Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines
Medical Benefit Drugs

Casgevy™ (exagamglogene autotemcel)

Effective: November 1, 2026

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988
☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988
☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939
☐ Tufts Health One Care-- A dual-eligible product; Fax 617-673-0956

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956
☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956
☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Sickle cell disease (SCD)

Sickle cell disease (SCD) is a group of inherited debilitating blood disorders caused by a mutation in the β-globin gene that leads to the production of abnormal sickle shaped hemoglobin (HbS). In SCD, the sickled RBCs become rigid, undergo premature hemolysis leading to anemia and become unable to transport oxygen to critical organs. The condition affects more than 100,000 people in the United States with an incidence of about 1 in every 365 Black births and 1 in every 16,300 Hispanic-American births.

Severely affected patients may experience diverse complications such as severe anemia, repeated acute painful vaso-occlusive events (VOEs) due to small-vessel obstruction (vaso-occlusive crises [VOCs]; sickle cell crises), acute chest syndrome (ACS; acute event with pneumonia-like symptoms), cerebral vasculopathy, chronic organ damage that may involve e.g., the bones, kidneys, heart, liver, and lungs or result in severe infectious complications such as functional hyposplenism and premature death. Treatment includes measures to control complications, relieve pain, prevent infections, and minimize organ damage. Standard pharmacologic treatment has included medications, such as hydroxyurea (Hydrea), analgesics and blood transfusions. Hematopoietic stem cell transplantation for patients with an appropriate donor, until the development of gene therapy, has been an option for cure. Gene therapies now offer a treatment option for members with severe sickle cell disease who do not have a willing HLA matched family donor.

Beta Thalassemia

Thalassemia refers to a range of diseases characterized by reduced or absent production of one or more globin chains. Beta thalassemia is caused by variants (mutations) in the hemoglobin beta locus (HBB, beta globin gene) that result in impaired production of beta globin chains. It varies in severity, with some patients being dependent on regular RBC transfusions, known as Beta Thalassemia Major; also called transfusion-dependent beta thalassemia (TDT). Thalassaemia affects approximately 2,000 patients living in the USA, with 1,500 having TDT.

Patients with TDT will typically present with symptoms during the first year of life and will need both regular transfusions to lessen severe anemia as well as subsequent chelation therapy to remove excess iron from the blood. Untreated infants with severe anemia can have jaundice, pallor, irritability, dark urine from hemolysis, and abdominal swelling from hepatosplenomegaly, which may be followed by infection, failure to thrive, and high-output heart failure. Treatments are limited and includes measures to

control the symptoms such as the drug Reblozyl to treat anemia. Allogeneic hematopoietic stem cell transplant (HSCT) has been available as a potentially curative treatment however, matched donors are often not available. Gene therapies now offer a treatment option for members with TDT who do not have a willing HLA matched family donor.

Food and Drug Administration (FDA) Approved Indications:

CASGEVY is an autologous genome edited hematopoietic stem cell-based gene therapy indicated for the treatment of patients aged 2 years and older with:

- sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs);
- transfusion-dependent beta thalassemia (TDT)

Casgevy is the first FDA-approved gene therapy that uses CRISPER technology for genetic modification, which has been shown to reduce or eliminate VOCs for patients with SCD. CRISPR/Cas9-editing technology allows for modification of defective genes by editing, removing, or replacing DNA from cells. CASGEVY is a non-viral, *ex vivo* CRISPR/Cas9 gene-edited cell therapy for eligible patients with SCD or TDT in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. The edited blood stem cells are transplanted back into the patient via a hematopoietic stem cell transplant, engraft (attach and multiply) within the bone marrow, and increase the production of fetal hemoglobin (HbF) in red blood cells. Hemoglobin F reduces intracellular hemoglobin S (Hbs) concentration, preventing the red blood cells from sickling and addressing the underlying cause of the disease. HbF is naturally present during fetal development and is a type of hemoglobin that facilitates oxygen delivery.

NOTE: Casgevy can only be administered at a Casgevy Authorized Treatment Center (ATC). Each Casgevy ATC has been carefully selected based on their expertise in areas such as transplant, cell and gene therapy. For information on locating an Authorized Treatment Center, please go to https://www.casgevy.com/sickle-cell-disease/find-an-ATC

Clinical Guideline Coverage Criteria

Sickle Cell Disease (for Commercial and Direct Products only)

For RITogether Coverage of Sickle Cell Disease see Gene Therapies for Sickle Cell Disease for RITogether Medical Necessity Guideline on our provider resource center.

