Molina Clinical Policy
Zynteglo (betibeglogene autotemcel)
Policy No. 420

Last Approval: 10/14/2026
Next Review Due By: October 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment. Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy addresses the use of Zynteglo gene therapy for the treatment of transfusion dependent beta thalassemia (TDT).

Thalassemia is a heterogeneous group of autosomal recessive genetic disorders characterized by decreased or absent synthesis of globin chains leading to anemia and microcytosis. There are two major forms of thalassemia: α-thalassemia and β-thalassemia.

Beta (β) thalassemia is a hereditary anemia caused by mutations in the β-globin (HBB) gene, resulting in impaired β-globin chain production. When β-globin is markedly reduced or absent, it leads to ineffective production and increased destruction of red blood cells, manifesting in clinically significant anemia. Individuals with β-thalassemia minor have a mutation in one HBB gene, while individuals with the intermediate and major forms have mutations in both HBB genes:

Minor (trait or carrier)	Mild Microcytosis
Intermedia (non-transfusion-dependent)	Moderate Microcytosis
Major (transfusion-dependent)	Severe microcytosis with target cells (typical Hb 3 to 4 g/dL)

β+ mutations result in reduced (but not absent) synthesis of β-globin. The degree of reduction in β-globin resulting from β+ mutations range from severe to mild. β0 mutations are severe and there is no detectable β-globin production from that mutated allele ([1]Benz and Angelucci 2025).

The Thalassemia International Federation (TIF) guidelines (2025) classify β-thalassemia phenotypically into two main groups based on clinical severity and transfusion requirement regardless of the underlying genotype: transfusion-dependent thalassemia and non-transfusion dependent thalassemia (Taher et al. 2025).

Transfusion-dependent β-thalassemia (TDT; previously thalassemia major) patients require life-long red-cell transfusions and have impaired quality of life. TDT can also cause ineffective erythropoiesis in pediatric patients, which can lead to bone deformities and growth retardation (National Organization for Rare Disorders 2023; [2]Benz and Angelucci 2025).

The clinical management of TDT focuses on reducing anemia-related symptoms and consists of lifelong, regular (usually every 2 to 5 weeks) blood transfusions to maintain a pre-transfusion hemoglobin level above 9 g/dL and iron chelation therapy to remove excess iron. Transfusion-induced iron overload causes widespread organ damage, most notably the cardiac, hepatic, and endocrine system and is the predominant cause of morbidity and mortality. Allogeneic hematopoietic stem cell transplantation (HSCT) was the only permanent curative option for TDT β-thalassemia patients, but only for those with an available HLA-matched donor. As a result, the viability of a HSCT is limited by a lack of suitable donors. Gene therapy, which involves autologous transplantation of genetically modified hematopoietic stem cells, is currently a novel therapeutic option.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

Zynteglo (betibeglogene autotemcel; beti-cel) is an ex vivo gene therapy that utilizes a lentiviral vector (LVV) to introduce a modified *β*-globin$^{A\text{-}T87Q}$ gene into autologous hematopoietic stem cells. Zynteglo is a sustainable and potentially curative alternative to chronic transfusion. Once the $\beta^{A\text{-}T87Q}$-globin gene of Zynteglo is incorporated, hematopoietic stem cells have the potential to produce HbA^{T87Q}, the gene therapy-derived adult Hb, at levels that can eliminate or significantly reduce the need for transfusions. The goal of beti-cel treatment is to correct ineffective erythropoiesis and enable lifelong, stable production of functional adult hemoglobin at levels sufficient to result in transfusion independence (TI).

Due to the significant risks associated with myeloablative conditioning therapy and the requirement that Zynteglo be administered in a specialized center with stem cell transplantation expertise, it is likely that Zynteglo will be reserved for patients with severe disease who cannot be managed with transfusions and chelation therapy (with or without Reblozyl) as an alternative to HSCT.

COVERAGE POLICY

All Gene Therapy requests require Molina Medical Director review.

