Clinical Policy: Deferasirox (Exjade, Jadenu)

Reference Number: CP.PHAR.145
Effective Date: 11.01.15
Last Review Date: 08.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Deferasirox (Exjade®, Jadenu®) is an iron chelator.

FDA Approved Indication(s)

Exjade and Jadenu are indicated for the treatment of:

- Chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older.
- 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.

Limitation(s) of use: The safety and efficacy of Exjade/Jadenu when administered with other iron chelation therapy have not been established.

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 Exjade and Jadenu are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Iron Overload due to Blood Transfusions (must meet all)**:**

1. Diagnosis of chronic iron overload due to blood transfusions;
2. Age ≥ 2 years;
3. Member must use generic deferasirox, unless contraindicated or clinically significant adverse effects are experienced;
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. At the time of the request, member has none of the following contraindications:
   a. Glomerular filtration rate (GFR) < 40 mL/min/1.73 m^2;
   b. Platelet count < 50 x 10^9/L;
   c. Severe hepatic impairment (Child-Pugh C);

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 the following (a or b):
   a. Exjade: 40 mg/kg per day (*see Appendix D for dose rounding guidelines*);
   b. Jadenu: 28 mg/kg per day (*see Appendix D for dose rounding guidelines*).

Approval duration: 6 months

B. Chronic Iron Overload due to Non-Transfusion-Dependent Thalassemia Syndromes (must meet all)**:**

1. Diagnosis of chronic iron overload due to NTDT;
2. Age ≥ 10 years;
3. Member must use generic deferasirox, unless contraindicated or clinically significant adverse effects are experienced;
4. Documentation of serum ferritin level > 300 mcg/L;
5. Documentation of LIC ≥ 5 mg Fe/g dw;
6. Therapy does not include concurrent use of other iron chelators;
7. At the time of the request, member has none of the following contraindications:
   a. GFR < 40 mL/min/1.73 m^2;
   b. Platelet count < 50 x 10^9/L;
   c. Severe hepatic impairment (Child-Pugh C);
8. Dose does not exceed the following (a or b):
   a. Exjade: 20 mg/kg per day (*see Appendix D for dose rounding guidelines*);
   b. Jadenu: 14 mg/kg per day (*see Appendix D for dose rounding guidelines*).

Approval duration: 6 months

C. 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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Iron Overload due to Blood Transfusions (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 serum ferritin level ≥ 500 mcg/L;
4. Member must use generic deferasirox, unless contraindicated or clinically significant adverse effects are experienced;
5. 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;
6. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Exjade: 40 mg/kg per day (*see Appendix D for dose rounding guidelines*);
   b. Jadenu: 28 mg/kg per day (*see Appendix D for dose rounding guidelines*).

Approval duration: 12 months

B. Chronic Iron Overload due to Non-Transfusion-Dependent Thalassemia Syndromes (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. Current documentation (serum ferritin within past 30 days; LIC within past 90 days) shows one of the following (a or b):
   a. If member has received < 6 months of Exjade/Jadenu, one of the following (i or ii):
      i. Serum ferritin level ≥ 300 mcg/L;
      ii. LIC ≥ 3 mg Fe/g dw;
   b. If member has received ≥ 6 months of Exjade/Jadenu, LIC ≥ 3 mg Fe/g dw;
3. Member must use generic deferasirox, unless contraindicated or clinically significant adverse effects are experienced;
4. Therapy does not include concurrent use of other iron chelators;
5. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Exjade: 20 mg/kg per day (*see Appendix D for dose rounding guidelines*);
   b. Jadenu: 14 mg/kg per day (*see Appendix D for dose rounding guidelines*).

Approval duration: 12 months

C. 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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, 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, HIM. PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Parkinson's disease.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
Fe/g dw: iron in milligrams per gram dry weight
GFR: glomerular filtration rate
LIC: liver iron concentration
NTDT: non-transfusion-dependent thalassemia

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Estimated GFR < 40 mL/min/1.73 m^2
  - Poor performance status
  - High-risk myelodysplastic syndromes
  - Advanced malignancies
  - Platelet count < 50 x 10^9/L
  - Known hypersensitivity to deferasirox or any component of Exjade or Jadenu
- Boxed warning(s): renal failure, hepatic failure, and gastrointestinal hemorrhage

