Reference number(s)
5548-A

Standard Medicare Part B Management Zynteglo

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Zynteglo	betibeglogene autotemcel

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Zynteglo is indicated for the treatment of adult and pediatric patients with beta-thalassemia who require regular blood cell (RBC) transfusions.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia

Documentation

The following documentation must be available, upon request, for all submissions:

- Molecular or genetic testing results documenting transfusion-dependent beta-thalassemia genotype.
- Chart notes or medical record documenting history of blood cell transfusions for the previous two years.

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Coverage Criteria

Transfusion-Dependent Beta-Thalassemia[1-4]

Authorization of 3 months for one dose total may be granted for transfusion-dependent beta-thalassemia when all of the following criteria are met:

- Member is 4 years of age or older and meets both of the following criteria:
  - Member weighs at least 6 kg.
  - Member is reasonably anticipated to provide at least the minimum number of cells required to initiate the manufacturing process.
- Member has a diagnosis of transfusion-dependent beta-thalassemia with a non-β0/β0 OR β0/β0 genotype confirmed via genetic testing (see Appendix for examples).
- Member requires regular blood cell transfusions and meets one of the following criteria within the previous two years:
  - Member has received at least 100 milliliter per kilogram of packed red blood cells (pRBCs) per year.
  - Member has received at least 8 transfusions events of packed red blood cells (pRBCs) per year.
- Member is eligible for a hematopoietic stem cell transplant (HSCT) but is unable to find a matched (10/10) human leukocyte antigen (HLA) related donor.
- Member has not received a prior hematopoietic stem cell transplant (HSCT).
- Member has not received Zynteglo or any other gene therapy previously.

Appendix[1-3]

Examples of non-β0/β0 OR β0/β0 genotypes

- β0/β0
- β0/β+
- βE/β0
- β0/IVS-I-110
- IVS-I-110/IVS-1-110

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Zynteglo.
- The available compendium

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    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- 2021 Guidelines for the management of transfusion dependent thalassaemia (TDT).

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Zynteglo are covered.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the member being eligible for a hematopoietic stem cell transplant but unable to find a related donor as well the member not previously receiving a hematopoietic stem cell transplant can be found in the clinical trial of Zynteglo.

References

1. Zynteglo [package insert]. Somerville, MA: Bluebird Bio; August 2022.
2. Locatelli F, Thompson AA, Kwiatkowski JL, et al. Betibeglogene Autotemcel Gene Therapy for Non-β0/β0 Genotype β-Thalassemia. N Engl J Med. 2022;386(5):415-427.
3. Ashutosh Lal, Franco Locatelli, Janet L. Kwiatkowski, Andreas E. Kulozik, Evangelia Yannaki, John B. Porter, Isabelle Thuret, Martin G. Sauer, Heidi Elliot, Ying Chen, Richard A. Colvin, Alexis A. Thompson; Northstar-3: Interim Results from a Phase 3 Study Evaluating Lentiglobin Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia and Either a β0 or IVS-I-110 Mutation at Both Alleles of the HBB Gene. Blood 2019; 134 (Supplement_1): 815.
4. Cappellini MD, Farmakis D, Porter J, Taher A. 2021 Guidelines for the management of transfusion dependent thalassaemia (TDT). Nicosia, Cyprus: Thalassaemia International Federation, 2021.

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