Zynteglo (beti-cel) for the treatment of transfusion dependent beta thalassemia (TDT) may be **considered medically necessary** when ALL the following clinical criteria with documentation are met:

1. A diagnosis of β-thalassemia
2. Member has **transfusion dependent disease** managed under standard thalassemia guidelines and documented by ONE of following**:**
   a. Receipt of ≥ 8 transfusions of packed red blood cells (pRBC) per year in the two previous years
   b. Receipt of at least 100 mL/kg/year of pRBCs in the two previous years
3. Age ≥ 4 years and ≤ 50 years at the time of infusion
4. A human leukocyte antigen (HLA)-matched related HSC donor is not available
5. No prior hematopoietic stem cell transplant (HSCT)
6. Clinical documentation with recent evaluation establishing eligibility for Zynteglo gene therapy that includes the following:
   a. Member is clinically stable and eligible for an allogeneic HSCT, and has Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1 (ambulatory and able to carry out work of a light or sedentary nature); OR Karnofsky or Lansky performance status (KPS) of at least 80
   b. Adequate and stable renal, hepatic, and cardiac function. Members with ANY of the following labs or imaging do not meet criteria:
      i. Renal impairment defined as creatinine clearance ≤ 70 mL/min/1.73 m^2
      ii. Persistent AST, ALT or direct bilirubin greater than 3 x the upper limit of normal. Positive for the presence of Hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), and HIV-1 / HIV-2
      NOTE: If a patient requires anti-retrovirals for HIV prophylaxis, then a negative test for HIV must be confirmed before beginning mobilization and apheresis of CD34+ cells
      iii. MRI or liver biopsy demonstrating bridging fibrosis, cirrhosis, or active hepatitis
      iv. Cardiac MRI findings of excess myocardial iron: T2* less than 10 milliseconds (msec)
      v. Any other evidence of severe iron overload, such as MRI findings in the liver or abnormal serum iron/ferritin studies
      NOTE: In clinical trials, MRI of the liver was performed on all patients. Patients older than 18 years with MRI results demonstrating liver iron content ≥ 15 mg/g underwent liver biopsy for further evaluation. Patients younger than 18 years with MRI results demonstrating liver iron content ≥ 15 mg/g were excluded from the studies unless a liver biopsy (at the discretion of the investigator) could provide additional data to confirm eligibility.
7. Absence of clinically significant active bacterial, viral, fungal or parasitic infections.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

8. Member has not received, or is being considered for other gene therapy, or investigational cellular therapy for β-Thalassemia

9. Females of childbearing potential and males capable of fathering a child: Member has been counseled on the use of effective contraception during treatment (from start of mobilization through at least 6 months after administration of Zynteglo) and advised of the risks associated with conditioning agents

10. Females of childbearing potential must not be pregnant or breastfeeding, AND must have a documented negative serum pregnancy test within the past 30 days
    NOTE: A negative serum pregnancy test must be confirmed prior to the start of mobilization and re-confirmed prior to conditioning procedures and before Zynteglo administration.

11. No history of uncorrected bleeding disorder

12. No history of prior or current malignancy

ADMINISTRATION:
1. **SETTING:** This gene therapy is ex-vivo. For ex-vivo route, *inpatient administration* is generally anticipated.
2. Zynteglo is considered a provider-administered therapy. It should be administered in a Qualified Treatment Center by a physician(s) with experience in HSCT and in the treatment of patients with TDT.
3. Refer to MHI Policy & Procedure: Specialty Medication Administration Site of Care Policy: MHI Pharm 11

CONTINUATION OF THERAPY:
The safety and efficacy of repeat treatment has not been studied and is currently not supported by any compendia nor indicated in the current FDA approved labeling. Requests for reauthorization or beyond one dose is considered experimental and will not be authorized.

Repeat administration is experimental and investigational since the safety and efficacy beyond one treatment has not been studied and is not indicated in the current FDA approval for Zynteglo. The evidence is insufficient to determine the effects on net health outcomes.

LIMITATIONS AND EXCLUSIONS:
There are no contraindications listed in the manufacturer's labeling at this time.

The following are considered **experimental, investigational, and unproven** based on insufficient evidence:
1. Prior treatment with Zynteglo, other gene therapy or being considered for treatment with other gene therapy, and any form of hematopoietic stem cell transplant

DURATION OF APPROVAL: Duration sufficient for **ONE** single course of treatment

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, a board-certified hematologist

QUANTITY LIMITATIONS: **ONE (1) single treatment course of Zynteglo per lifetime.** Additional infusions of Zynteglo will not be authorized.

