Gene Therapy Treatments for Beta Thalassemia

Humana

Medicaid Medical Coverage Policy

Original Effective Date: 01/01/2025
Effective Date: 03/09/2026
Review Date: 11/04/2025
Policy Number: HUM-2239-001
Line of Business: Medicaid
State(s): SC

Table of Contents

Description

Thalassemias are a diverse group of inherited recessive disorders caused by abnormal synthesis of either the alpha- or beta-globin chains of hemoglobin.[4] **Beta-thalassemia** (also known as β-thalassemia or Cooley's anemia) is a rare inherited blood disorder where the body does not produce enough hemoglobin, the protein responsible for carrying oxygen throughout the bloodstream. Common symptoms include anemia, fatigue, pale skin, weakness and an increased risk of blood clots.[5] Thalassemias are now commonly classified as either transfusion-dependent (TDT) or non-transfusion-dependent. Traditionally, β-thalassemia is categorized into three types: thalassemia minor, intermedia and major.[4]

Chronic transfusion therapy is regularly used in the management of β-thalassemia major, with individuals typically receiving 1 to 3 units of packed red blood cells (RBC) every 3 to 5 weeks.[3] Regular RBC transfusions in individuals with transfusion-dependent beta thalassemia can lead to iron accumulation in the body. To manage this, iron chelation therapy is commonly used to help reduce the risk of iron-related organ toxicity. Splenomegaly may also develop because of increased RBC breakdown by the spleen, particularly in individuals with β-thalassemia major.[9]

Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative therapy available, with cure rates between 80% to 90%. However, access to matched donors can be challenging due to limited availability and some are not ideal candidates due to age or iron-related complications. Additionally, HSCT carries risks of serious complications, such as graft-versus-host disease.[10] Gene therapy is a medical approach that involves introducing a functional gene or modifying the expression of a gene associated with

disease. It aims to deliver lasting therapeutic effects by continuously producing proteins that influence the development and progression of the targeted disease and is currently used in treating conditions such as β-thalassemia.[9]

Casgevy (exagamglogene autotemcel) is a one-time gene therapy used to treat individuals 12 years of age and older with β-thalassemia who need regular blood transfusions. This therapy uses a gene-editing method called CRISPR, which works by guiding a special protein (Cas9) to a specific spot in the DNA. Once there, it makes a precise cut, allowing specialists to change how certain genes work.[17]

Zynteglo (betibeglogene autotemcel) is a one-time gene therapy product administered as a single dose. This autologous hematopoietic stem cell-based gene therapy is indicated for the treatment of adult and pediatric individuals with β-thalassemia who require regular RBC transfusions.[18] This works by introducing functional copies of the beta-globin gene into an individuals' own stem cells. Once reinfused, the modified cells are intended to enable the body to produce hemoglobin more effectively, reducing or eliminating the need for regular blood transfusions.[8]

Requests for Casgevy (exagamglogene autotemcel) AND Zynteglo (betibeglogene autotemcel) *require review by a medical director*.

Coverage Determination

Refer all requests or questions regarding gene therapy treatments for beta thalassemia to the Corporate Transplant Department.

Phone	Fax	Email
1-866-421-5663	502-508-9300	transplant@humana.com

Humana members may be eligible under the Plan for **Casgevy (exagamglogene autotemcel) (J3392) one-time, single dose** when the following requirements are met[17]:

- Absence of limitations; **AND**
- Individual has diagnosis of TDT; **AND**
- Individual is 12 through 65 years of age; **AND**

Humana members may be eligible under the Plan for **Zynteglo (betibeglogene autotemcel) (J3393) one-time, single dose** when the following requirements are met[18]:

- Absence of limitations; **AND**
- Individual has β-thalassemia, requiring RBC transfusions; **AND**

- Individual is 4 through 65 years of age

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **Casgevy (exagamglogene autotemcel) (J3392)** for any indications other than those listed above including, but may not be limited to[16]:

- Individual has desire to become pregnant/reproduce OR unwilling to use effective contraception; **OR**
- Individual is pregnant or breastfeeding; **OR**
- Hepatic impairment; **OR**
- Prior allogenic or autologous HSC transplant; **OR**
- Renal impairment; **OR**
- Seropositive for HIV-1, HIV-2, HBV or HCV