*Appendix D: Dose Rounding Guidelines**

Weight-based Dose Range	Tablet for Oral Solution Quantity Recommendation
≤ 131.24 mg	125 mg tablet
131.25 mg – 262.49 mg	250 mg tablet
262.5 mg – 392.99 mg	125 mg tablet and 250 mg tablet
393 mg – 524.99 mg	500 mg tablet
525 mg – 655.99 mg	125 mg tablet and 500 mg tablet
656 mg – 787.49 mg	250 mg tablet and 500 mg tablet
787.5 mg – 917.99 mg	125 mg tablet, 250 mg tablet and 500 mg tablet
918 mg – 1,049.99 mg	2 x 500 mg tablets
1,050 mg – 1,180.99 mg	125 mg tablet and 2 x 500 mg tablets
1,181 mg – 1,312.49 mg	250 mg tablet and 2 x 500 mg tablets
1,312.5 mg – 1,442.99 mg	125 mg tablet, 250 mg tablet and 2 x 500 mg tablets
1,443 mg – 1,574.99 mg	3 x 500 mg tablets
Weight-based Dose Range	**Oral Granules (sachets) Quantity Recommendation**
≤ 94.49 mg	90 mg sachet
94.5 mg – 188.99 mg	180 mg sachet
189 mg – 283.49 mg	90 mg sachet and 180 mg sachet
283.5 mg – 377.99 mg	360 mg sachet
378 mg – 472.49 mg	90 mg sachet and 360 mg sachet
472.5 mg – 566.99 mg	180 mg sachet and 360 mg sachet
567 mg – 661.49 mg	90 mg sachet, 180 mg sachet and 360 mg sachet
661.5 mg – 755.99 mg	2 x 360 mg sachets
756 mg – 850.49 mg	90 mg sachet and 2 x 360 mg sachets
850.5 mg – 944.99 mg	180 mg sachet and 2 x 360 mg sachets
945 mg – 1,039.49 mg	90 mg sachet, 180 mg sachet and 2 x 360 mg sachets
1,039.5 mg – 1,133.99 mg	3 x 360 mg sachets

**This is part of a dose rounding guideline on select drug classes as part of an initiative conducted on a larger scale with multiple references and prescriber feedback.*

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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Deferasirox (Exjade)	Transfusional iron overload	20 mg/kg body weight (calculate dose to the nearest whole tablet) PO QD	40 mg/kg/day
	NTDT syndromes	10 mg/kg body weight (calculate dose to the nearest whole tablet) PO QD	20 mg/kg/day
Deferasirox (Jadenu)	Transfusional iron overload	14 mg/kg body weight (calculated to nearest whole tablet/sachet) PO QD	28 mg/kg/day
	NTDT syndromes	7 mg/kg body weight (calculated to nearest whole tablet/sachet) PO QD	14 mg/kg/day

VI. Product Availability

Drug	Availability
Deferasirox (Exjade)	Tablets for oral suspension: 125 mg, 250 mg, 500 mg
Deferasirox (Jadenu)	Tablets/sprinkle (sachets): 90 mg, 180 mg, 360 mg

VII. References

1. Exjade Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/exjade.pdf. Accessed April 14, 2023.
2. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/jadenu.pdf. Accessed April 14, 2023.
3. 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.
4. Hoffbrand AV, Taher A, Cappellini MD. How I treat tranfusional iron overload. Blood. November 1, 2012; 120(18): 3657-3669.
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6. Taher A, Musallam K, Cappellini MD. Guidelines for the management of non-transfusion dependent thalassaemia (NTDT) 2nd edition. Thalassaemia International Federation. 2018. TIF publication No. 22.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: contraindications caveat added to required Jadenu trial; the following contraindications are added: platelets, GFR; Child Pugh C restriction is removed; added requirement that	05.14.19	08.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
member does not have severe hepatic impairment; references reviewed and updated. References reviewed and updated.		
Added appendix D: dose rounding guidelines; added reference to appendix D within criteria.	03.05.20	05.20
3Q 2020 annual review: no significant changes; references reviewed and updated.	04.20.20	08.20
Per July SDC and prior clinical guidance, modify redirection to require medical justification why generic deferasirox cannot be used for Exjade, brand Jadenu and Jadenu Sprinkle requests.	07.09.20	
3Q 2021 annual review: no significant changes; revised medical justification language for not using generic deferasirox to "must use" language; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	05.16.21	08.21
3Q 2022 annual review: no significant changes; 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: per competitor analysis for continuation of therapy in chronic iron overload due to blood transfusions added requirement that member is responding positively to therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline, added clarification that concurrent therapy with other iron chelators is allowable if member has excess cardiac iron as evidence by cardiac T2* < 20 millisecond or iron-induced cardiomyopathy; added requirement for generic use for continuation of therapy; references reviewed and updated.	04.14.23	08.23

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.