Corporate Medical Policy: Exagamglogene autotemcel (Casgevy®) **"Notification"** **POLICY EFFECTIVE APRIL 1, 2026**

Restricted Product(s):

- exagamglogene autotemcel (Casgevy®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of patients aged 12 years and older with:
  - Sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs)
  - Transfusion-dependent β-thalassemia (TDT)

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient is 12 years of age or older; **AND**
2. ONE of the following:
   a. The patient has a diagnosis of **sickle cell disease (SCD) [medical record documentation required]**; **AND**
      i. The diagnosis has been confirmed by BOTH of the following:
         1. ONE of the following:
            a. Identification of significant quantities of HbS with or without an additional abnormal β-globin chain variant by hemoglobin assay **[medical record documentation required]**; **OR**
            b. Identification of biallelic *HBB* pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing **[medical record documentation required]**; **AND**
         2. Molecular genetic testing demonstrating ONE of the following genotypes:
            a. β^S/β^S or β^S/β^0 or β^S/β^+ genotype **[medical record documentation required]**; **OR**
            b. The prescriber has submitted written clinical rationale to support that use of the requested agent is clinically appropriate for the patient's genotype and disease severity **[medical record documentation required]**; **AND**
      ii. The patient has experienced at least four severe vaso-occlusive crisis (VOC) events*** in the past 24 months in the setting of appropriate supportive care measures for SCD (e.g., pain management plan) **[medical record documentation required]**; **AND**
      iii. ONE of the following:
         1. The patient has uncontrolled disease despite treatment with hydroxyurea OR crizanlizumab at any point in the past **[medical record documentation required]**; **OR**

2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to hydroxyurea OR crizanlizumab **[medical record documentation required]**; **AND**

iv. The patient will discontinue any disease-modifying therapies for SCD (e.g., crizanlizumab, hydroxyurea, voxelotor) at least 8 weeks prior to the planned start of hematopoietic stem cell (HSC) mobilization and myeloablative conditioning **[medical record documentation required]**; **OR**

b. The patient has a diagnosis of **transfusion-dependent β-thalassemia (TDT) [medical record documentation required]**; **AND**

i. The diagnosis has been confirmed by BOTH of the following:

1. ONE of the following:

a. Identification of biallelic *HBB* pathogenic variants by sequence gene analysis **[medical record documentation required]**; **OR**

b. The patient has severe microcytic hypochromic anemia, absence of iron deficiency, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A (HbA) and increased HbA_2 with or without increased amounts of hemoglobin F (HbF) **[medical record documentation required]**; **AND**

2. Molecular genetic testing demonstrating either homozygous β-thalassemia or compound heterozygous β-thalassemia, including β-thalassemia/hemoglobin E (HbE) **[medical record documentation required]**; **AND**

ii. The patient has required regular red blood cell (RBC) transfusions defined as the following **[medical record documentation required]**:

1. A history of at least 100 mL/kg/year of packed RBC transfusions during the past 2 years **[medical record documentation required]**; **OR**

2. A history of at least 10 units/year of packed RBC transfusions in the past 2 years **[medical record documentation required]**; **AND**

iii. The patient does NOT have a history of iron overload demonstrated by cardiac T2* less than 10 msec by magnetic resonance imaging (MRI) or left ventricular ejection fraction (LVEF) less than 45% by echocardiogram **[medical record documentation required]**; **AND**

iv. The patient does NOT have associated α-thalassemia and > 1 alpha chain deletion **[medical record documentation required]**; **AND**

v. The patient will discontinue any disease-modifying therapies for TDT (e.g., mitapivat) prior to the planned start of hematopoietic stem cell (HSC) mobilization and myeloablative conditioning **[medical record documentation required]**; **AND**

3. The patient is clinically fit to undergo autologous hematopoietic stem cell transplantation **[medical record documentation required]**; **AND**
4. The patient has NOT received prior allogeneic hematopoietic stem cell transplantation **[medical record documentation required]**; **AND**
5. The patient is a candidate for an allogeneic hematopoietic cell transplantation but has NO available willing and healthy 10/10 human leukocyte antigen (HLA)-matched related hematopoietic-cell donor **[medical record documentation required]**; **AND**

6. The patient has adequate bone marrow function, as defined by a white blood cell count of 3,000/µL or greater or a platelet count of 50,000/µL or greater **[medical record documentation required, including lab tests within the past 3 months]**; **AND**
7. The patient is able to receive red blood cell (RBC) transfusions **[medical record documentation required]**; **AND**
8. The patient has been assessed for renal impairment to ensure hematopoietic stem cell transplantation is appropriate (i.e., the patient's estimated glomerular filtration rate is > 60 mL/min/1.73 m^2) **[medical record documentation required]**; **AND**
9. The patient does NOT have severe cerebral vasculopathy, as defined by a history or presence of Moyamoya disease that puts the patient at risk of bleeding **[medical record documentation required]**; **AND**
10. The patient does NOT have advanced liver disease, defined as clear evidence of liver cirrhosis, active hepatitis, or significant fibrosis on liver biopsy **[medical record documentation required]**; **AND**
11. The patient is NOT human immunodeficiency virus type 1 or 2 (HIV-1 or HIV-2) positive **[medical record documentation required, including lab tests within the past 3 months]**; **AND**
12. ONE of the following **[medical record documentation required, including lab results within the past 3 months]**:
    a. The patient's hepatitis B surface antigen is negative; **OR**
    b. The patient has been previously vaccinated against hepatitis B virus (HBV) (i.e., HBV surface antibody [Ab]-positive) AND is negative for other markers of prior HBV infection (e.g., negative for HBV core Ab); **OR**
    c. The patient is negative for HBV DNA; **AND**
13. ONE of the following **[medical record documentation required, including lab results within the past 3 months]**:
    a. The patient's hepatitis C virus (HCV) antibody is negative; **OR**
    b. The patient's HCV antibody is positive AND the patient's HCV viral load is undetectable; **AND**
14. The patient does NOT have any prior or current malignancy or immunodeficiency disorder, with the exception of non-melanoma skin cancers, nor a history of Familial Cancer Syndrome **[medical record documentation required]**; **AND**
15. The patient does NOT have any clinically significant and active bacterial, viral, fungal, or parasitic infection **[medical record documentation required]**; **AND**
16. The patient does NOT have any contraindications to use of plerixafor during the mobilization of hematopoietic stem cells nor any contraindications to use of busulfan and any other medications required during the myeloablative conditioning, including hypersensitivity to the active substances or to any of the excipients **[medical record documentation required]**; **AND**
17. The patient has NOT received any previous gene therapy for the requested and/or approved indications, including the requested agent **[medical record documentation required]**; **AND**
18. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist, SCD or TDT specialist, transplant specialist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
19. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]**.

