PROVIDER POLICIES & PROCEDURES

CASGEVY® (exagamglogene autotemcel)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for gene therapy with Casgevy (exagamglogene autotemcel). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Sickle cell disease (SCD) is a single-gene inherited blood disorder in which the sickle mutation is coinherited with a pathogenic variant at the other beta-globin allele that reduces or abolishes normal beta-globin production. There are several variants of SCD including sickle cell anemia (homozygous sickle mutation [Hb SS]), sickle-beta thalassemia, hemoglobin SC disease, and others. The key feature of all types of SCD is that the Hb S proportion is typically >50 percent, and Hb S is the predominant hemoglobin. The major clinical features are related to hemolytic anemia and vaso-occlusion, which can lead to acute and chronic pain and tissue ischemia or infarction.

Beta-thalassemia (β-thalassemia) is a hemoglobinopathy in which the normal ratio of alpha globin to beta globin production is disrupted due to a genetic variant in one or more alpha or beta globin genes. Individuals typically inherit two beta globin genes, one from each parent. β-thalassemia is caused by reduced production of beta chains and accumulation of excess alpha chains, and the severity of disease correlates with the amount of normal beta globin production. Individuals with β-thalassemia who require regular transfusions due to severe anemia and/or significant complications of extramedullary hematopoiesis are referred to as having transfusion-dependent β-thalassemia.

Casgevy is a single dose CRISPR/Cas9-modified hematopoietic stem cell-based autologous CD34+ cellular gene therapy indicated for the treatment of patients aged 12 years and older with:

- sickle cell disease with recurrent vaso-occlusive crises; OR
- transfusion-dependent β-thalassemia

Casgevy targets the erythroid-specific enhancer region of the BCL11A gene causing reduced expression of BCL11A which results in an increase in γ-globin expression and fetal hemoglobin (HbF) protein production. In individuals with SCD, HbF expression reduces intracellular HbS concentration, thereby preventing the red blood cells (RBC) from sickling. In individuals with transfusion-dependent β-thalassemia, γ-globin production improves the α-globin to non-α-globin imbalance thereby reducing ineffective erythropoiesis and hemolysis and increasing total hemoglobin levels.

CLINICAL GUIDELINE

Coverage decisions for the use of Casgevy will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage decisions are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

I. Treatment with Casgevy will be considered medically necessary for individuals with *sickle cell*

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disease when ALL of the following criteria are met:

A. The individual is 12 years of age or older; **AND**
B. The individual has a diagnosis of sickle cell disease with one of the following genotypes confirmed by genetic testing:
    a. β^S/β^S
    b. β^S/β^0
    c. β^S/β^+; **AND**
C. The treatment is prescribed by or in consultation with a hematologist; **AND**
D. The treatment will be administered at an authorized treatment center; **AND**
E. The individual has a history of ≥ 2 severe vaso-occlusive episodes per year in the 2 years prior to screening in the setting of appropriate supportive care defined as:
    a. Acute pain event requiring a visit to a medical facility and administration of pain medications (opioids or intravenous non-steroidal anti-inflammatory drugs [NSAIDs]) or RBC transfusions; **OR**
    b. Acute chest syndrome; **OR**
    c. Priapism lasting >2 hours and requiring a visit to a medical facility; **OR**
    d. Hepatic sequestration; **OR**
    e. Splenic sequestration; **AND**
F. The individual is eligible for a hematopoietic stem-cell transplant (HSCT) as determined by the hematologist; **AND**
G. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
H. The individual has not previously received a hematopoietic stem-cell transplant; **AND**
I. The individual has not previously received Casgevy or any other gene therapy; **AND**
J. The individual does not have any of the following:
    a. Advanced liver disease as defined by the following:
        i. Alanine transaminase (ALT) >3 × the upper limit of normal (ULN) or direct bilirubin value >2.5 × ULN; **OR**
        ii. Baseline prothrombin time (PT) (international normalized ratio [INR]) >1.5 × ULN, **OR**
        iii. History of cirrhosis or any evidence of bridging fibrosis, or active hepatitis on liver biopsy; **AND**
    b. A history or presence of Moyamoya disease; **AND**
    c. Bacterial, viral, fungal or parasitic infection including HIV-1, HIV-2, hepatitis B or hepatitis C; **AND**
    d. Any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
    e. A history of abnormal transcranial doppler (TCD) (TAMMV ≥200 cm/sec for non-imaging TCD and ≥185 cm/sec for imaging TCD) in individuals 12 to 18 years of age; **AND**
K. The individual has previously trialed at least one pharmacologic treatment for SCD including hydroxyurea, l-glutamine, crizanlizumab-tmca or voxelotor; **AND**
L. The provider will follow all FDA recommendations for usage, dosage, preparation, administration, monitoring and patient education; **AND**

II. Treatment with Casgevy will be considered medically necessary for individuals with *transfusion-dependent β-thalassemia* when ALL of the following criteria are met:

