Clinical Policy: Deferiprone (Ferriprox)

Reference Number: CP.PHAR.147
Effective Date: 11.01.15
Last Review Date: 08.20
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 patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate.

Limitation(s) of use: Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias.

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 due to Thalassemia Syndromes (must meet all)**:**

1. Diagnosis of transfusional iron overload due to thalassemia syndromes;
2. Age ≥ 18 years;
3. 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) and a serum ferritin level > 1,000 mcg/L;
4. Failure of deferoxamine and either Exjade® or Jadenu®, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for deferoxamine, Exjade, Jadenu*
5. Dose does not exceed 99 mg/kg per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Transfusional Iron Overload due to Thalassemia Syndromes (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Current documentation (within the past 30 days) shows a serum ferritin level ≥ 500 mcg/L;
3. 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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.

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®)	1000 mg x 1 dose, then 500 mg Q4 hr x 2 doses PRN, then 500 mg Q4-12 hr PRN.* _____ **IM route if patient not in shock; IV infusion limited to patients in cardiovascular collapse.*	6000 mg/24 hr
	1000-2000 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)
	500-1000 mg IM/day.	1000 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Exjade (deferasirox)	20 to 40 mg/kg (calculated to the nearest whole tablet) PO QD	40 mg/kg/day
Jadenu (deferasirox)	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/Neutropenia
  - Can cause agranulocytosis that can lead to serious infections and death. Neutropenia may precede the development of agranulocytosis.
  - Measure the absolute neutrophil count (ANC) before starting Ferriprox therapy and monitor the ANC weekly on therapy.
  - Interrupt Ferriprox if infection develops, and monitor the ANC more frequently.
  - Advise patients taking Ferriprox to report immediately any symptoms indicative of infection.

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 thalassaemia 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Transfusional iron overload	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	99 mg/kg/day

VI. Product Availability

- Oral solution: 100 mg/mL
- Tablets: 500 mg, 1,000 mg (three times a day) with functional scoring, 1000 mg (twice a day) with functional scoring

VII. References

1. Ferriprox Tablets Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; May 2020. Available at www.ferriprox.com. Accessed June 4, 2020.

2. Ferriprox Oral Solution Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; May 2017. Available at http://www.ferriprox.com/us/pdf/ferriprox_full_pi.pdf. Accessed April 20, 2020.
3. Desferal Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2019. Available at https://dailymed.nlm.nih.gov/dailymed/. Accessed April 20, 2020.
4. Exjade Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2019. Available at http://www.us.exjade.com/. Accessed April 20, 2020.
5. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2019. Available at https://www.jadenu.com/. Accessed April 20, 2020.
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.
8. Maggio A, Vitrano A, Capra M, et al. Long-term sequential deferiprone-deferoxamine versus deferiprone alone for thalassaemia major patients: a randomized clinical trial. Br J Haematol. 2009;145:245-54.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Moved Ferriprox to independent policy Ferriprox criteria - added age criteria (adults); removed requests for documentation; reformatted using appendices and added question about ferritin levels in the continuation of therapy section.	11.15	11.15
Converted policy to new template. **Age removed and documentation requests added; "current documentation" is defined as "within the last 30 days" for follow-up serum ferritin levels and recommended monthly ferritin tests. Initiation of therapy: transfusion history and serum ferritin level per the PI dosing information; the wording "and consistent ferritin levels >1,000" is changed to "or a serum ferritin level >1,000."**	10.16	11.16
Converted to new template. Approval duration extended to 6 and 12 months, from 3 and 6 months initial and re-auth respectively. Added weight-based max dose per PI; safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.	05.17	P&T: 08.17 CPC: 11.17
3Q 2018 annual review: policies combined for Centene Medicaid, HIM (new) and Commercial (new) lines of business; no significant changes; references reviewed and updated.	04.27.18	08.18
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

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.