

Clinical Policy: Deferasirox (Exjade, Jadenu)

Reference Number: ERX.SPA.90

Effective Date: 11.01.15

Last Review Date: 08.21

Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] 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. Member must use generic deferasirox, unless contraindicated 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 m²;
 - b. Platelet count $<$ 50 x 10⁹/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 \geq 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 a 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 m²;
 - b. Platelet count < 50 x 10⁹/L;
 - a. 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 ERX.PA.01 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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met 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 per kg per day (*see Appendix D for dose rounding guidelines*);
 - b. Jadenu: 28 mg per 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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met 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 is ≥ 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 per kg per day (*see Appendix D for dose rounding guidelines*);
 - b. Jadenu: 14 mg per 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

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

2. Refer to ERX.PA.01 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 – ERX.PA.01 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 m²
 - Poor performance status
 - High-risk myelodysplastic syndromes
 - Advanced malignancies
 - Platelet count < 50 x 10⁹/L
 - Known hypersensitivity to deferasirox or any component of Exjade or Jadenu
- Boxed warning(s):
 - Acute kidney 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

*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.

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 Name	Availability
Deferasirox (Exjade)	Tablets for oral suspension: 125 mg, 250 mg, 500 mg
Deferasirox (Jadenu)	Tablets/sprinkles (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 13, 2021.
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 13, 2021.
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, Viprasit 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added requirement that therapy does not include concurrent use of other iron chelators per PI; added requirement related to contraindications that can be objectively measured/confirmed (initial); added weight based max dose; Added "current documentation" in re-auth (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); for NTDT: increased initial/continued approval from 3/6 to 6/12 months; added LIC ≥ 3 mg Fe/g dw as an option if member has received < 6 months of Exjade/Jadenu and removed < 300 mcg/L and LIC is ≥ 3 mg Fe/g dw. Updated references.	07.17	08.17
3Q 2018 annual review: no significant changes; increased approval durations for chronic iron overload due to blood transfusions from 3/6 to 6/12 months; removed contraindications; removed limitation for use with other iron chelators; references reviewed and updated.	04.30.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: the following contraindications are added: platelets, GFR; restriction of concurrent use with other iron chelators added to criteria to reconcile with PI and other lines of business; added requirement that member does not have severe hepatic impairment; 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.	05.08.20	08.20
3Q 2021 annual review: added redirection to preferred generic deferasirox; references reviewed and updated.	05.16.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2015 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.