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or rendering a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The Biologics License Application (BLA) for Zynteglo is supported by results from the Phase 3 trials, Northstar-2 (HGB-207) and Northstar-3 (HGB-212), the Phase 1/2 studies Northstar HGB-204 and HGB-205, and a Phase 4 long-term follow-up study (LTF303).

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

Phase 1/2 Studies

HGB-204 and **HGB-205,** two single-arm, phase 1/2 trials, evaluated the safety and efficacy of single-dose beti-cel in a total of 22 patients with TDT of any genotype: both non-β0/β0 TDT (n=13) and β0/β0 TDT (n=9) patients. Participants were 35 years of age or younger, with lower age limits of 12 and 5 years in the HGB-204 (n=18) and HGB-205 (n=4) trials, respectively. Patients were deemed transfusion-dependent if they received at least 8 transfusions per year, or at least 100 mL/kg of body weight of packed red cells per year, in the two years prior to enrollment. Of the 23 enrolled patients in these two trials who underwent mobilization and apheresis, all but one patient continued on to receive beti-cel. The reported AEs were similar to those associated with autologous stem cell transplantation, and no identified safety issues were related to the LVV used in the manufacture of gene therapy, according to the researchers (Thompson et al. 2018).

These trials were primarily designed for safety and engraftment endpoints, but Magrin et al. (2022) also reported early results of HGB-205 on 4 participants receiving betibgelogene for TDT. All four patients in HGB-205 receiving betibgelogene for TDT were transfusion independent at the time of publication. Three patients had non-β0/β0 genotype and the fourth was homozygous B^+ IVS1-110. Kwiatkowski et al. (2019) reported very initial results from HGB-204 indicating 3 of 8 participants with β0/β0 genotype achieved transfusion independence compared to 8 of 10 for non-β0/β0 genotype. Long term follow-up data from these trials are below under LTF-303 trial data.

Phase 3 Studies

NorthStar-2 (HGB-207) and **NorthStar-3 (HGB-212)** were identically designed phase 3 open-label, single-arm, 24-month studies in TDT β-thalassemia. NorthStar-2 enrolled patients with a non-β0/β0 genotype, while NorthStar-3 enrolled patients with a β0/β0 genotype or severe non-β0/β0. Patients were eligible if they were up to 50 years old, transfusion dependent (at least 8 transfusions annually for the previous two years, or at least 100 mL/kg/year of packed red blood cells) and were HSCT-eligible. Patients who had a previous HSCT or a known or available HLA-matched family donor were excluded. These two trials used the most recent formulation of beti-cel.

Northstar-2 (NCT02906202) details: The efficacy and safety of beti-cel was evaluated in 23 adult and pediatric patients (n=23) with TDT β-thalassemia and a non-β0/β0 genotype. A total of 23 patients ages 4 to 34 years were treated, with a median follow-up duration of 29.5 months (range: 13.0 to 48.2). Prior to the infusion of beti-cel, patients undergo myeloablative chemotherapy, as with HSCT. Patients in this trial were hospitalized for an average of 45 days and underwent myeloablation with busulfan (with doses adjusted based on pharmacokinetic analysis) and then received beti-cel intravenously.

The primary end point was TI (the weighted average hemoglobin level of ≥ 9 g per deciliter without red-cell transfusions for ≥12 months). Only 19 patients were evaluable for TI (the other participants were not followed up for sufficient time yet) and 89% (17/19) of patients achieved TI, with median weighted average total Hb levels of 11.9 g/dL (min-max: 9.4 – 12.9 g/dL). Before gene therapy these 17 patients required between 11.5 to 37 transfusions per year. The beti-cel safety profile was comparable to that of busulfan-based myeloablation. At least one AE assessed by the investigators to be due to or possibly associated to beti-cel occurred in 4 patients; all occurrences were nonserious except for thrombocytopenia (in 1 patient). There were no observed cases of cancer. There were no confirmed cancer cases (Locatelli et al. 2022). Per study information reported in the FDA label 7 participants that achieved transfusion independence continued phlebotomy for iron removal.