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A. The individual is 12 years of age or older; **AND**
B. The individual has a diagnosis of β-thalassemia as confirmed by genetic testing; **AND**
C. The individual has a history of ≥100 mL/kg/year or ≥10 units/year of RBC transfusions in the previous 2 years; **AND**
D. The treatment is prescribed by or in consultation with a hematologist; **AND**
E. The treatment will be administered at an authorized treatment center; **AND**
F. The individual is eligible for a hematopoietic stem-cell transplant (HSCT) as determined by the hematologist; **AND**
G. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
H. The individual has not previously received a hematopoietic stem-cell transplant; **AND**
I. The individual has not previously received Casgevy or any other gene therapy; **AND**
J. The individual does not have any of the following:
    a. Advanced liver disease as defined by:
        1. Alanine transaminase (ALT) >3 × the upper limit of normal (ULN) or direct bilirubin value >2.5 × ULN; **OR**
        2. Baseline prothrombin time (PT) (international normalized ratio [INR]) >1.5 × ULN, **OR**
        3. History of cirrhosis or any evidence of bridging fibrosis, or active hepatitis on liver biopsy; **AND**
    b. Bacterial, viral, fungal or parasitic infection including HIV-1, HIV-2, hepatitis B or hepatitis C; **AND**
    c. Any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
K. The provider will follow all FDA recommendations for usage, dosage, preparation, administration, monitoring and patient education

Investigational and Not Medically Necessary

Casgevy is considered investigational and therefore not medically necessary for all other indications not specified in this policy.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of Casgevy is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Casgevy:
1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program

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Casgevy Prior Authorization Request form (to include physician's order and signature)

2. Clinical documentation supporting the medical necessity of treatment with Casgevy for *sickle cell disease* ONLY should include the following:
    a. Genetic testing confirming the diagnosis of sickle cell disease with one of the following genotypes: β^S/β^S, β^S/β^0 or β^S/β^+; **AND**
    b. Medical record documenting a history of ≥ 2 severe vaso-occlusive episodes per year in the prior 2 years; **AND**
    c. Laboratory data confirming the absence of:
        i. HIV-1, HIV-2, HBV, HCV infection; **AND**
        ii. Advanced liver disease; **AND**
    d. Medical record documentation of prior pharmacologic therapies trialed for SCD; **AND**
    e. Signed provider attestation confirming the following:
        i. The individual is eligible for a hematopoietic stem-cell transplant (HSCT); **AND**
        ii. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
        iii. The individual has not previously received a HSCT; **AND**
        iv. The individual has not previously received Casgevy or any other gene therapy; **AND**
        v. The individual does not have a history or presence of Moyamoya disease; **AND**
        vi. The individual does not have any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
    f. For individuals 12-18 years of age ONLY: documentation confirming the absence of abnormal transcranial doppler (TCD)
3. Clinical documentation supporting the medical necessity of treatment with Casgevy for *β-thalassemia* ONLY should include the following:
    a. Genetic testing results confirming the diagnosis of β-thalassemia; **AND**
    b. Medical record documenting a history of ≥100 mL/kg/year or ≥10 units/year of RBC transfusions in the previous 2 years; **AND**
    c. Laboratory data confirming the absence of:
        i. HIV-1, HIV-2, HBV, HCV infection; **AND**
        ii. Advanced liver disease; **AND**
    d. Signed provider attestation confirming the following:
        i. The individual is eligible for a hematopoietic stem-cell transplant (HSCT); **AND**
        ii. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
        iii. The individual has not previously received a HSCT; **AND**
        iv. The individual has not previously received Casgevy or any other gene therapy; **AND**
        v. The individual does not have any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
4. Other information as requested

Requesting Authorization

Requests for the prior authorization of Casgevy must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

Initial Authorization

If approved, authorization will be given for a one-time, single-dose intravenous infusion of Casgevy

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Reauthorization
Casgevy is indicated as a one-time infusion only. Repeat administration of Casgevy is not supported by FDA labeling or compendia and is therefore not considered medically necessary.

EFFECTIVE DATE
This Policy for the prior authorization of gene therapy with Casgevy for individuals covered under the HUSKY Health Program is effective May 1, 2025.

LIMITATIONS
N/A

CODES:

Code	Definition
J3392	Injection, exagamglogene autotemcel, per treatment

DEFINITIONS

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness,

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injury or disease; and (5) based on an assessment of the individual and his or her medical condition.

8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

- Angelucci E, Benz EJ. Hematopoietic stem cell transplantation and other curative therapies for transfusion-dependent thalassemia. In *UpToDate.* Negrin RS, Chao NJ, Tirnauer JS (Eds), Wolters Kluwer. Updated December 3, 2024. Accessed on March 4, 2025
- Benz EJ, Angelucci E. Diagnosis of thalassemia (adults and children). In *UpToDate.* Vichinsky EP, Tirnauer JS (Eds), Wolters Kluwer. Updated November 21, 2024. Accessed on February 25, 2025.
- CASGEVY [prescribing information]. Boston, MA: Vertex Pharmaceuticals; Revised January 2024
- Frangoul H, Locatelli F, Sharma A, et al. Exagamglogene autotemcel for severe sickle cell disease. *N Engl J Med*. 2024;390(18):1649-1662. doi:10.1056/nejmoa2309676
- Locatelli F, Lang P, Wall D, et al. Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia. *N Engl J Med*. 2024;390(18):1663-1676. doi:10.1056/NEJMoa2309673
- Vichinsky EP, Field JJ. Overview of the clinical manifestations of sickle cell disease. In *UpToDate.* DeBaun MR, Tirnauer JS (Eds), Wolters Kluwer. Updated January 23, 2025. Accessed on February 25, 2025

PUBLICATION HISTORY

Status	Date	Action Taken
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