

Pharmacy Policy Bulletin

Title: Chelation Agents

Policy #: Rx.01.22

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **deferasirox (Exjade®/Jadenu®)** and **deferiprone (Ferprx®, Ferriprox®)** as provided under the member's prescription drug benefit.

Description:

Individuals, who are transfusion-dependent, receive excess iron with each transfusion. In non-transfusion-dependent thalassemia (NTDT), elevated iron levels are related to suppression of hepcidin levels, increased intestinal iron absorption, and increased release of recycled iron from the reticuloendothelial system. The excess iron accumulates in various tissues, including cardiac, liver, pulmonary, and endocrine glands, due to lack of an active mechanism to excrete iron. The goal of iron chelation therapy in iron overload is to reduce iron levels, prevent complications, and reduce morbidity.

Deferasirox (Exjade®/Jadenu®) is indicated for the treatment of transfusional hemosiderosis (chronic iron overload due to blood transfusions) in individuals who are 2 years of age or older and for the treatment of chronic iron overload in patients 10 years of age and older with NTDT syndromes and with a liver iron concentration (LIC) of at least 5 mg Fe per gram of dry weight (Fe/ g dw) and a serum ferritin greater than 300 mcg/L.

Deferiprone (Ferriprox®, Ferprx®) is an iron chelator indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate.

Deferasirox (Exjade®/Jadenu®) is an orally active chelator that is selective for iron (as Fe³⁺). It is a tridentate ligand that binds iron with high affinity in a 2:1 ratio. Although deferasirox has very low affinity for zinc and copper, there are variable decreases in the serum concentration of these trace metals after the administration of deferasirox. The clinical significance of these decreases is uncertain.

Deferiprone (Ferriprox®, Ferprx®) is a chelating agent with an affinity for ferric ion (iron III). Deferiprone binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable over a wide range of pH values.

Policy:

INITIAL CRITERIA

Deferasirox (Exjade®/Jadenu®) is approved when documentation of ANY of the following is provided:

- A. Diagnosis of chronic iron overload due to blood transfusions with BOTH of the following:
 - 1. Member is 2 years of age or older; and
 - 2. serum ferritin levels are consistently greater than 1000 mcg/L (as demonstrated with at least two lab values within two months prior to treatment)
- B. Diagnosis of chronic iron overload in Non-Transfusion-Dependent Thalassemia Syndromes with BOTH of the following:
 - 1. Member is 10 years of age or older; and
 - 2. Serum ferritin levels are consistently greater than 300 mcg/L and liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) (as demonstrated with at least two lab values within 2 months prior to treatment)

Initial authorization length: 3 months

CONTINUATION CRITERIA

Deferasirox (Exjade®/Jadenu®) is re-approved when ANY the following inclusion criteria are met:

- A. Documentation of a decreased serum ferritin level compared with the baseline level for transfusion dependent anemia; or
- B. Documentation of a decreased serum ferritin level compared with the baseline level or reduction in LIC (liver iron concentration) for Non-transfusion dependent thalassemia syndrome

Authorization length for continuation of therapy: 6 month increments if a benefit is demonstrated

Deferiprone (Ferroprox®, Ferprx®) is approved when documentation is provided of ALL of the following:

- A. Diagnosis of transfusional iron overload due to thalassemia syndromes; and
- B. Current chelation therapy is inadequate

Black Box Warning as shown in the drug Prescribing Information:

Deferasirox (Exjade/ Jadenu)

Renal failure: Deferasirox can cause acute renal failure and death, particularly in patients with comorbidities and those who are in the advanced stages of their hematologic disorders. Deferasirox is contraindicated in adults and pediatric patients with eGFR less than 40 ml/min/1.73m². Use caution

in pediatric patients with eGFR between 40 and 60 ml/min/1.73m². For patients with renal impairment (eGFR 40-60 ml/min/1.73m²) reduce starting dose by 50%. Measure serum creatinine and determine creatinine clearance (CrCl) prior to initiation of therapy and monitor renal function at least monthly thereafter. For patients with baseline renal impairment or increased risk of acute renal failure, monitor creatinine weekly for the first month, then at least monthly thereafter. Monitor serum ferritin monthly to evaluate for overchelation. Use the minimum dose to establish and maintain a low iron burden. Consider dose reduction, interruption, or discontinuation based on increases in serum creatinine. Interrupt deferasirox therapy when acute kidney injury is suspected and during volume depletion.

Hepatic failure: Deferasirox can cause hepatic injury including hepatic failure and death. Measure serum transaminases and bilirubin in all patients prior to initiating treatment, every 2 weeks during the first month, and at least monthly thereafter. Avoid use of deferasirox in patients with severe (Child-Pugh class C) hepatic impairment and reduce the dose in patients with moderate (Child-Pugh class B) hepatic impairment. Interrupt deferasirox therapy when acute liver injury is suspected and during volume depletion.

GI hemorrhage: Deferasirox can cause GI hemorrhages, which may be fatal, especially in elderly patients who have advanced hematologic malignancies and/or low platelet counts. Monitor patients and discontinue deferasirox for suspected GI ulceration or hemorrhage.

Deferiprone (Ferriprox, Ferprx®)

Agranulocytosis/Neutropenia: Deferiprone can cause agranulocytosis that can lead to serious infections and death. Neutropenia may precede the development of agranulocytosis. Measure the absolute neutrophil count (ANC) before starting deferiprone therapy and monitor the ANC weekly during therapy. Interrupt deferiprone therapy if neutropenia develops. If infection develops, interrupt deferiprone and monitor the ANC more frequently. Advise patients taking deferiprone to report immediately any symptoms indicative of infection. For neutropenia, instruct the patient to immediately discontinue deferiprone and all other medications with potential to cause neutropenia. Obtain a complete blood count (CBC), white blood count (WBC corrected for the presence of nucleated red blood cells, ANC and a platelet count daily until recovery. For agranulocytosis, consider hospitalization and other clinically appropriate management.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

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Exjade (deferasirox) [package insert]. East Hanover NJ. Novartis Pharmaceuticals Corporation. Revised July 2020. Available at:

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Ferriprox (deferiprone) [package insert]. Rockville MD. ApoPharma USA, Inc. Revised May 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=97f7bfcb-8666-464c-87b6-9621ceca5ee2&type=display>. Accessed November 16, 2020.

Gilroy RK. Wilson Disease. Available at: <http://emedicine.medscape.com/article/183456-overview#a1>. Accessed November 16, 2020.

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Mir M. Transfusion induced iron overload. Available at: <http://emedicine.medscape.com/article/1389732-overview>. Accessed November 16, 2020.

Musallam KM, Rivella S, Vichinsky E, Rachmilewitz. Non-transfusion-dependent thalassemias. Haematologica. June 2013;98:833-844. DOI: 10.3324/haematol.2012.066845

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Exjade	Deferasirox
Jadenu	Deferasirox
Ferriprox, Ferprx	Deferiprone

Cross References:

Off-Label Use policy Rx.01.33

Policy Version Number:	12.00
P&T Approval Date:	October 08, 2020
Policy Effective Date:	January 01, 2021
Next Required Review Date:	July 09, 2021

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

