BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 12/01/22**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 11/16/23**
	CURRENT EFFECTIVE DATE: 02/15/24
	LAST CRITERIA REVISION DATE: 02/15/24
NEXT ANNUAL REVIEW DATE: 4TH QTR 2024	**ARCHIVE DATE:**

GENE THERAPY FOR BETA THALASSEMIA AND SICKLE CELL DISEASE:

- **CASGEVY™ (exagamglogene autotemcel)**
- **LYFGENIA™ (lovotibeglogene autotemcel)**
- **ZYNTEGLO™ (betibeglogene autotemcel)**

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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GENE THERAPY FOR BETA THALASSEMIA AND SICKLE CELL DISEASE:

- **CASGEVY™ (exagamglogene autotemcel)**
- **LYFGENIA™ (lovotibeglogene autotemcel)**
- **ZYNTEGLO™ (betibeglogene autotemcel)**

Criteria:

Refer to FDA website for current indications and dosage.

CASGEVY (exagamglogene autotemcel)

- **Criteria for initial therapy:** Casgevy (exagamglogene autotemcel) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist or transplant specialist

  2. Individual is 12 of age or older

  3. Individual has a confirmed diagnosis of **ONE** of the following:

     - Severe sickle cell disease (SCD) in an individual with recurrent vaso-occlusive crisis (VOCs) as indicated by **BOTH** of the following:

       a. Confirmed diagnosis of sickle cell disease (e.g., βS/βS, βS/B0, or βS/B+)
       b. Two vaso-occlusive crisis events per year in the previous two years despite treatment with hydroxyurea or is unable to take hydroxyurea due to contraindication or intolerance

     - Transfusion-dependent β-thalassemia (TDT) as indicated by **BOTH** of the following:

       a. Confirmed diagnosis of β-thalassemia by globin gene testing
       b. History of at least 100ml/kg/year or 10 units/year of red blood cells transfusion s in the prior 2 years

  4. Individual has received and completed **ALL** the following baseline tests before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

     - Serologic tests for hepatitis B and C (HB surface Ag, anti-HB surface Ab, anti-HB core Ab, and hepatitis C antibody tests)
     - HIV test
     - Pregnancy test in individual of child-bearing potential
     - For TDT indication only: MRI of the heart and liver to evaluate for severe iron overload

  5. Individual meets **ALL** of the following:

     - Does NOT have a known 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic hematopoietic stem cell transplantation (HSCT)

- Iron chelators will be stopped 7 days prior to initiation of conditioning
- Hydroxyurea, Oxbryta and Adakveo will be stopped 8 weeks prior to mobilization and conditioning

6. Individual does **NOT** have **ANY** of the following:

   - Active bacterial, fungal, parasitic, or viral infection, including active/uncontrolled HBV and HCV
   - Prior gene therapy or is being considered for treatment with any other gene therapy
   - Prior hematopoietic stem cell transplant
   - Advanced liver disease (See Definitions Section)
   - Creatinine clearance less than 60 ml/min/1.73m^2
   - Presence of untreated Moyamoya disease
   - For TDT indication only: Severely elevated iron in the heart (cardiac T2* less than 10 milliseconds by MRI) or Left Ventricular Ejection Fraction (LVEF) < 45% by echocardiogram

7. The Attestation for Casgevy Treatment form (see below) has been signed by a physician (or designee) [Note: The form may be completed by the physician who is requesting and administering Casgevy or by the referring hematologist who will resume follow-up care.]

Approval duration: One-time treatment per lifetime
The safety and effectiveness of repeat administration of Casgevy (exagamglogene autotemcel) has not been evaluated.

Approval conditions:
If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider and/or referring provider attests and agrees to submit clinical outcomes data and information.

- Casgevy (exagamglogene autotemcel) for all other indications not previously listed is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

LYFGENIA (lovotibeglogene autotemcel)

- **Criteria for initial therapy:** Lyfgenia (lovotibeglogene autotemcel) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual is 12 to 50 years of age

3. Individual has a confirmed diagnosis of severe sickle cell disease (SCD) in an individual with recurrent vaso-occlusive crisis (VOCs) as indicated by **ALL** of the following:

   - Confirmed diagnosis of sickle cell disease (e.g., βS/βS, βS/B0, or βS/B+)
   - Four vaso-occlusive events in the previous two years despite treatment with hydroxyurea or is unable to take hydroxyurea due to contraindication or intolerance

4. Individual has received and completed **ALL** the following baseline tests before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

   - Serologic tests for hepatitis B and C (HB surface Ag, anti-HB surface Ab, anti-HB core Ab, and hepatitis C antibody tests)
   - HIV test
   - Pregnancy test in individual of child-bearing potential

5. Individual meets **ALL** of the following:

   - Does NOT have a known 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic hematopoietic stem cell transplantation (HSCT)
   - Iron chelators will be stopped 7 days prior to initiation of conditioning
   - Hydroxyurea, Oxbryta, Adakveo and L-glutamine will be stopped 2 months prior to mobilization and conditioning
   - Karnofsky performance status of ≥ 60 (≥16 years of age) or a Lansky performance status of ≥60 (<16 years of age)