Humana members may **NOT** be eligible under the Plan for **Zynteglo (betibeglogene autotemcel) (J3393)** for any indications other than those listed above including, but may not be limited to[Error! Reference source not found.]:

- Individual has desire to become pregnant/reproduce OR unwilling to use effective contraception; **OR**
- Individual is pregnant or breastfeeding; **OR**
- Hepatic impairment; **OR**
- Renal impairment; **OR**
- Seropositive HIV-1, HIV-2, HTLV-1, or HTLV-2

A review of the current medical literature shows that there is **no evidence** to determine that these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
No code(s) identified		
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
J3392	Injection, exagamglogene autotemcel, per treatment	
J3393	Injection, betibeglogene autotemcel, per treatment	
ICD-10-PCS Code(s)	**Description**	**Comments**
XW133B8	Transfusion of Betibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 8	
XW133J8	Transfusion of Exagamglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 8	
XW143B8	Transfusion of Betibeglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8	
XW143J8	Transfusion of Exagamglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8	

References

1. ClinicalKey. Drug Monograph. Betibeglogene autotemcel. https://clinicalkey.com. Updated August 15, 2025.

2. ClinicalKey. Drug Monograph. Exagamglogene autotemcel. https://clinicalkey.com. Updated May 8, 2025.

3. ClinicalKey. Holstein SA, Hohl RJ. Thalassemia. In: Kellerman RD, Heidelbaugh MD, Lee EM. *Conn's Current Therapy*. Elsevier; 2025:528-533. https://clinicalkey.com.

4. ClinicalKey. Onukogu ID. Thalassemias. In: Ferri FF. *Ferri's Clinical Advisor.* Elsevier; 2026:1169e12-1169e21. https://clinicalkey.com.

5. ECRI Institute. Genetic Test Assessment. Zynteglo (betibeglogene autotemcel) (bluebird bio, inc.) for treating transfusion-dependent beta-thalassemia. https://home.ecri.org. Published November 7, 2022.

6. Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. *N Engl J Med.* 2021;384(3):252-260.

7. Frangoul H, Stults A, Bruce K, et al. Best practices in gene therapy for sickle cell disease and transfusion-dependent β-thalassemia. *Transplant Cell Ther*. 2025;31(6):352.e1-352.e10. doi:10.1016/j.jtct.2025.02.025.

8. Hayes, Inc. Emerging Technology Report. Betibeglogene autotemcel (Zynteglo) for beta thalassemia. https://evidence.hayesinc.com. Published August 19, 2022.

9. Hayes, Inc. Emerging Technology Report. Exagamglogene autotemcel (Casgevy; Vertex/CRISPR) for transfusion-dependent beta thalassemia. https://evidence.hayesinc.com. Published January 19, 2024.

10. IBM Micromedex. Betibeglogene autotemcel. DrugPoint summary. https://micromedexsolutions.com. Updated August 20, 2025.

11. IBM Micromedex. Exagamglogene autotemcel. DrugPoint summary. https://micromedexsolutions.com. Updated August 20, 2025.

12. 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.

13. Papaioannou I, Owen JS, Yáñez-Muñoz RJ. Clinical applications of gene therapy for rare diseases: a review. *Int J Exp Pathol*. 2023;104(4):154-176.

14. Thompson AA, Walters, MC, Kwiatkowski J, et al. Gene therapy in patients with transfusion-dependent β-Thalassemia. *N Engl J Med*. 2018;378(16):1479-1493.

15. UpToDate, Inc. Hematopoietic stem cell transplantation and other curative therapies for transfusion-dependent thalassemia. https://uptodate.com. Updated December 3, 2024.

16. UpToDate, Inc. Management of thalassemia. https://uptodate.com. Updated August 2025.

17. US Food & Drug Administration (FDA). Full prescribing information: Casgevy (exagamglogene autotemcel). Revised January 2024.

18. US Food & Drug Administration (FDA). Full prescribing information: Zynteglo (betibeglogene autotemcel). https://fda.gov. Revised August 2022.

Change Summary

01/01/2025 New Policy
01/01/2025 Annual Review, Coverage Change Updated Coding Information.