

## Clinical Policy: Deferasirox (Exjade, Jadenu)

Reference Number: CP.PHAR.145

Effective Date: 11.01.15

Last Review Date: 08.19

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<sup>®</sup>, Jadenu<sup>®</sup>) 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. This indication is based on achievement of an LIC less than 5 mg Fe/g dw. An improvement in survival or disease-related symptoms has not been established.

Limitation(s) of use:

- Controlled clinical trials of Exjade/Jadenu with myelodysplastic syndromes (MDS) and chronic iron overload due to blood transfusions have not been performed.
- 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<sup>®</sup> 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  $\geq$  2 years;
3. If request is for Exjade, failure of Jadenu unless contraindicated (e.g., excipients) or clinically significant adverse effects are experienced;
4. Transfusion history of  $\geq$  100 mL/kg of packed red blood cells (e.g.,  $\geq$  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<sup>2</sup>;
  - b. Platelet count  $<$  50 x 10<sup>9</sup>/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;
  - b. Jadenu: 28 mg/kg per day.

**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  $\geq$  10 years;
- 3. If request is for Exjade, failure of Jadenu unless clinically significant adverse effects are experienced;
- 4. Documentation of serum ferritin level  $>$  300 mcg/L and a LIC  $\geq$  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<sup>2</sup>;
  - b. Platelet count  $<$  50 x 10<sup>9</sup>/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;
  - b. Jadenu: 14 mg/kg per day.

**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.PHAR.21 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 a serum ferritin level  $\geq$  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;
  - b. Jadenu: 28 mg/kg per day.

**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, a serum ferritin level  $\geq 300$  mcg/L or an LIC  $\geq 3$  mg Fe/g dw;
  - b. If member has received  $\geq 6$  months of Exjade/Jadenu, an LIC is  $\geq 3$  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;
  - b. Jadenu: 14 mg/kg per day.

**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.PHAR.21 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.PHAR.21 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<sup>2</sup>
  - Poor performance status
  - High-risk myelodysplastic syndromes
  - Advanced malignancies
  - Platelet count < 50 x 10<sup>9</sup>/L
  - Known hypersensitivity to deferasirox or any component of Exjade of Jadenu
- Boxed warning(s):
  - Acute liver injury, including acute renal failure requiring dialysis and renal tubular toxicity including Fanconi syndrome

- Hepatic toxicity, including failure
- Gastrointestinal hemorrhage
- Therapy requires close patient monitoring, including laboratory tests of renal and hepatic function.

**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; December 2018. Available at <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/exjade.pdf>. Accessed April 30, 2019.
2. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018. Available at <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/jadenu.pdf>. Accessed April 30, 2019.
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 transfusional 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to independent policy Removed intermediate dose adjustment stratifications per serum ferritin levels; added failure of Jadenu; removed requests for documentation to allow for attestations per appendices; removed	08.15	11.15

Reviews, Revisions, and Approvals	Date	P&T Approval Date
questions re evidence of transfusion within the last six weeks and allow for attestation of transfusion history of at least 100 mL/kg and a serum ferritin consistently >1000 mcg/L per PI		
<p>CP.PHAR.144 Jadenu incorporated into CP.PHAR.145 Exjade policy and converted to new template. Age removed and documentation requests added; “current documentation” is defined as “within the last 30 days” in the context of follow-up serum ferritin levels– 90 days is provided for follow-up LIC documentation request (section B).</p> <p>Section A: Initiation of therapy: the wording “and consistent ferritin levels &gt;1,000” is changed to “or a serum ferritin level &gt;1,000.”</p> <p>Section B: Jadenu preference over Exjade, in 2015 policy’s section A, is newly added to section B (Chronic Iron Overload Due to NTDT Syndromes).</p> <p>Approval durations for NTDT increased from 3 and 6 months to 6 and 12 months respectively. Serum ferritin and LIC options under continuation of therapy are consolidated for clarity. Definitions of “poor performance status” and “high-risk MDS” are removed.</p>	09.16	11.16
Converted to new template. Added weight-based max dose; safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Updated references.	09.17	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.	04.30.18	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

**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.

**For Health Insurance Marketplace members,** when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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