Gene Therapy Treatments for Sickle Cell Disease

Humana

Medicaid Medical Coverage Policy

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Description

A group of genetic disorders known as sickle cell disease (SCD) are brought on by an abnormal type of hemoglobin (Hb), hemoglobin S (*HbS*), or sickle hemoglobin. Red blood cells contain Hb and in some situations (such as cold temperatures, infection or dehydration), the *HbS* molecules bind together to form long polymers, which gives the red blood cell a sickle shape. Because sickled red blood cells are rigid and can stick to blood vessel walls, they can impede blood flow and result in hypoxia (low levels of oxygen) in the surrounding tissues. This event is known as a vaso-occlusive crisis (VOC) and organ harm may result from oxygen deprivation over time. SCD is a chronic condition that has a high morbidity and mortality rate.[6,7]

About 8% of people of African descent carry the *HbS* gene, which is the highest prevalence of all affected groups. The *HbS* gene is also found in certain Hispanic populations (Caribbean, Central America and South America), people of Mediterranean descent (Greek, Italian and Turkish), Indian and Saudi Arabian populations. In the United States (US), there are about 100,000 cases of sickle cell disease which is associated with a 20–30 year shorter life expectancy.[6,7]

The mainstays of treatment for SCD have been supportive care to manage complications and preventive measures to reduce the incidence of VOCs. SCD treatment options primarily consist of hydroxyurea, pain management and transfusion. Currently, the only potential cure is hematopoietic stem-cell transplantation

(HSCT) using cells from a healthy donor. Allogeneic (donor) HSCT is the most successful potentially curative treatment for SCD, but its use is limited because of the lack of donors, concerns for transplant-related toxicities (including death), and preferences of the individual and family.[6,7]

The landscape of SCD treatment continues to evolve rapidly, with new disease-modifying therapies in development and potentially curative options now available. Gene therapy is being explored as a potential approach to addressing disease complications.**Error! Reference source not found.** Gene therapy is a technique that i ntroduces a normal gene or alters the expression of a disease-causing gene. The goal of gene therapy is to provide a sustained therapeutic benefit via continual expression of the proteins that reduce the pathogenesis of the relevant disease.**Error! Reference source not found.**

Casgevy (exagamglogene autotemcel) is an autologous, genome-edited, HSC based gene therapy indicated for the treatment of SCD in individuals 12 years of age and older with recurrent VOCs. Casgevy uses clustered regularly interspaced short palindromic repeats (CRISPR) technology to edit blood stem cells to increase the production of fetal hemoglobin. To cut DNA or deoxyribonucleic acid at a specific site, CRISPR collaborates with a produced guide RNA (gRNA) and an accompanying endonuclease (Cas9).[6]

This gene therapy procedure requires the individual to receive medications causing the stem cells to leave the bone marrow and enter the bloodstream and then apheresis is performed to collect the stem cells specifically to harvest HSCs. After that, CRISPR-Cas9 with gRNA that targets the *BCL11A* gene is electroporated into the HSCs. To create room for the gene therapy HSCs, the individual must go through a conditioning program once the gene therapy product is available. After being administered into the individual, the gene therapy HSCs will settle in the bone marrow. The altered *BCL11A* gene will be present in the new blood cells that are produced by transplanted HSCs.[6]

Lyfgenia (lovotibeglogene autotemcel) is an autologous HSC based gene therapy indicated for the treatment of individuals 12 years of age or older with sickle cell disease and a history of VOCs.[14]

This gene therapy utilizes a viral vector to carry the desired genetic information to target cells; vectors that are successfully transduced into target cells use the cell to express the desired proteins. By continuously expressing the proteins that alter the pathophysiology of the relevant disease, gene therapy aims to produce a long-lasting therapeutic benefit. Lyfgenia introduces lentiviral vectors containing a normal Hb gene into the individual's HSCs. The HSCs are transfected with Lyfgenia, which inserts the normal Hb gene into the HSCs' DNA. After being administered into the individual, the gene therapy HSCs establish themselves in the bone marrow. New blood cells with the normal Hb gene are produced by transplanted HSCs.[7]

Requests for Casgevy (exagamglogene autotemcel) AND Lyfgenia (lovotibeglogene autotemcel) *require review by a medical director*.

