Exjade and Jadenu are an oral medication that binds to iron in the blood. Once the iron is bound the body is able to get rid of it. Exjade and Jadenu are used for the treatment of patients who have too much iron in their blood due to repeated blood transfusions or for patients with an inherited disorder called non-transfusion-dependent thalassemia (NTDT). Too much iron in the blood results in the formation of insoluble ferritin which over time can lead to organ damage. Although NTDT usually does not require individuals to get frequent red blood cell transfusions, some patients with NTDT are still at risk for iron overload that can lead to organ damage (1-2).

Regulatory Status
FDA-approved indications: Exjade and Jadenu are iron chelators indicated for:

1. Treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older. This indication is based on reduction in serum ferritin and liver iron concentration (LIC).
2. Treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron (Fe) concentration (LIC) of at least 5 mg Fe per gram of dry weight and a serum ferritin greater than 300 mcg/L (1-2).

Exjade and Jadenu have a boxed warning regarding the development of renal failure, hepatic failure and gastrointestinal hemorrhage, fatal in some patients. Creatinine clearance (estimated by the Cockcroft-Gault method) must be determined before initiating therapy in all patients in order to establish a reliable pretreatment baseline. Monitor serum creatinine weekly during the first month after initiation or modification of therapy and at least monthly thereafter (1-2).
Exjade and Jadenu are contraindicated in patients with creatinine clearance less than 40 mL/min or serum creatinine greater than 2 times the age appropriate upper limit of normal. Baseline serum transaminases and bilirubin should also be obtained in all patients before the initiation of treatment and every 2 weeks during the first month and at least monthly thereafter (1-2).

Avoid the use of Exjade and Jadenu in patients with severe (Child-Pugh C) hepatic impairment. Patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment may be at higher risk for hepatic toxicity. Closely monitor patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment for efficacy and adverse reactions that may require dose titration (1-2).

GI hemorrhage, including deaths, has been reported, especially in elderly patients who had advanced hematologic malignancies and/or low platelet counts. Non-fatal upper GI irritation, ulceration and hemorrhage have been reported in patients, including children and adolescents, receiving Exjade or Jadenu. Patients should be monitored for suspected GI ulceration or hemorrhage during Exjade or Jadenu therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. The risk of gastrointestinal hemorrhage may be increased when administering Exjade or Jadenu in combination with drugs that have ulcerogenic or hemorrhagic potential, such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, oral bisphosphonates, or anticoagulants (1,2).

Exjade and Jadenu are contraindicated in patients with any of the following: serum creatinine greater than 2 times the age-appropriate upper limit of normal, creatinine clearance less than 40 mL/min, high-risk myelodysplastic syndromes (MDS), advanced malignancies and platelet counts below 50 x 10^9/L (1-2).

Related policies
Ferriprox

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Exjade and Jadenu may be considered medically necessary for the treatment of chronic iron overload or for non-transfusion-dependent thalassemia (NTDT) and if the conditions indicated below are met.
Exjade and Jadenu may be considered investigational for all other indications.

**Prior - Approval Requirements**

**Diagnoses**

The patient must have **ONE** of the following:

1. Chronic iron overload due to blood transfusions  
   a. 2 years of age and older  
   b. Serum ferritin >1000mcg/L

2. Non-transfusion-dependent thalassemia (NTDT)  
   a. 10 years of age and older  
   b. Liver iron concentration (LIC) of at least 5 milligrams of iron per gram of dry liver tissue weight  
   c. Serum ferritin >300 mcg/L

**AND ALL** of the following:  
1. Platelet counts >50,000 per microliters  
2. Obtain baseline transaminases (AST and ALT) and bilirubin before initiation of therapy and every 2 weeks during the first month and at least monthly thereafter

**AND NONE** of the following:  
1. High-risk myelodysplastic syndromes (MDS)  
2. Advanced malignancies  
3. Severe (Child-Pugh C) hepatic impairment  
4. Serum creatinine greater than 2 times the age-appropriate upper limit of normal  
5. Creatinine clearance less than 40 mL/min  
6. Concurrent therapy with another iron chelating agent (see Appendix 1)

**Prior – Approval Renewal Requirements**

**Diagnoses**

The patient must have **ONE** of the following:
1. Chronic iron overload due to blood transfusions
   a. 2 years of age and older
   b. Serum ferritin >500 mcg/L
2. Non-transfusion-dependent thalassemia (NTDT)
   a. 10 years of age and older
   b. Liver iron concentration (LIC) of at least 5 milligrams of iron per gram of dry liver tissue weight
   c. Serum ferritin >300 mcg/L

AND ALL of the following:
1. Platelet count >50,000 per microliters
2. Transaminases (AST and ALT) and bilirubin monitored monthly

AND NONE of the following:
1. High-risk myelodysplastic syndromes (MDS)
2. Advanced malignancies
3. Severe (Child-Pugh C) hepatic impairment
4. Serum creatinine greater than 2 times the age-appropriate upper limit of normal
5. Creatinine clearance less than 40 mL/min
6. Concurrent therapy with another iron chelating agent (see Appendix 1)

Policy Guidelines

Pre – PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 12 months

Rationale

Summary
Exjade and Jadenu are FDA approved for treating chronic iron overload due to blood transfusions in patients 2 years of age and older. This orally active iron chelator is most commonly used in patients with b-thalassemia, who, with repeated red blood cell transfusions, accumulate iron. Exjade and Jadenu is also approved to treat patients 10 years of age and older who have chronic iron overload resulting from a genetic blood disorder called non-transfusion-dependent thalassemia (NTDT) (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Exjade and Jadenu while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td>December 2011</td>
<td>New Policy</td>
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<tr>
<td>December 2012</td>
<td>Annual editorial review</td>
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<tr>
<td>March 2013</td>
<td>Annual editorial review and reference update, addition of non-transfusion-dependent thalassemia (NTDT) to criteria</td>
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<tr>
<td>December 2014</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>April 2015</td>
<td>Addition of Jadenu</td>
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<tr>
<td>June 2015</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>September 2015</td>
<td>Annual review and reference update</td>
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<tr>
<td>December 2016</td>
<td>Annual review and reference update, policy number change from 5.11.02 to 5.99.02</td>
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<tr>
<td>June 2017</td>
<td>Annual editorial review and reference update, separation of MDS and advanced malignancies in renewal section</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.
### Appendix 1 - List of Iron Chelating Agents

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<th>Generic Name</th>
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<tr>
<td>deferiprone</td>
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