Mass General Brigham
Health Plan

Casgevy
(exagamglogene autotemcel)

Policy Number: 075

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization Required	X	X	X
No Prior Authorization			X (38207, 38208)
Not payable		X (38207)	

Overview
Casgevy (exagamglogene autotemcel) is an autologous hematopoietic stem cell-based gene therapy for sickle-cell disease (SCD) and for transfusion-dependent beta thalassemia (TBT). In this therapy, autologous CD34+ hematopoietic stem cells are edited with CRISPR/Cas9 technology at the erythroid specific enhancer region of *BCL11A* to reduce BCL11A expression in erythroid lineage cells, leading to increased expression of fetal hemoglobin (HbF).

FDA-approved indications
For the treatment of patients aged 12 and older with:

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

Coverage guidelines
Mass General Brigham Health Plan covers Casgevy when all general eligibility criteria have been met, and all criteria have been met for either SCD or for TDT.

General eligibility:

1. Member is ≥12 years of age; and
2. Treatment will be administered in a qualified treatment facility as per product website; and
3. Laboratory evaluation without evidence of advanced liver disease; and
4. No active/uncontrolled infections, including HIV, HBV, and HCV; and

Sickle Cell Disease:

1. Genetic test confirms SCD; and
2. At least 4 VOC/VOE in the past 24 months, including but not limited to:
    a. Acute pain event requiring a visit to a medical facility for pain medication(s) or red blood cell (RBC) transfusions;
    b. Acute chest syndrome;
    c. Acute splenic and/or hepatic sequestration;
    d. Priapism lasting longer than 2 hours and requiring a visit to a medical facility; and
3. One of the following:
    a. Inadequate response to treatment with hydroxyurea for at least 3 months, with good adherence to therapy based on pharmacy claims or provider documentation, or
    b. Adverse reaction or contraindication to the use of hydroxyurea, or
    c. Chronic transfusion therapy without hydroxyurea for primary or secondary stroke prevention; or

Transfusion-dependent β-thalassemia:

1. Diagnosis of TDT requiring at least 100 ml/kg body weight (or 10 units of packed red blood cells) per year for the previous two years to maintain target hemoglobin levels; and
2. No evidence of severe iron overload.

Mass General Brigham Health Plan considers Casgevy to be experimental/investigational for all other indications.

Exclusions

1. History of HSCT
2. History of gene therapy for SCD

Medicaid variation

Prior authorization requests for Casgevy for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Casgevy are found in Table 45: Beta Thalassemia, Myelodysplastic Syndrome, and Sickle Cell Disease Agents.

Medicare variation

Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for its Medicare Advantage plan members. 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 there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, Medicare had no NCD or LCD for Casgevy (exagamglogene autotemcel).**

Codes

The following codes are included for informational purposes only; inclusion of a code does not constitute or imply coverage.

The list of codes applies to commercial and MassHealth plans only.

Authorized CPT/HCPCS Codes	Code Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
J3392	INJECTION, EXAGAMGLOGENE AUTOTEMCEL, PER TREATMENT

Summary of Evidence

The pivotal trials of exagamglogene autotemcel (Casgevy, exa-cel) were CLIMB SCD-121, for patients aged 12-35 with severe SCD, and CLIMB THAL-111, for patients aged 12-35 with TBT. Both were open-label, single-arm, phase 1/2/3 trials. As reported in early reports on phases 1 and 2 of these trials by Frangoul et al. (2021) and Sharma et al. (2023), myeloablative conditioning followed by exa-cel therapy produced engraftment, induction of fetal hemoglobin production, and improvement in disease manifestations in the initial patients with both conditions. The FDA approved Casgevy in December 2023 for treatment of both severe SCD and TBT.

Subsequent reports on CLIMB SCD-121 and its companion long-term follow-up study CLIMB SCD-131 showed that exa-cel produced complete or near-complete resolution of VOCs and hospitalization for VOCs (Frangoul et al. *NEJM* 2024), and that these benefits were sustained over up to 4.7 years of follow-up (Frangoul et al. *Blood* 2024). Reports on CLIMB THAL-111 and its companion long-term followup study CLIMB THAL-121 showed that exa-cel produced transfusion independence for 12 months in 91% of patients, and also hemoglobin levels >9g/dL for 6 months in 91% of patients (Locatelli et al. *NEJM* 2024), and that these benefits were sustained over up to 5 years of follow-up (Locatelli et al. *Blood* 2024). Additional reports on these studies by de la Fuente (2024) and Sharma (2024) show substantial benefits in health-related quality of life in both patient populations.

MGB Health Plan considers exa-cel to be medically necessary for members with SCD or TBT who meet criteria similar to those used in the pivotal trials CLIMB SCD-121 and CLIMC THAL-111.

Effective
April 2025: Annual review. Codes and code list updated. FDA-approved indications and medical necessity criteria updated. MassHealth variation updated to include new prior authorization process.
March 2025: Summary of evidence added. References updated.
September 2024: Ad hoc review. Updated medical necessity criteria.
April 2024: Effective date.

References
Casgevy (exagamglogene autotemcel), suspension for intravenous infusion [prescribing information]. Boston, MA: Vertex, 2023.

de la Fuente J, Locatelli F, Lang P, et al. Health-related quality-of-life improvements after exagamglogene autotemcel in patients with transfusion-dependent beta-thalassemia. *Blood* 2024;144(Suppl 1):7454.

Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. *NEJM* 2021;384:252-60.

Frangoul H, Locatelli F, Sharma A, et al. Durable clinical benefits with exagamglogene autotemcel for severe sickle cell disease. *Blood* 2024;144(Suppl 1):4954.

Frangoul H, Locatelli F, Sharma A, et al. Exagtamglogene autotemcekl for severe sickle cell disease. *NEJM* 2024;390(18):1649-62.

Locatelli F, Lang P, Meisel R, et al. Durable clinical benefits with exagamglogene autotemcel for transfusion-dependent β-thalassemia. *Blood* 2024;144(Suppl 1):512.

Locatelli F, Lang P, Wall D, et al. Exagamglogene autotemcel for transfusion-dependent β-Thalassemia. *NEJM* 2024;390(18):1663-76.

Sharma A, Boelens JJ, Cancio M, et al. CRISPR-Cas9 editing of the *HGB1* and *HGB2* promoters to treat sickle cell disease. *NEJM* 2023;389:820-32.

Sharma A, Frangoul H, Locatelli F, et al. Health-related quality-of-life improvements after exagamglogene autotemcel in patients with severe sickle cell disease. *Blood* 2024;144(Suppl 1):7453.