Northstar-3 (NCT03207009, HGB-212**)** is a non-randomized, single arm, single dose efficacy and safety study of betibeglogene in patients with TDT. This phase three trial enrolled 18 patients with either a β0/β0 genotype or IVS-I-110 mutation (genotypes: 12 β0/β0, 3 β0/β+ IVS1-110, 3 homozygous IVS-1-110 mutation). The participants ages ranged from 4-33 years of age. Post treatment the median follow-up was 47.9 months.

The primary endpoint was transfusion independence. Sixteen of the 18 patients achieved TI, with median weighted average total Hb levels of 10.5 g/dL (min-max: 9.5 – 13.5 g/dL) and continued to maintain TI for a median duration of 24 months. Peripheral blood vector copy number was stable over time. Only six of 16 patients that became transfusion independent remained on chelation therapy.

Two adverse events of fever post-infusion were reported. No instances of insertional oncogenesis or hematologic malignancy have been observed. The safety profile was generally consistent with known side effects from HSCT, mobilization, conditioning and apheresis.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

Phase 4 Long-Term Follow-Up

LTF-303 (NCT02633943) is a multi-center phase 4 long-term follow-up study that included patients from the four trials (HGB-204, HGB-205, HGB 207, and HGB212). After participating in and completing the two-year follow-up in either phase 1/2 studies (HGB-204, HGB-205) or one of the phase 3 studies (HGB-207, HGB-212), patients were invited to enroll in the 13-year long-term follow-up study. Patients were initially followed every 6 months for the first 5 years following product infusion, and then annually from Year 5 to Year 15. Sixty-three patients with transfusion-dependent β-thalassemia were followed for a median of 5.9 years (Kwiatkowski et al. 2026).

- TI was achieved in:
  - 68.2% (15/22) of patients in the Phase 1/2 studies.
  - 90.2% (37/41) of patients in the Phase 3 studies.
- Patients who achieved TI maintained it through their last follow-up visit, demonstrating durable efficacy.
- Among patients who became transfusion independent:
  - 73% (38/52) were able to discontinue iron chelation therapy by the last follow-up.

No cases of malignancy, insertional oncogenesis, or replication-competent lentivirus were reported during long-term follow-up. There were 4 cases of oligoclonality that are being monitored.

Mirza et al. (2026) published their real-world experience with Zynteglo from a German cohort. Patients aged 12 years and older with transfusion-dependent β-thalassemia who did not have a β0/β0 genotype and lacked an HLA-matched sibling donor were evaluated before the marketing authorization for betibeglogene autotemcel (beti-cel) was voluntarily withdrawn for reasons unrelated to safety. Treatment effectiveness in routine clinical practice was comparable to that reported in clinical trials; however, several unexpected post-treatment complications were observed. One patient developed unexplained polycythemia that could not be attributed to known genetic or acquired causes. Another experienced depression and anxiety after treatment that prevented a return to employment, while a third developed severe fatigue that significantly impaired both quality of life and work performance. No other new safety signals were reported. Overall, these real-world findings reinforce the efficacy and safety profile of beti-cel while also highlighting adverse events encountered outside the clinical trial setting. Preservation of fertility was an important concern for younger patients considering therapy. Some chose not to proceed with gene therapy because of the risk of infertility associated with busulfan conditioning. The challenges posed by busulfan, particularly its potential detrimental effects on gonadal function, underscore the need for the development of safer and less toxic conditioning regimens.

National and Specialty Organizations

The **Thalassaemia International Federation (TIF)** addressed gene therapies for TDT treatment in its *Guidelines for the Management of Transfusion Dependent Thalassaemia* (Taher et al. 2025), and noting the following regarding gene therapy such as Zynteglo (beti-cel):

- *Allogeneic HSCT from HLA-identical sibling donors* is highly effective for children up to 14 years with transfusion-dependent thalassemia (TDT), especially in regions without access to gene therapy for those under 12. It remains the preferred curative option (Grade B, Class I).
- *HSCT from fully HLA-matched unrelated donors* can yield outcomes comparable to sibling donors in specialized centers. However, this option should be carefully discussed with families due to higher risks of immune complications and the emerging availability of gene therapies (Grade B, Class IIa).
- *Gene therapy* is considered optimal for:
  - Patients aged 14 and older
  - Those without HLA-identical family donors
  - Studies on beti-cel and exa-cel show consistent safety and efficacy across age groups and clinical profiles, with no clear indicators for prioritizing one product over the other (Grade C, Class IIa)
  - Autologous gene therapy presents unique challenges that require new treatment frameworks beyond traditional HSCT models

