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). Thalassemia 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 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.

The Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for its Medicare Advantage plan members. CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations. When CMS does not provide guidance, the Plan's internally developed medical necessity guidelines are used. CMS coverage guidelines is not established for this service. Point32Health covers Casgevy in accordance with MassHealth coverage criteria.

For the therapy Casgevy, evidence is sufficient for coverage. Casgevy was FDA approved in December 2023 for SCD based on the results of an ongoing single-arm, multicenter CLIMB-121 trial. This study found that 29 out of the 31 patients enrolled, or 93.5%, achieved the primary outcome meaning the patients had no VOCs for 12 consecutive months during the 2 years of follow up. Casgevy was FDA approved in January 2024 for transfusion-dependent beta thalassemia based on results of an ongoing open-label, multicenter, single-arm CLIMB THAL-111 trial. This study found that out of 35 patients eligible for the primary efficacy analysis (i.e., the primary efficacy set), the transfusion independence for 12 consecutive months (TI12) rate was 32/35 (91.4%, 98.3% one-sided CI: 75.7%, 100%). The primary outcome was the proportion of patients achieving transfusion independence for 12 consecutive months defined as maintaining weighted average Hb ≥9 g/dl without transfusions for at least 12 consecutive months any time within the first 24 months after Casgevy infusion.

The use of this criteria in the utilization management process will ensure access to evidence based clinically appropriate care. See References section below for all evidence accessed in the development of these criteria.

Clinical Guideline Coverage Criteria

Sickle Cell Disease

The Plan may cover Casgevy for Severe Sickle Cell Disease when all the following clinical criteria is met:

1. Diagnosis of SCD (βS/βS, βS/β0 genotype)**; and**
2. Copy of genetic test confirming diagnosis of SCD**; and**
3. Prescriber is a hematologist or consult notes from a specialist are provided**; and**
4. Member is ≥ 2 years of age and weighs ≥ 12 kg**; and**
5. History of ≥ 2 sickle cell crises per year in the last 2 years**; and**
6. ONE of the following:
    a. Inadequate response to hydroxyurea therapy at the maximally tolerated dose*# for at least three months*
    b. Adverse reaction or contraindication to hydroxyurea**; and**
7. Appropriate dosing and treatment dates**; and**
8. Infusion will take place in a qualified treatment facility**; and**
9. Member is clinically stable and eligible for HSCT**; and**
10. Member does not have active HIV, HBV, or HCV infection**; and**
11. Member has not received any prior SCD gene therapy

Transfusion-dependent beta thalassemia (TDT)

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

1. Diagnosis of transfusion dependent β-thalassemia (TDT or β-thalassemia major); **and**
2. Copy of genetic test confirming diagnosis; **and**
3. Prescriber is a hematologist or consult notes from a hematologist are provided; **and**
4. Member is ≥ 2 years of age and weighs ≥ 12 kg; **and**
5. Appropriate dosing and treatment dates; **and**
6. Member has required ≥ 100 mL/kg/year of pRBC or ≥ 10 units per year in the previous 2 years; **and**
7. Member does not have active HIV, HBV or HCV infection; **and**
8. Infusion will take place in a qualified treatment center; **and**
9. Member will receive pre-infusion conditioning with busulfan; **and**
10. Member is clinically stable and eligible for HSCT; **and**
11. Member has not received any prior TDT gene therapy

Limitations

- 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

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: 90'Accessed @ 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. MassHealth Drug List- Health and Human Services. Table 45: Beta Thalassemia, Myelodysplastic Syndrome, and Sickle Cell Disease Agents. April 2024. Accessed June 7, 2024. https://mhdl.pharmacy.services.conduent.com/MHDL/pubtheradetail.do?id=45
9. New Drug Review: Casgevy (exagamglogene autotemcel). IPD Analytics. January 2024.
10. 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.
11. 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.
12. 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.

13. 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.
14. 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 MPAC, MNG update to include Beta- thalassemia effective July 1, 2024
- May 15, 2024: Reviewed by MPAC, SCD criteria update to align with MassHealth criteria effective July 1, 2024
- June 13, 2024: Reviewed and approved by UM Committee effective July 1, 2024
- July 22, 2024: Reviewed by MPAC, administrative update, effective September 1, 2024
- November 21, 2024: Reviewed by MPAC, TDT criteria update to align with MassHealth criteria effective January 6, 2025. Coding updated: Per CMS HCPCS, effective January 1, 2025: the following code added: J3392.
- December 13, 2024: Reviewed and approved by the UM Committee 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 8, 2025: Reviewed by UM Committee for annual review, renewed without changes 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.