OVERVIEW
Reblozyl is an erythroid maturation agent indicated for the treatment of anemia in adults with beta-thalassemia who require regular red blood cell transfusions. Reblozyl is not indicated for use as a substitute for red blood cell transfusions in patients who require immediate correction of anemia.

Disease Overview
Beta-thalassemia, an inherited blood disorder, is characterized by reduced levels of functional hemoglobin (Hb). Patients with a severe form (beta-thalassemia major) become symptomatic due to low Hb level (e.g., increased cardiac effort, tachycardia, poor growth) or ineffective erythropoiesis (e.g., bone changes, massive splenomegaly). Even with treatment, severe complications may arise due to iron overload secondary to increased intestinal absorption and frequent blood transfusions. The frequency of symptomatic patients with beta-thalassemia is estimated at approximately 1 in 100,000 individuals in the general population but is less common in the US.

Guidelines
Guidelines do not address luspatercept for treatment of beta-thalassemia. Standards of Care Guidelines for Thalassemia (2012) are published by the Children’s Hospital and Research Center of Oakland. Life-long blood transfusions and iron chelation are the main treatments for beta-thalassemia. Transfusions are usually needed every 3 to 4 weeks and are recommended to maintain the pre-transfusion Hb level above 9 to 10 g/dL and post-transfusion Hb level should not exceed 14 g/dL. Blood transfusions are given to improve anemia as well as suppress ineffective erythropoiesis. Most serious growth, bone, and neurologic complications are prevented with regular transfusions. Once transfusions are started, transfusion-related complications become a major source of morbidity. Hydroxyurea is described as an experimental agent for beta-thalassemia. The Thalassaemia International Federation (2014) also recommends transfusions and iron chelation for treatment of beta-thalassemia. These guidelines state that transfusions are usually administered every 2 to 5 weeks and are recommended to maintain the pre-transfusion Hb level above 9 to 10.5 g/dL and post-transfusion Hb level below 14 to 15 g/dL. The primary goal of chelation therapy is to maintain safe levels of body iron by balancing iron from blood transfusion with iron excretion by chelation. Despite literature suggesting hydroxyurea may be beneficial in certain patients with beta-thalassemia, use is not recommended outside of a clinical trial.

POLICY STATEMENT
Prior authorization is recommended for medical benefit coverage of Reblozyl. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Reblozyl as well as the monitoring required for adverse events and long-term efficacy, approval requires Reblozyl to be prescribed by or in consultation with a physician who specializes in the condition being treated.
RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Reblozyl is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Beta-Thalassemia. Approve for the duration noted if the patient meets one of the following criteria (A or B):
   A) Initial Therapy. Approve for 4 months if the patient meets all of the following criteria (i, ii, and iii):
      i. The patient is ≥ 18 years of age; AND
      ii. According to the prescriber, the patient requires regular red blood cell transfusions.  
         Note: This includes patients who are transfusion-dependent; AND
      iii. The medication is being prescribed by or in consultation with a hematologist.
   B) Continuation of Therapy. Approve for 1 year if according to the prescriber, the patient has experienced a clinically meaningful decrease in transfusion burden.

   Dosing. Approve up to 1.25 mg/kg by subcutaneous injection, not more frequently than once every 3 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Reblozyl has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.
REFERENCES

HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Date Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Policy</td>
<td>--</td>
<td>11/13/2019</td>
</tr>
<tr>
<td>Revision</td>
<td>Note added to clarify that the requirement for regular blood cell transfusions includes patients who are transfusion-dependent.</td>
<td>11/18/2019</td>
</tr>
</tbody>
</table>