferiprone . Approve for 1 year if the patient meets the following (i AND ii)
i. The patient is benefiting from deferiprone therapy for sickle cell disease (e.g., reduction in the serum ferritin levels, stable disease, reduced organ iron load), as confirmed by the prescribing physician.
ii. If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):
a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.

**Other Uses with Supportive Evidence**

3. **Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes.** Approve deferiprone for 1 year if the patient meets the following criteria (A or B).
**A)** Initial Therapy. Approve deferiprone if the patient meets all the following criteria (i, ii, and iii):
**i.** Prior to starting chelating therapy, the patient's serum ferritin level was > 300 micrograms/liter (mcg/L) **[documentation required]**; AND
**ii.** Deferiprone is prescribed by or in consultation with a hematologist.
**iii.** If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):
a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.

**B)** Patients Currently Receiving deferiprone. Approve for 1 year if the patient meets the following (i AND ii):

a. The patient is benefiting from deferiprone therapy (e.g., reduction in the serum ferritin levels, stable disease, reduced organ iron load), as confirmed by the prescribing physician.
b. If brand Ferriprox is prescribed, the patient must meet the following criteria (a, b, OR c):
    a. The patient has previously failed or is intolerant to generic deferiprone tablets; OR
    b. Brand Ferriprox is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required]; OR
    c. Brand Ferriprox oral solution is being requested due to the patient having difficulty swallowing or cannot swallow tablets [documentation required] OR the prescribed dose cannot be attained with deferiprone tablets.

**II.** Coverage of **deferasirox products** is recommended in those who meet the following criteria:

**FDA-Approved Indications**

1. **Iron Overload, Chronic – Transfusion-Related.** Approve deferasirox for 1 year if the patient meets the following criteria (A or B):
   **A)** Initial Therapy. Approve deferasirox if the patient meets all the following criteria:
   i. Patient is receiving blood transfusions at regular intervals for a chronic condition (e.g., thalassemia syndromes, myelodysplastic syndrome, chronic anemia, sickle cell disease); AND
   ii. Prior to starting chelating therapy, the patient's serum ferritin level was > 1,000 micrograms/liter (mcg/L) **[documentation required]**; AND
   iii. Deferasirox is prescribed by or in consultation with a hematologist; OR

   **B)** Patients Currently Receiving the requested product. Approve for 1 year if the patient meets the following:
   **a.** The patient is benefiting from deferasirox therapy (e.g., reduction in the serum ferritin levels, stable disease, reduced organ iron load), as confirmed by the prescribing physician;

2. **Iron Overload, Chronic – Non-Transfusion-Dependent Thalassemia Syndromes.** Approve deferasirox for 1 year if the patient meets the following criteria (A or B).
   **A)** Initial Therapy. Approve deferasirox if the patient meets all the following criteria:
   i. Prior to starting chelating therapy, the patient's serum ferritin level was > 300 micrograms/liter (mcg/L) **[documentation required]**; AND
   ii. The drug is prescribed by or in consultation with a hematologist; OR

   **B)** Patients Currently Receiving the requested product. Approve for 1 year if the patient meets the following:
   a. The patient is benefiting from deferasirox therapy (e.g., reduction in the serum ferritin levels, stable disease, reduced organ iron load), as confirmed by the prescribing physician;

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Deferasirox and deferiprone have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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

**Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

**REFERENCES**

1. Ferriprox® tablets [prescribing information]. Rockville, MD: ApoPharma USA, Inc.; May 2020.
2. Algren AD. Review of oral iron chelators (deferiprone and deferasirox) for the treatment of iron overload in pediatric patients. Available at: http://www.who.int/selection_medicines/committees/expert/18/applications/OralIronChelators.pdf. Accessed on 13 June 2021.
3. Brittenham GM. Iron-chelating therapy for transfusional iron overload. *N Engl J Med*. 2011;364:146-156.
4. 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.
5. Chalmers AW, Shammo JM. Evaluation of a new tablet formulation of deferasirox to reduce chronic iron overload after long-term blood transfusions. *Ther Clin Risk Manag.* 2016;12:201-208.
6. The NCCN Myelodysplastic Syndrome Clinical Practice Guidelines in Oncology (Version 3.2021 – January 15, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed 13 June 2021.
7. 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.
8. 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.
9. Calvaruso G, Vitrano A, Di Maggio R, et al. Deferiprone versus deferoxamine in sickle cell disease: results from a 5-year long-term Italian multi-center randomized clinical trial. *Blood Cells Mol Dis.* 2014;53:265-271.
10. Consorzio per Valutazioni Biologiche e Farmacologiche. Efficacy/safety study of deferiprone compared with deferasirox in paediatric patients. . In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 March 22]. Available at: https://www.clinicaltrials.gov/ct2/show/NCT01825512?term=NCT01825512&rank=1. NLM Identifier: NCT01825512.
11. Marsella M, Borgna-Pignatti C. Transfusional iron overload and iron chelation therapy in thalassemia major and sickle cell disease. *Hematol Oncol Clin N Am.* 2014;28:703-727.
12. Cappellini MD, Porter J, El-Beshlawy A, et al. Tailoring iron chelation by iron intake and serum ferritin: the prospective EPIC study of deferasirox in 1744 patients with transfusion-dependent anemias. *Haematologica.* 2010;95:557-566.
13. Ferriprox® oral solution [prescribing information]. Rockville, MD: ApoPharma USA, Inc.; February 2020.