Clinical Policy: Deferiprone (Ferriprox)

Reference Number: CP.PHAR.147
Effective Date: 11.01.15
Last Review Date: 08.23
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Deferiprone (Ferriprox®) is an iron chelator.

FDA Approved Indication(s)

Ferriprox is indicated for the treatment of transfusional iron overload in adult and pediatric patients (tablets: 8 years of age and older; oral solution: 3 years of age and older) with thalassemia syndromes, sickle cell disease, or other anemias.

Limitation(s) of use: Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Ferriprox is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Transfusional Iron Overload (must meet all)**:**

1. Diagnosis of transfusional iron overload due to one of the following (a, b, or c):
   a. Thalassemia syndromes;
   b. Sickle cell disease;
   c. Other anemia;
2. Member does not have transfusional iron overload due to myelodysplastic syndrome or Diamond Blackfan anemia;
3. Member meets one of the following (a or b):
   a. For Ferriprox tablets: Age ≥ 8 years;
   b. For Ferriprox oral solution: Age ≥ 3 years;
4. Transfusion history of ≥ 100 mL/kg of packed red blood cells (e.g., ≥ 20 units of packed red blood cells for a 40 kg person);
5. Serum ferritin level > 1,000 mcg/L;
6. Failure of deferoxamine and deferasirox (Exjade®, Jadenu®), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for deferoxamine and deferasirox*

7. Therapy does not include concurrent use of other iron chelators, unless member has excess cardiac iron as evidence by cardiac T2* < 20 millisecond or iron-induced cardiomyopathy;
8. Dose does not exceed 99 mg/kg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Transfusional Iron Overload (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline;
3. Current documentation (within the past 30 days) shows a serum ferritin level ≥ 500 mcg/L;
4. Therapy does not include concurrent use of other iron chelators, unless member has excess cardiac iron as evidence by cardiac T2* < 20 millisecond or iron-induced cardiomyopathy;
5. If request is for a dose increase, new dose does not exceed 99 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Parkinson's disease.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DFO-DFP: deferiprone-deferoxamine
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
deferoxamine (Desferal®)	1,000-2,000 mg SC QD (20-40 mg/kg/day) over 8-24 hours.	See dosing regimen
	20-40 mg/kg IV daily (children*) and 40-50 mg/kg IV daily (adults) for 5-7 days per week. _____ **Average dose should not exceed 40 mg/kg/day until growth has ceased.*	40 mg/kg/day (children) 60 mg/kg/day (adults)
	500-1,000 mg IM/day	1,000 mg/day
deferasirox (Exjade)	20 to 40 mg/kg (calculated to the nearest whole tablet) PO QD	40 mg/kg/day
deferasirox (Jadenu)	14 mg/kg (calculated to the nearest whole tablet/sachet) PO QD	28 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Box Warnings

- Contraindication(s): hypersensitivity to deferiprone or to any of the excipients in the formulation.
- Boxed warning(s): agranulocytosis and neutropenia

Appendix D: Combination Therapy

- A multicentre randomized open-label trial was designed to assess the effectiveness of long-term sequential deferiprone-deferoxamine (DFO-DFP) versus DFP alone to treat thalassemia major. The decrease of serum ferritin levels during the treatment period was statistically significantly higher in sequential DFP-DFO patients compared with DFP-alone patients (P = 0.005). Kaplan-Meier survival analysis for the two chelation treatments did not show any statistically significant differences (long-rank test, P = 0.3145). Evidence exists to support the use of combination therapy with Ferriprox (deferiprone) and Desferal (deferoxamine) in patients with severe iron overload or overt iron-related morbidity.

Appendix E: General Information

- In FAIRPARK-II, deferiprone, an iron chelator, was associated with worse scores in measures of parkinsonism compared to placebo over a 36-week period in participants with newly diagnosed Parkinson's disease who had never received levodopa.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Transfusional iron overload	Oral tablets: 75 mg/kg PO in 2 or 3 divided doses for a total daily dose of 75 to 99 mg/kg/day in 2 or 3 divided doses Oral solution: 25 mg/kg to 33 mg/kg PO TID for a total daily dose of 75 mg/kg to 99 mg/kg	99 mg/kg/day

VI. Product Availability

- Oral solution: 100 mg/mL
- Tablets: 500 mg with functional scoring, 1,000 mg (three times a day) with functional scoring, 1,000 mg (twice a day) with functional scoring

VII. References

1. Ferriprox Tablets Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; November 2021. Available at www.ferriprox.com. Accessed April 19, 2023.
2. Ferriprox Oral Solution Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; November 2021. Available at www.ferripox.com. Accessed April 19, 2023.
3. Desferal Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2022. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a7174843-5965-49fc-b842-f7eff7b48bbc. Accessed April 19, 2023.
4. Exjade Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at https://www.us.exjade.com/. Accessed April 19, 2023.
5. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at https://www.jadenu.com/. Accessed May 4, 2023.
6. Musallam KM, Angastiniotis M, Eleftheriou A, Porter JB. Cross-talk between available guidelines for the management of patients with beta-thalassemia major. Acta Haematol. 2013; 130: 64-73. DOI: 10.1159/000345734.

7. Hoffbrand AV, Taher A, Cappellini MD. How I treat tranfusional iron overload. Blood. November 1, 2012; 120(18): 3657-3669.
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9. Cappellini MD, Farmakis D, Porter J, et al. 2021 Guidelines for the management of transfusion dependent thalassaemia (TDT) 4th edition. Thalassaemia International Federation. 2021. Available at: https://www.thalassemia.org/wp-content/uploads/2021/06/TIF-2021-Guidelines-for-Mgmt-of-TDT.pdf. Accessed May 4, 2022.
10. Devos D, Labreuche J, Rascol O, et al. Trial of deferiprone in Parkinson's disease. N Engl J Med 2022; 387:2045-2055.
11. Children's Hospital & Research Center Oakland. 2012 Standards of Care Guidelines for Thalassemia. Available at: https://thalassemia.com/documents/SOCGuidelines2012.pdf. Accessed May 4, 2023.
12. Sheth S. Strategies for managing transfusional iron overload: conventional treatments and novel strategies. Curr Opin Hematol. 2019 May; 26(3): 139-144.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: HIM line of business removed as does not require PA; references reviewed and updated.	05.14.19	08.19
RT4: added new 1,000 mg tablet to Section VI.	08.07.19	
3Q 2020 annual review: no significant changes; added new tri-scored 1,000 mg tab formulation; references reviewed and updated.	06.04.20	08.20
3Q 2021 annual review: RT4: added new indication for sickle cell and other anemias transfusional iron overload with pediatric expansions; references reviewed and updated.	05.13.21	08.21
3Q 2022 annual review: no significant changes; clarified redirection to Exjade/Jadenu is for generic deferasirox; references reviewed and updated.	05.03.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.30.22	
Added Parkinson disease to section III with rationale in Appendix E.	02.24.23	05.23
3Q 2023 annual review: added requirement that therapy does not include concurrent use of other iron chelators, unless member has excess cardiac iron as evidence by cardiac T2* < 20 millisecond or iron-induced cardiomyopathy; per competitor analysis added requirement that member is responding positively to therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline; per prescribing information limitation of use and competitor analysis added requirement that member does not have transfusional iron overload due to myelodysplastic	04.19.23	08.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
syndrome or Diamond Blackfan anemia; references reviewed and updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.