Protocol for Zynteglo® (betibeglogene autotemcel)

Approved April 2023

Background: *Beta thalassemia is an inherited blood disorder characterized by reduced levels of functional hemoglobin.*

Zynteglo *is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.*

Criteria for approval:

1. Patient has a documented diagnosis of transfusion-dependent beta thalassemia (TDT) and requires regular red blood cell (RBC) transfusions.
2. Transfusion-dependent is defined as:
    a. For all ages: Documented history of ≥ 100 ml/kg/year of pRBCs in the past two years **OR**
    b. For patients aged ≥ 12 years: ≥ 8 transfusions of pRBCs per year for the past 2 years; **AND**
3. Diagnosis is confirmed by molecular genetic testing; **AND**
4. Patient is a candidate for hematopoietic stem cell transplantation (HSCT), but does NOT have access to matched family donor; **AND**
5. Medication is prescribed by or in consultation with a hematologist or a provider specializing in thalassemia; **AND**
6. Patient will undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for Zynteglo manufacturing
7. Perform screening for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2) in accordance with clinical guidelines before collection of cells for manufacturing
8. Patient is not on anti-retrovirals or hydroxyurea for one month prior to mobilization. If a patient requires anti-retrovirals for HIV prophylaxis, then confirm a negative test for HIV before beginning mobilization and apheresis of CD34+ cells.
9. Medication will only be approved for a single one-time dose.

10. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence
11. Patient has been counselled regarding need for lifelong monitoring for hematological malignancies

Approval Duration: one time approval

References:

1. Zyntelgo [prescribing information]. Bluebird Bio, Inc. Somerville, MA. August 2022
2. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2019. Updated periodically
3. Galanello, R., Origa, R. Beta-thalassemia. Orphanet J Rare Dis 5, 11 (2010). https://doi.org/10.1186/1750-1172-5-11
4. Benz EJ, Angelucci E. Management of thalassemia. UpToDate, Aug 24, 2022.
5. Weiss MJ. Update on the Diagnosis and Management of Thalassemia. Clinical Advances in Hematology & Oncology Volume 12, Issue 1 January 2014.
6. National Organization for Rare Disorders. Beta-thalassemia. 2018. Available at: https://rarediseases.org/rarediseases/thalassemia-major/. Accessed on February 10, 2023.