Clinical Policy: Deferasirox (Exjade, Jadenu)

Reference Number: CP.PHAR.145
Effective Date: 11.15
Last Review Date: 11.17
Line of Business: 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.
- For the treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia 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 of use: Controlled clinical trials of Exjade/Jadenu with myelodysplastic syndromes 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 (including office chart notes and lab results) 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 as may occur in the treatment of chronic anemia, including thalassemia;
2. Age ≥ 2 years old;
3. If request is for Exjade, failure of Jadenu unless clinically significant adverse effects are experienced;
4. Documentation shows a 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 or more in individuals weighing more than 40 kg) and a serum ferritin level > 1,000 mcg/L;
5. Therapy does not include concurrent use of other iron chelators;
6. Dose does not exceed the following:
   a. If request is for Exjade: 40 mg/kg/day;
   b. If request is for Jadenu: 28 mg/kg/day;

7. At the time of request, member has none of the following contraindications:
   a. Serum creatinine > 2 times the age-appropriate upper limit of normal (ULN) or creatinine clearance < 40 mL/min*;*
   b. Platelet count < 50 x 10^9/L.

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 non-transfusion-dependent thalassemia;
2. Age ≥ 2 years old;
3. If request is for Exjade, failure of Jadenu unless clinically significant adverse effects are experienced;
4. Documentation shows a serum ferritin level > 300 mcg/L and a LIC ≥ 5 mg Fe/g dw;
5. Therapy does not include concurrent use of other iron chelators;
6. Member does not have severe (Child-Pugh C) hepatic impairment;
7. Dose does not exceed the following:
   a. If request is for Exjade: 20 mg/kg/day;
   b. If request is for Jadenu: 14 mg/kg/day;
8. At the time of request, member has none of the following contraindications:
   a. Serum creatinine > 2 times the age-appropriate ULN or creatinine clearance < 40 mL/min;
   b. Platelet count < 50 x 10^9/L.

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 last 30 days) shows a 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. If request is for Exjade: 40 mg/kg/day;
   b. If request is for Jadenu: 28 mg/kg/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 30 days; LIC within 90 days) shows one of the following:

a. If member has received < 6 months of Exjade/Jadenu, a serum ferritin level ≥ 300 mcg/L or an LIC ≥ 3 mg Fe/g dw;
b. If member has received ≥ 6 months of Exjade/Jadenu, an 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. If request is for Exjade: 20 mg/kg/day;
   b. If request is for Jadenu: 14 mg/kg/day.

Approval duration: 12 months

C. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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 policy – CP.PHAR.57 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

Fe/g dw: iron in milligrams per gram dry weight
IM: intramuscular
IV: intravenous
LIC: liver iron concentration
ULN: upper limit of normal

V. Dosage and Administration

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

VI. Product Availability

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

VII. References

1. Exjade Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at http://www.us.exjade.com/. Accessed May 8, 2017.
2. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at https://www.jadenu.com/. Accessed May 8, 2017.
3. Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. http://ecog-acrin.org/resources/ecog-performance-status.
4. 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.
5. Hoffbrand AV, Taher A, Cappellini MD. How I treat tranfusional iron overload. Blood. November 1, 2012; 120(18): 3657-3669.
6. Taher AT, Viprakasit V, Musallam KM, Cappellini MD. Treating iron overload in patients with non-transfusion-dependent thalassemia: Critical Reivew. Am J Hematol. 2013; 88: 409-415. DOI: 10.1002/ajh.23405.

Reviews, Revisions, and Approvals	Date	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 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	08.15	11.15
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). Section A: Initiation of therapy: the wording "and consistent ferritin levels >1,000" is changed to "or a serum ferritin level >1,000." 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). 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.	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

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.