The **European Bone Marrow Transplantation Group** updated their guidance for gene therapies in beta thalassemia (Franceschi et al., 2026). It is important to note that Zynteglo's conditional marketing authorization in Europe and the UK was withdrawn by the developer. The expert panel recommended delaying gene therapy in the case of liver iron content > 15 mg/g until iron chelation therapy can reduce iron content and re-evaluation can occur. They noted that it isn't the iron overload alone that is the greatest concern, it's the organ damage that occurs with

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

extended periods of exposure that leads to poor outcomes. Cardiac complications related to iron overload are one of the biggest causes of morbidity in transfusion dependent beta thalassemia. Reversibility of iron overload cardiac disease has been demonstrated after intensive iron chelation therapy.

The **Institute for Clinical and Economic Review (ICER)** published a final evidence report supporting the long-term value of beti-cel for the treatment of beta thalassemia (July 2022). The report focused on the clinical benefits of beti-cel and its cost-effectiveness compared to standard clinical management for TDT beta thalassemia, which includes lifelong blood transfusions and iron chelation therapy. The systematic review comprised 5 studies of beti-cel: two phase 1/2 trials (HGB-204 and HGB-205), two phase 3 trials (NorthStar 2 and NorthStar 3), and one cohort study that followed trial participants over the long duration (LTF-303). All 4 trials were open-label, single-arm studies. The evidence suggests beti-cel is generally superior to standard of care for patients with β-thalassemia, but the magnitude of this superiority is still uncertain due to known risks with myeloablative conditioning and unknown durability. Even if beti-cel proves to be a long-lasting treatment with an excellent safety profile, many patients will likely continue transfusion and chelation, according to the authors. In the phase 3 trials, 90% of patients (n = 56) achieved and maintained TI for a median of 42 months. The LTFU indicated that independence from transfusion was maintained for a mean of 42 months (range: 23-87). The report notes that this duration is insufficient to confirm long-term durability, and while the analysis concludes that beti-cel is superior to the current standard of care, its long-term health benefits are unknown. Most of the serious AEs were attributable to known risks associated with myeloablative conditioning, the degree of risk of beti-cel infusion in real-world practice remains unknown. In light of these considerations, ICER assigned beti-cel gene therapy a rating of moderate certainty (incremental or better), which indicates a point estimate of small or substantial net health benefit.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
J3393	Injection, betibeglogene autotemcel, per treatment

AVAILABLE DOSAGE FORMS: Injection, suspension: minimum of 5 × 10^6 CD34+ cells/kg; Each infusion bag contains approximately 20 mL of Zynteglo.

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

10/14/2026	Policy reviewed. No changes to coverage criteria. IRO Peer Review performed on October 12, 2026 by a practicing physician board certified in Hematology.
06/10/2026	Policy revised. Inpatient setting recommendation added to Administration section of coverage criteria.
10/08/2025	Policy revised. Expanded criteria, allowing the use of Zynteglo in those with the most serve beta thalassemia genotype (β0/β0) given HGB-212 trial results. Further defined labs for advanced liver disease and removed redundant criteria for HIV testing.
12/11/2024	Policy revised. Added requirement of Molina Medical Director review.
10/09/2024	Policy reviewed. No changes to coverage criteria.
10/12/2023	Policy reviewed. No changes to coverage criteria.
10/12/2022	New policy. IRO Peer Review. 8/26/2022. Policy reviewed by practicing physician Board-certified in Hematology & Oncology.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