The Plan may cover Casgevy for sickle cell disease when **all** the following clinical criteria is met:

1. Member has a diagnosis of sickle cell disease with recurrent vaso-occlusive crises (VOCs)**; and**
2. Member is at least 2 years of age and weighs ≥ 12 kg; **and**
3. Casgevy is prescribed by or in consultation a hematologist who specializes in the treatment of sickle cell disease; **and**
4. Member has documentation of recurrent severe vaso-occlusive crises (VOC) as defined by at least 2 vaso-occlusive events per year in the 2 years prior to screening for administration that required care at a medical facility. * Examples of VOCs include:
    a. Acute pain event requiring pain medication(s) or RBC transfusions
    b. Acute chest syndrome
    c. Priapism lasting >2 hours
    d. Acute splenic sequestration
    e. Acute hepatic sequestration
5. Member has tried and failed, has a contraindication, or intolerance to treatment with hydroxyurea or another disease modifying therapy (e.g., Adakveo (crizanlizumab), Endari (L-glutamine)); **and**
6. Member has not previously been treated with a gene therapy for sickle cell disease; **and**
7. Member has not previously been treated with any other gene therapies for any other disorder; **and**
8. Member is clinically stable and would be considered a candidate for allogenic hematopoietic stem cell transplantation (HSCT), but is ineligible due to the absence of a willing/acceptable HLA-matched family donor or any other condition(s) that the provider attests to which makes the member ineligible for HSCT; **and**
9. Member has not received previous allogenic stem cell transplant for sickle cell disease; **and**
10. The provider attests that the Member has adequate organ function with no anticipated decline in organ function in close proximity to apheresis timeframe; **and**
11. The Member has no active infection (e.g., viral, bacterial, fungal, parasitic) including presence of HIV-1 and HIV-2, active hepatitis B or active hepatitis C. Screening must be completed at the time of apheresis; **and**
12. Casgevy will be administered at an Authorized Treatment Center

Note: *For Members who have been stabilized on continuous red blood cell transfusions because of chronic SCD complications and have history of recurrent VOCs may meet medical necessity with additional documentation provided.

Transfusion-dependent beta thalassemia (TDT)

The Plan may cover Casgevy for TDT when **all** of the following clinical criteria are met and supporting documentation is provided:

1. Member has a diagnosis of beta thalassemia; **and**
2. Member is at least 2 years of age and weighs ≥ 12 kg; **and**
3. Casgevy is prescribed by or in consultation with a hematologist who specializes in the treatment of beta thalassemia; **and**
4. Member has transfusion-dependent disease (defined as needing at least 10 units or at least 100 ml per kilogram of bodyweight of packed red cells per year within the previous 2 years); **and**
5. Member is clinically stable and would be considered a candidate for allogenic hematopoietic stem cell transplantation (HSCT), but is ineligible due to the absence of a willing HLA-matched family donor or any other condition(s) that the provider attests to which makes the member ineligible for HSCT; **and**
6. Member has no evidence of severe iron overload as established by:
    a. Cardiac T2* less than 10 msec by magnetic resonance imaging [MRI]; **or**
    b. Left ventricular ejection fraction [LVEF] < 45% by echocardiogram); **or**
    c. Advanced liver disease as confirmed by liver function test (aspartate transaminase [AST], alanine transaminase [ALT] > 3 × the upper limit of normal [ULN], or direct bilirubin value; **or**
    d. Liver biopsy demonstrated bridging fibrosis or cirrhosis.
7. In Members with chronic kidney disease, renal status is documented as stable and controlled with treatment; **and**
8. Member has not had a prior HSCT; **and**
9. Member has not previously been treated with a gene therapy for TDT; **and**
10. Member has not previously been treated with any other gene therapies for any other disorder; **and**
11. The Member has no active infection (e.g., viral, bacterial, fungal, parasitic) including presence of HIV-1 and HIV-2, active hepatitis B or active hepatitis C. Screening must be completed at the time of apheresis; **and**
12. Casgevy will be administered at an Authorized Treatment Center

Limitations

- Casgevy will not be covered if the Member demonstrates clinical decompensation from time of authorization to time of infusion and no longer meets clinical coverage criteria.
- Any indications for Casgevy other than those outlined above are considered investigational and will not be covered.
- Authorization of Casgevy is limited to one single dose treatment.
- Members who have received prior gene therapy for sickle cell disease or TDT, including in clinical trial settings, will not be approved for Casgevy.