Duration of Approval: 365 days (1 year); one-time, single-dose treatment per lifetime

Please note, for certain identified gene and cellular therapies such as exagamglogene autotemcel (Casgevy®), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC to coordinate this therapy.

***A severe VOC event is defined as an acute episode of pain with no medically determined cause other than a vaso-occlusion, requiring a medical facility visit and treatment with pain medications (i.e., oral or parenteral opioids, or parenteral NSAIDs) or red blood cell (RBC) transfusions. Severe VOC events may include acute chest syndrome, acute hepatic sequestration, acute splenic sequestration, and/or acute priapism lasting more than 2 hours and requiring care at a medical facility

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
exagamglogene autotemcel (Casgevy®) intravenous (IV) infusion	• Sickle cell disease (SCD) in patients ≥12 years old with recurrent vaso-occlusive crises • Transfusion-dependent β-thalassemia in patients ≥12 years old	IV: Minimum recommended dose of 3 x 10^6 CD34+ cells per kg of body weight, as a single dose	J3392	**1**

***Maximum units allowed for duration of approval**

Other revenue codes that may be applicable to this policy: 0891, 0892

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-Cas9 gene editing for sickle cell disease and beta-thalassemia. *N Engl J Med*. 2021;384(3):252-260.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). **Policy notification given 2/1/2026 for effective date 4/1/2026**.
January 2026: Criteria change: For TDT indication: Added a requirement to discontinue any disease-modifying therapies for TDT (e.g., mitapivat) prior to initiating treatment, due to the recent FDA approval of a new therapy for TDT.
December 2025: Criteria update: Adjusted formatting to clarify that no presence of associated α-thalassemia and > 1 alpha chain deletion criterion is specific to TDT indication. Removed specified liver iron concentration from criteria defining no presence of advanced liver disease.
December 2025: Criteria change: For SCD indication: Added diagnostic confirmation criteria of either presence of significant quantities of HbS with or without an additional abnormal β-globin chain variant on hemoglobin assay OR molecular genetic testing showing biallelic *HBB* pathogenic variants with at least one allele as the p.Glu6Val pathogenic variant. Updated genotype-specific requirement to allow for prescriber submission of adequate written clinical rationale to support use of the requested agent for the patient's genotype and disease severity. Adjusted required trial and failure of hydroxyurea (HU) to specify uncontrolled disease despite treatment with HU or crizanlizumab at any point in the past. Added required discontinuation of any disease-modifying therapies for SCD at least 8 weeks prior to mobilization and conditioning. For TDT indication: Added diagnostic confirmation criteria of either sequence gene analysis showing biallelic *HBB* pathogenic variants OR presence of severe microcytic hypochromic anemia, absence of iron deficiency, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of HbA and increased HbA_2 with or without increased amounts of HbF. Reformatted criteria for no history of iron overload to only apply to TDT indication and added LVEF < 45% as additional indication of iron overload. For all indications: Removed Karnofsky/Lansky performance status defining ability to undergo autologous HSCT. Adjusted formatting of criteria for no associated alpha-thalassemia and > 1 alpha chain deletion for clarity. Removed requirement of no CKD and added required assessment for renal impairment to ensure HSCT is appropriate (i.e., eGFR > 60 mL/min/1.73m^2). Removed requirement of no pulmonary hypertension. Adjusted no cerebral vasculopathy requirement to only indicate no history or presence of Moyamoya disease putting patient at risk of bleeding. Adjusted no HBV criteria for clarity to allow for vaccinated patients (HBV surface antibody-positive) who are negative for other HBV markers (HBV core antibody-negative) and for past HBV exposure if patient is negative for HBV DNA. Adjusted HCV antibody-positive criteria with negative HCV RNA to undetectable viral load for clarity. Adjusted criteria for no immediate family members with a known or suspected Familial Cancer Syndrome to no history of Familial Cancer Syndrome. Added that no previous gene therapy requirement is for the requested and/or approved indications. Other minor updates made throughout policy for clarity. **Policy notification given 10/15/2025 for effective date 12/15/2025**.
January 2025: Coding change: Added HCPCS code J3392 to dosing reference table effective 1/1/2025; deleted C9399, J3490, and J3590 termed 12/31/2024.
February 2024: Original medical policy criteria issued.