Coverage Determination

Refer all requests or questions regarding Gene Therapy Treatments for Sickle Cell Disease to the Corporate Transplant Department.

Phone	Fax	Email
1-866-421-5663	502-508-9300	transplant@humana.com

Humana members may be eligible under the Plan for **Casgevy (exagamglogene autotemcel)** when the following criteria are met[18]:

- Absence of contraindications; **AND**
- Individual is 12 through 65 years of age; **AND**
- Individual is a candidate for an autologous HSC transplantation, but lacks an available matched donor; **AND**
- Individual with diagnosis of SCD with recurrent vaso-occlusive crises (VOCs), **as indicated by**:
    - History of at least two ***severe*** VOC events per year for the previous two years ***Severe VOC*** is defined as an occurrence of at least one of the following events:
        - Acute pain event requiring a visit to a medical facility and administration of pain medications (opioids, intravenous or non-steroidal anti-inflammatory drugs [NSAIDs]) or RBC transfusions; **OR**
        - Acute chest syndrome; **OR**
        - Priapism lasting greater than 2 hours and requiring a visit to a medical facility; **OR**
        - Splenic sequestration

Humana members may be eligible under the Plan for **Lyfgenia (lovotibeglogene autotemcel)** when the following criteria are met[19]:

- Absence of contraindications; **AND**
- Individual is 12 through 65 years of age; **AND**
- Individual is a candidate for an autologous HSC transplantation, but lacks an available matched donor; **AND**
- Individual has diagnosis of SCD and a history of vaso-occlusive events (VOEs), as indicated by:
    - History of at least four VOEs per year for the previous two years.
      VOE is defined as any of the following event requiring evaluation at a medical facility:

- Acute pain event with no medically determined cause other than vaso-occlusion, lasting greater than 2 hours; **OR**
- Acute chest syndrome; **OR**
- Acute hepatic sequestration; **OR**
- Acute splenic sequestration; **OR**
- Priapism requiring any level of medical attention; **OR**
- VOE requiring hospitalization or multiple visits to an emergency department/urgent care over 72 hours and receiving intravenous medications at each visit

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **Casgevy (exagamglogene autotemcel)** for any indications other than those listed above including, but may not be limited to[18]:

- Individual is seropositive for hepatitis B or C (HBV, HCV), or human immunodeficiency virus (HIV); **OR**
- Individual has desire to become pregnant/reproduce **OR** unwilling to use effective contraception; **OR**
- Individual is pregnant or breastfeeding; **OR**
- Hepatic impairment; **OR**
- Renal impairment (eg, estimated glomerular filtration rate less than 60 mL/min/1.73 m2); **OR**
- Prior HSC transplant; **OR**

This is considered experimental/investigational as they are not identified as widely used and generally accepted for any other proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for **Lyfgenia (lovotibeglogene autotemcel)** for any indications other than those listed above including, but may not be limited to[19]:

- Individual is seropositive for human immunodeficiency virus (HIV); **OR**
- Individual has desire to become pregnant/reproduce **OR** unwilling to use effective contraception; **OR**
- Individual is pregnant or breastfeeding; **OR**

- Hepatic impairment; **OR**
- Renal impairment (eg, creatinine clearance less than or equal to 70 mL/min/1.73 m2)

This is considered experimental/investigational as they are not identified as widely used and generally accepted for any other proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
No code(s) identified		
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
C9399	Unclassified drugs or biologicals	
J3394	Injection, lovotibeglogene autotemcel, per treatment	
J3490	Unclassified drugs	
J3590	Unclassified biologics	
ICD-10-PCS Code(s)	**Description**	**Comments**
XW133H9	Transfusion of Lovotibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 9	
XW133J8	Transfusion of Exagamglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 8	
XW143H9	Transfusion of Lovotibeglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 9	
XW143J8	Transfusion of Exagamglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8	

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Change Summary

01/01/2025 New Policy.
02/04/2025 Update, Coverage Change.