FDA Approved > Zynteglo® Gene Therapy for β-Thalassemia

The U.S. Food and Drug Administration (FDA) approved Zynteglo (betibeglogene autotemcel), a curative gene therapy for the treatment of patients with β-thalassemia who require regular red blood cell (RBC) transfusions. Zynteglo is the third gene therapy approved by the FDA.

Although Zynteglo is only administered one time, the treatment process involves several steps, including a lengthy hospitalization. The cost of therapy is $2.8 million per treatment not including the cost of hospitalization. The manufacturer, bluebird bio, estimates that there are approximately 1,500 patients with transfusion-dependent β-thalassemia in the United States — of whom 850 are expected to be treatment eligible — with a smaller number expected to pursue treatment.

Background

A curative therapy

β-thalassemia is a rare blood disorder caused by a mutation in the beta-globin gene leading to reduced or absent hemoglobin production and subsequent insufficient delivery of oxygen throughout the body. Patients with severe β-thalassemia require lifelong RBC transfusions every 2-5 weeks; transfusions increase risk the risk for complications due to chronic iron overload, including damage to the heart, liver, and other organs. The median age of death for patients with severe β-thalassemia who require regular transfusions is 37 years. The manufacturer of Zynteglo, bluebird bio, estimates that there are approximately 1,500 patients with transfusion-dependent β-thalassemia in the United States (of whom 850 are expected to be treatment eligible). The lengthy hospital stay and conditioning regimen is expected to limit uptake to approximately 50 patients in the first year.

Zynteglo is a curative therapy that uses an engineered virus to deliver a functioning gene to the bone marrow of β-thalassemia patients, allowing the body to produce normal hemoglobin levels. Zynteglo is only administered one time, however, the treatment process takes several steps, including the collection of stem cells to which the functional gene is added to the patient's cells outside of the body, and then infused to the patient following myeloablative chemotherapy to kill the patient's non-functioning stem cells. Following Zynteglo infusion, patients stay in the hospital for several months as they regain functioning immune systems. The entire process, from preparation to recovery, takes

approximately six months. In clinical trials, 89% of 41 patients with β-thalassemia who were treated with Zynteglo no longer required RBC transfusions.

Studies found the drug to be well-tolerated with serious adverse events being attributed to the chemotherapy regimen required prior to treatment. The FDA also indicated a potential risk of blood cancer associated with the treatment; however, no cases were found in studies of Zynteglo. Patients who receive Zynteglo are required to have their blood monitored for at least 15 years following treatment for evidence of cancer.

Cost and availability

Potential additional volatility in the Medicaid drug rebate program

The manufacturer estimates that a patient with transfusion dependent β-thalassemia will incur total health care costs that are approximately 23 times higher than the general population, an average $6.4 million over the patient's lifetime. In May 2022, the Institute for Clinical and Economic Review (ICER), an independent organization that provides clinical and cost-effectiveness analyses of treatments, found that Zynteglo would be cost-effective up to a price of approximately $2.9 million. ICER evaluated Zynteglo using an anticipated price of $2.1 million, and stated "beti-cel meets commonly accepted value thresholds at an anticipated price of $2.1 million — if that price is subject to an 80% payback for treatment failure."

The manufacturer has priced Zynteglo at $2.8 million per patient, not including the costs of the conditioning regimen and hospitalization required for patients receiving the therapy. Bluebird bio is negotiating with payers including state Medicaid agencies on a reimbursement model to refund up to 80% of the cost of therapy if the patient is required to restart blood transfusions within two years of treatment with Zynteglo. Challenges related to the reimbursement model include addressing member enrollment switches to another plan or payer and maintenance of data and health outcomes tracking. Zynteglo was previously approved in Europe, with a cost of $1.8 million; however, bluebird bio removed it from marketing in 2021 due to difficulties with reimbursement.

Bluebird bio is planning to launch Zynteglo in October 2022 where it will be available at manufacturer designated treatment centers that the company has indicated are "preeminent transplant institutions" across the United States. The FDA is expected to decide on a second gene therapy from bluebird bio in September for the treatment of a rare neurological disorder.

Please contact Bethany Holderread at Bethany.holderread@mercer.com or Abigail Charlier at Abigail.charlier@mercer.com for questions on Zynteglo or other high cost drugs.

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