REFERENCES

1. Benz E.J., Angelucci E. Diagnosis of thalassemia (adults and children). Updated October 5, 2026. www.uptodate.com
2. de Franceschi, L., Aljurf, M., Baronciani, D. et al. Update of the decision-making algorithm on selecting transfusion-dependent β-thalassemic patients for gene therapy approaches: joint consensus report on behalf of EHA-specialized working group and EBMT hemoglobinopathies working party. Bone Marrow Transplant (2026). https://doi.org/10.1038/s41409-026-02947-5
3. Farmakis D, Giakoumis A, Angastiniotis M, Eleftheriou A. The changing epidemiology of the ageing thalassaemia populations: A position statement of the Thalassaemia International Federation. Eur J Haematol. 2020 Jul;105(1):16-23. doi: 10.1111/ejh.13410. Epub 2020 Apr 15. PMID: 32198891.
4. Institute for Clinical and Economic Review (ICER). Beaudoin FL, Richardson M, Synnott PG, et al. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review, July 19, 2022. https://icer.org/wp-content/uploads/2021/11/ICER_Beta-Thalassemia_Final-Report_071922.pdf.
5. Kwiatkowski JL, Thompson AA, Rasko JEJ, et al. Long-Term Clinical Outcomes of Lentiglobin Gene Therapy for Transfusion-Dependent β-Thalassemia in the Northstar (HGB-204) Study. Blood. 2019;134(Supplement_1):4628-4628.
6. Kwiatkowski JL, Thompson AA, Schneiderman J, et al. Long-term efficacy and safety results of betibeglogene autotemcel gene therapy for transfusion-dependent β-thalassemia. Blood. 2026 May 7;147(19):2203-2214. doi: 10.1182/blood.2025029196. PMID: 41525466.
7. Kwiatkowski JL, Walters MC, Hongeng S, et al. Betibeglogene autotemcel gene therapy in patients with transfusion-dependent, severe genotype β-thalassaemia (HGB-212): a non-randomized, multicentre, single-arm, open-label, single-dose, phase 3 trial. Lancet. 2024 Nov 30;404(10468):2175-2186. doi: 10.1016/S0140-6736(24)01884-1. Epub 2024 Nov 8. PMID: 39527960.
8. Locatelli F, Thompson AA, Kwiatkowski JL, et al. Betibeglogene Autotemcel Gene Therapy for Non-β0/β0 Genotype β-Thalassemia. N Engl J Med. 2022 Feb 3;386(5):415-427. doi: 10.1056/NEJMoa2113206. Epub 2021 Dec 11. PMID: 34891223.
9. Magrin E, Semeraro M, Hebert N, et al. Long-term outcomes of lentiviral gene therapy for the β-hemoglobinopathies: the HGB-205 trial. Nat Med. 2022;28(1):81-88. doi:10.1038/s41591-021-01650-w.
10. Mirza A, Ritsert ML, Tao G. Gene therapy in transfusion-dependent non-β0/β0 genotype β-thalassemia: first real-world experience of beti-cel. Blood Adv. 2025 Jan 14;9(1):29-38. doi: 10.1182/bloodadvances.2024014104. PMID: 39418614; PMCID: PMC11732601.
11. National Organization for Rare Disorders (NORD). Beta thalassemia. Updated 2023. https://rarediseases.org/rare-diseases/thalassemia-major/
12. NCT02906202. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia, who do not have a β0/β0 genotype (NCT02906202; Northstar-2). Updated June 18, 2023. https://clinicaltrials.gov/ct2/show/NCT02906202
13. NCT03207009. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia. (NCT03207009). Updated March 7, 2024. https://clinicaltrials.gov/study/NCT03207009?id=NCT03207009&rank=1
14. NCT02633943. ClinicalTrials.gov. Long-term follow-up of subjects with transfusion-dependent β-thalassemia treated with ex vivo gene therapy. Updated April 9, 2025. https://clinicaltrials.gov/study/NCT02633943?id=NCT02633943&rank=1
15. Taher, A.T, Farmakis, D., Porter, J.B., Cappellini, M.D., Musallam, K.M. Guidelines for the management of transfusion-dependent B-Thalassemia (TDT). Thalassemia International Federation: 5th Edition. 2025
16. 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. doi:10.1056/NEJMoa1705342.
17. United States Food and Drug Administration (FDA). Cellular, Tissue, and Gene Therapies Advisory Committee Meeting. FDA Briefing Document. BLA 125717 betibeglogene autotemcel. June 9-10, 2022. https://www.fda.gov/media/159009/download
18. Zynteglo (betibeglogene autotemcel) [prescribing information]. Somerville, MA: Bluebird Bio Inc; August 2022. https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Package-Insert-ZYNTEGLO.pdf

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*