This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

**Drug:** Exjade, Jadenu (deferasirox), Ferriprox (deferiprone), Desferal (deferoxamine)

**Class:** Iron Chelators

**Formulary medication:** N/A

**Line of business:** Non-Medicare

**Effective Date:** August 2015

**Revision Date:** August 2015

**Policy/Criteria:**

**Exjade, Jadenu (deferasirox)**

1. FDA approved indications AND
   a. Treatment of chronic iron overload due to non-transfusion dependent thalassemia syndromes evidenced by baseline serum ferritin level > 300 mcg/L OR Liver Iron Concentration (LIC) > 5mg/g dw
   b. Treatment of chronic iron overload due to blood transfusions evidenced by baseline serum ferritin level > 1000 mcg/L (record of transfusions required) OR Liver Iron Concentration (LIC) > 7mg/g dw
2. Prescribed by hematologist
3. Jadenu can be administered with or without food, no need to dissolve tablet
4. Duration of Approval: 6 months

**Ferriprox (deferiprone)**

1. FDA approved indications AND
   a. Treatment of transfusional iron overload due to thalassemia syndromes evidenced by baseline serum ferritin level > 300 mcg/L OR Liver Iron Concentration (LIC) > 5mg/g dw
2. Prescribed by hematologist
   a. deferasirox and deferoxamine are preferred over deferiprone
3. Duration of Approval: 6 months

**Desferal (deferoxamine)**

1. FDA approved indications
   a. Treatment of chronic iron overload due to blood transfusions evidenced by baseline serum ferritin level > 1000 mcg/L (record of transfusions required) OR Liver Iron Concentration (LIC) > 7mg/g dw
   b. Treatment of acute iron toxicity
2. Prescribed by hematologist
3. Duration of Approval: 6 months
Clinical Justification:

<table>
<thead>
<tr>
<th>Pharmacology</th>
<th>Exjade/Jadenu (Deferasirox)</th>
<th>Ferriprox (Deferiprone)</th>
<th>Desferal (Deferoxamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecule: 2:1 stoichiometry for iron</td>
<td>3:1 stoichiometry for iron</td>
<td>Molecule: 1:1 stoichiometry for iron</td>
<td></td>
</tr>
<tr>
<td>Route of Administration</td>
<td>Oral</td>
<td>Oral</td>
<td>IV or slow SQ infusion</td>
</tr>
</tbody>
</table>

Comparative Efficacy

- *Noninferiority to deferoxamine was demonstrated for deferasirox at 20 and 30mg/kg/day dosages.*
- *Deferiprone is limited to second-line therapy as indicated by FDA*
- *No outcome studies (mortality/morbidity) are available*
- *Only deferoxamine has been proved to improve survival in treatment of iron overload in thalassemia.*

Comparison of FDA-Approved Indications

<table>
<thead>
<tr>
<th>FDA-Approved Indications</th>
<th>Exjade/Jadenu (Deferasirox)</th>
<th>Ferriprox (Deferiprone)</th>
<th>Desferal (Deferoxamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of chronic iron overload due to blood transfusions</td>
<td>Patients 2 year and older</td>
<td>--</td>
<td>Patients 3 year and older</td>
</tr>
<tr>
<td>Treatment of transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate</td>
<td>Patients 10 year and older</td>
<td>Adults only</td>
<td>--</td>
</tr>
<tr>
<td>Treatment of acute iron intoxication</td>
<td>--</td>
<td>--</td>
<td>Patients 3 year and older</td>
</tr>
</tbody>
</table>

Comparison of Contraindications, Warning and Precautions

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Exjade (Deferasirox)</th>
<th>Ferriprox (Deferiprone)</th>
<th>Desferal (Deferoxamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CrCl &lt; 40 mL/min or serum creatinine &gt; 2 times ULN</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe renal disease or anuria</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Poor performance status and high risk MDS or advanced malignancies</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet &lt; 50 x 10^9/L</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Black Box Warnings

- Agranulocytosis: X
- Infection Risk: X
- Renal Failure: X
- Hepatic Failure: X
- GI hemorrhage: X

Warnings and Precautions

- Infection: X
- Fetal Risk: X
May cause renal impairment | X | X
May cause hepatic impairment | X |
GI hemorrhage | X |
Cytopenias (e.g. agranulocytosis, neutropenia, thrombocytopenia) | X |
Infusion reactions | X |
Respiratory distress syndrome | X |

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exjade (deferasirox)</td>
<td>20mg/kg/day orally</td>
</tr>
<tr>
<td>Jadenu (deferasirox)</td>
<td>14mg/kg/day orally</td>
</tr>
<tr>
<td>Ferriprox (deferiprone)</td>
<td>75mg/kg/day orally in 3 divided doses</td>
</tr>
<tr>
<td>Desferal (deferoxamine)</td>
<td>0.5—1 g IM daily, IV</td>
</tr>
</tbody>
</table>

**Desferal (deferoxamine)**

Deferoxamine is the only FDA-approved product for the treatment of acute iron intoxication. IM administration is preferred and should be used of ALL PATIENTS NOT IN SHOCK. IV administration SHOULD ONLY BE USED FOR PATIENTS IN A STATE OF CARDIOVASCULAR COLLAPSE AND THEN ONLY BY SLOW INFUSION THAT DOES NOT EXCEED 15MG/KG/HR.

**Exjade/Jadenu (deferasirox)**

Deferasirox has been developed as an alternative to deferoxamine, the standard treatment of chronic iron overload, which is administered parenterally. Deferasirox is an orally active chelator that is selective for iron. It binds iron with high affinity in a 2:1 ratio. Iron excretion is predominantly fecal. Clinical trials designed to confirm a clinical benefit or increased survival has not been completed. Clinical trials have demonstrated that deferasirox was effective in reducing liver iron concentrations in patients with transfusional hemosiderosis secondary to betathalassemia and chronic anemias. The benefit of deferasirox over the alternative therapy (deferoxamine) is that the oral route of administration may increase compliance and improve the quality of life in patients with transfusion hemosiderosis. For continuation of therapy, serum ferritin levels should be monitored monthly.

**Ferriprox (deferiprone)**

Deferiprone is FDA-approved for the treatment of adults with transfusional iron overload secondary to thalassemia syndromes when current chelation therapy is inadequate. There is insufficient safety and efficacy data established for the treatment of transfusional iron overload in patients with other chronic anemias. Despite the ease of oral administration, a Cochrane review of 10 studies involving 398 patients with thalassemia supported second line treatment of deferiprone when deferoxamine is contraindicated or inadequate. Furthermore, outcome studies such as mortality are not established for deferiprone therapy. Serum ferritin should be monitored periodically for efficacy, along with CBC, ANC, LFT and zinc level monitoring during therapy.

**References:**