# Clinical Policy: Deferasirox (Exjade, Jadenu)

Reference Number: CP.PHAR.145
Effective Date: 11.01.15
Last Review Date: 08.22
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) and a serum ferritin level > 1,000 mcg/L;
5. 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);
6. Therapy does not include concurrent use of other iron chelators;
7. 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 and LIC ≥ 5 mg Fe/g dw;
5. Therapy does not include concurrent use of other iron chelators;
6. 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);
7. 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**

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, 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Current documentation (within the past 30 days) shows serum ferritin level ≥ 500 mcg/L;
3. Therapy does not include concurrent use of other iron chelators;
4. 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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, serum ferritin level ≥ 300 mcg/L or LIC ≥ 3 mg Fe/g dw;

b. If member has received ≥ 6 months of Exjade/Jadenu, LIC ≥ 3 mg Fe/g dw;
3. Therapy does not include concurrent use of other iron chelators;
4. 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. 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, 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.

## 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 |

| Weight-based Dose Range | Tablet for Oral Solution Quantity Recommendation |
|---|---|
| 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.*

## 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 May 9, 2022.
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 May 9, 2022.
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.
5. Taher AT, Viprakasit V, Musallam KM, Cappellini MD. Treating iron overload in patients with non-transfusion-dependent thalassemia: Critical Review. Am J Hematol. 2013; 88: 409-415. DOI: 10.1002/ajh.23405.
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.
7. Cappellini MD, Farmakis D, Porter J, et al. 2021 Guidelines for the management of transfusion dependent thalassemia (TDT) 4th edition. Thalassaemia International Federation. 2021. Available at: https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-4th-edition-2021/. Accessed May 4, 2022.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 3Q 2018 annual review: policies combined for Centene Medicaid, HIM (new) and Commercial (new) lines of business; no significant changes; references reviewed and updated. | 04.30.18 | 08.18 |
| 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 member does not have severe hepatic impairment; references reviewed and updated. References reviewed and updated. | 05.14.19 | 08.19 |
| 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 | 05.16.21 | 08.21 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| use" language; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated. | | |
| 3Q 2022 annual review: no significant changes; references reviewed and updated. | 05.03.22 | 08.22 |

**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.

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**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.