Reblozyl® (luspatercept-aamt) – New orphan drug approval

- On November 8, 2019, the FDA announced the approval of Celgene and Acceleron's Reblozyl (luspatercept-aamt), for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.
    - Reblozyl is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.
- Beta thalassemia is a rare, inherited blood disorder that reduces the production of hemoglobin. In people with beta thalassemia, low levels of hemoglobin lead to a lack of oxygen in many parts of the body and anemia.
    - Supportive treatment for people with beta thalassemia often consists of lifelong regimens of chronic blood transfusions for survival and treatment for iron overload due to the transfusions.
    - People with beta thalassemia are also at an increased risk of developing abnormal blood clots.
- Reblozyl is a first-in-class erythroid maturation agent and the first FDA-approved treatment for anemia in beta thalassemia.
- The efficacy of Reblozyl was established in the BELIEVE trial, a randomized, double-blind, placebo-controlled study in 336 patients with beta thalassemia. All patients were eligible to receive best supportive care, which included RBC transfusions. The primary endpoint was the proportion of patients achieving RBC transfusion burden reduction (≥ 33% reduction from baseline) with a reduction of at least 2 units from week 13 to week 24.
    - In the Reblozyl arm, 21.4% of patients met the primary endpoint during weeks 13 to 24 vs. 4.5% in the placebo arm (risk difference 17.0; 95% CI: 10.4, 23.6; $p < 0.0001$).
- Warnings and precautions for Reblozyl include thrombosis/thromboembolism, hypertension, and embryo-fetal toxicity.
- The most common adverse reactions (> 10%) with Reblozyl use were headache, bone pain, arthralgia, fatigue, cough, abdominal pain, diarrhea, and dizziness.
- The recommended dose of Reblozyl is 1 mg/kg once every 3 weeks by subcutaneous injection.
    - Reblozyl should be reconstituted and administered by a healthcare professional.
    - Hemoglobin results should be assessed and reviewed prior to each administration. If an RBC transfusion occurred prior to dosing, the pre-transfusion hemoglobin must be considered for dosing purposes.
    - If the pre-dose hemoglobin is ≥ 11.5 g/dL and the Hgb level is not influenced by recent transfusion, dosing should be delayed until the hemoglobin is ≤ 11 g/dL.
    - Refer to the Reblozyl drug label for additional dosing and administration recommendations.
- Acceleron announced that the Wholesale Acquisition Cost (WAC) for Reblozyl will be $3,441 for a 25 mg vial and $10,324 for a 75 mg vial.

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- The FDA is also evaluating Reblozyl for the treatment of anemia in adults with very low- to intermediate-risk myelodysplastic syndromes who have ring sideroblasts and require RBC transfusions. The FDA is expected to make an approval decision by April 4, 2020 for this indication.

- Celgene and Acceleron plan to launch Reblozyl one week following the FDA approval. Reblozyl will be available as a 25 mg and 75 mg lyophilized powder in single-dose vials for reconstitution (for injection).