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J3392	Injection, exagamglogene autotemcel, per treatment

References:

1. A Safety and Efficacy Study Evaluating CTX001 in Subjects With Severe Sickle Cell Disease; PEV259674: 90Accessed @ https://clinicaltrials.gov/study/NCT03745287?intr=(exagamglogene%20autotemcel)&rank=6 accessed January 25, 2024.
2. Casgevy (exagamglogene autotemcel). [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; July 2026.
3. Evaluation of Safety and Efficacy of CTX001 in Pediatric Participants With Severe Sickle Cell Disease (SCD); NCT05329649. Accessed at Study Details | Evaluation of Safety and Efficacy of CTX001 in Pediatric Participants With Severe Sickle Cell Disease (SCD) | ClinicalTrials.gov accessed January 25, 2024.
4. A Safety and Efficacy Study Evaluating CTX001 in Subjects With Transfusion-Dependent β-Thalassemia; NCT03655678. Accessed @ https://clinicaltrials.gov/study/NCT03655678#study-overview accessed February 28, 2024.
5. Frangoul H, Altshuler D, Cappellini MD, et. al., CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia. *N Engl J Med.* 2021 Jan 21;384(3):252-260. doi: 10.1056/NEJMoa2031054. Epub 2020 Dec 5

6. Muncie, Herbert M. Beta thalassemia. National Organization for Rare Disorders (NORD). Available at: https://rarediseases.org/rarediseases/thalassemia-major/. Published 2023. Updated May 23, 2023. Accessed February 28, 2024.
7. Luspatercept: Drug information. UpToDate.com/login [via subscription only]. Accessed February 26, 2024.
8. New Drug Review: Casgevy (exagamglogene autotemcel). IPD Analytics. January 2024.
9. Handgretinger R, Mezger M. An evaluation of exagamglogene autotemcel for the treatment of sickle cell disease and transfusion-dependent beta-thalassaemia. Expert Opin Biol Ther. 2024 Sep;24(9):883-888. doi: 10.1080/14712598.2024.2399134. Epub 2024 Sep 2. PMID: 39222044.
10. Lesmana H, Kim SY, Corado AM, Poskanzer SA; ACMG Therapeutics Committee8∗documents@acmg.net. Casgevy (exagamglogene autotemcel) and Lyfgenia (lovotibeglogene autotemcel) for individuals 12 years and older with sickle cell disease (SCD) and recurrent vaso-occlusive crises (VOC): A therapeutics bulletin of the American College of Medical Genetics and Genomics (ACMG). Genet Med Open. 2024 Sep 10;2:101875. doi: 10.1016/j.gimo.2024.101875. PMID: 39822266; PMCID: PMC11736165.
11. de la Fuente J, et. al. Improvements in Health-Related Quality of Life in Patients with Transfusion-Dependent β-Thalassemia After Exagamglogene Autotemcel. Blood Adv. 2025 Aug 19:bloodadvances.2025016702. doi: 10.1182/bloodadvances.2025016702. Epub ahead of print. PMID: 40862696.
12. Locatelli F, Lang P, et. al. CLIMB THAL-111 Study Group. Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia. N Engl J Med. 2024 May 9;390(18):1663-1676. doi: 10.1056/NEJMoa2309673. Epub 2024 Apr 24. PMID: 38657265.
13. Frangoul H, et. al. CLIMB THAL-141 and CLIMB SCD-151 Study Groups. Exa-cel in Children with Transfusion-Dependent β-Thalassemia or Sickle Cell Disease. N Engl J Med. 2026 Jun 11. doi: 10.1056/NEJMoa2603387. Epub ahead of print. PMID: 42274009.

Approval And Revision History

February 21, 2024: Reviewed by the Medical Policy Approval Committee (MPAC) effective April 1, 2024.

Subsequent endorsement date(s) and changes made:

- April 17, 2024: Reviewed by Medical Policy Approval Committee, MNG updated to include Transfusion-dependent beta thalassemia (TDT) based on FDA label expansion effective June 1, 2024
- July 22, 2024: Reviewed by MPAC, administrative update, effective September 1, 2024
- November 21, 2024: Reviewed by MPAC, updated criteria, under Sickle Cell Disease, removed Oxbryta as disease modifying therapy, under Transfusion-dependent beta thalassemia, added criteria that members with chronic kidney disease must have stable and controlled renal status. Coding updated: Per CMS HCPCS the following code added J3392, effective January 1, 2025
- November 19, 2025: Reviewed by MPAC for annual review, renewed without changes, references updated, effective January 1, 2026
- December 2025: Administrative updates effective January 1, 2026
- December 17, 2025: Reviewed by MPAC, RITogether coverage of Sickle Cell Disease moved to Gene Therapies for Sickle Cell Disease for RITogether effective January 1, 2026
- September 16, 2026: Reviewed by MPAC and revised to expand eligibility to individuals aged 2 years and older who weigh at least 12 kg with sickle cell disease or transfusion-dependent beta thalassemia, consistent with the FDA label. Changes effective November 1, 2026.

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment, or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.