6. Individual does **NOT** have **ANY** of the following:

    - Active bacterial, fungal, parasitic, or viral infection, including active/uncontrolled HBV and HCV
    - Prior gene therapy or is being considered for treatment with any other gene therapy
    - Prior hematopoietic stem cell transplant
    - Advanced liver disease (See Definitions Section)
    - Creatinine clearance less than 70ml/min/1.73m^2
    - Absolute neutrophil count (ANC) less than 1000/µL or < 500/µL if taking hydroxyurea
    - Platelet count less than 100,000/µL
    - History of cardiac iron overload (cardiac T2* less than 10 milliseconds by MRI)
    - Clinically significant pulmonary hypertension at baseline
    - Presence of genetic mutations that result in the inactivation of 2 or more α-globin genes
    - Any prior or current malignancy or immunodeficiency disorder, with the exception of non-melanoma skin cancers OR immediate family member with a known or suspected Familial Cancer Syndrome
    - Severe cerebral vasculopathy, defined by **ONE** or more of the following:

        a. History of overt or hemorrhagic stroke
        b. Greater than 50% stenosis or occlusion in the circle of Willis
        c. Presence of Moyamoya disease

7. The Attestation for Lyfgenia Treatment form (see below) has been signed by a physician (or designee) [Note: The form may be completed by the physician who requesting and administering Lyfgenia or by the referring hematologist who will resume follow-up care.]

Approval duration: One-time treatment per lifetime
The safety and effectiveness of repeat administration of Lyfgenia (lovotibeglogene autotemcel) has not been evaluated.

Approval conditions:
If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider and/or referring provider attests and agrees to submit clinical outcomes data and information.

- Lyfgenia (lovotibeglogene autotemcel) for all other indications not previously listed is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or

2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

ZYNTEGLO (betibeglogene autotemcel)

- **Criteria for initial therapy:** Zynteglo (betibeglogene autotemcel) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual is 50 years of age or younger and weighs at least 6 kilograms

3. Individual has a confirmed diagnosis of beta thalassemia who require regular red blood cell (RBC) transfusions with **ONE** of the following:

   - History of at least 100ml/kg/year of packed red blood cells or in the past 12 months
   - History of at least 8 or greater packed red blood cell transfusions in the past 12 months

4. Individual has received and completed **ALL** the following baseline tests before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

   - Serologic tests for hepatitis B and C (HB surface Ag, anti-HB surface Ab, anti-HB core Ab, and hepatitis C antibody tests)
   - HIV test
   - Pregnancy test in individual of child-bearing potential (all individuals should be using dual contraception prior to mobilization and for 6 months after Zynteglo administration)
   - Hemoglobin (must be 11g /dl or greater for 30 days prior to mobilization and myeloablative conditioning)
   - MRI of the heart and liver to evaluate for severe iron overload

5. Individual meets **ALL** of the following:

- Does NOT have a known 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic hematopoietic stem cell transplantation (HSCT)
- Iron chelators will be stopped 7 days prior to initiation of myeloablative conditioning
- Not taking hydroxyurea or HIV anti-retroviral medications for prophylaxis or plan to stop at least 1 month prior to mobilization
- Karnofsky performance status of ≥ 80 or greater for individuals ≥ 16 years or older or a Lansky performance status of 80 or greater for individuals < 16 years of age

6. Individual does **NOT** have **ANY** of the following:

   - White blood cell (WBC) less than 3 x 10^9/L
   - Platelet countless than 100 x 10^9/L not related to hypersplenism
   - Severely elevated iron in the heart (cardiac T2* less than 10 milliseconds by MRI)
   - Advanced liver disease (see Definitions section)
   - Creatinine clearance less than 70ml/min/1.73m^2
   - Active infection, including but not limited to HIV or hepatitis B or C
   - Prior gene therapy or is being considered for treatment with any other gene therapy
   - Prior allogenic hematopoietic stem cell transplant
   - Any prior or current malignancy or immunodeficiency disorder, with the exception of non-melanoma skin cancers OR immediate family member with a known or suspected Familial Cancer Syndrome

7. The Attestation for Zynteglo Treatment form (see below) has been signed by a physician (or designee) [Note: The form may be completed by the physician who is requesting and administering Zynteglo or by the referring hematologist who will resume follow-up care.]

Approval duration: One-time treatment per lifetime
The safety and effectiveness of repeat administration of Zynteglo (betibeglogene autotemcel) have not been evaluated.

Approval conditions:
If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider attests and agrees to submit clinical outcomes data and information.

Required Outcomes Measurements:

- Provider submits **documentation** of any packed Red Blood Cell transfusion episodes occurring after month 7 through month 24 following Zynteglo infusion
- Note: Packed Red Blood Cell transfusions occurring within a two-week timeframe of each other will be considered one transfusion episode

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- **ZYNTEGLO™ (betibeglogene autotemcel)**

- Zynteglo (betibeglogene autotemcel) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any one or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Attestations for Casgevy, Lyfgenia, or Zynteglo Treatment

Physician Name: _____

Individual Name: _____ DOB**:** _____

Treatment requested: _____

- The Physician is responsible for filling out this form. This form may be completed by the physician requesting and administering Casgevy, Lyfgenia, or Zynteglo or by the referring hematologist who will resume follow-up care for beta thalassemia or sickle cell disease.
- All elements must be initialed, and the form must be signed by the Physician (or designee).
- Incomplete forms will be returned to acquire missing information, initial, signature, or date.
- Return completed form to BCBSAZ.

Physician Agreement:

- Physician to initial by each element and date and sign to show willingness to participate.
- Documentation may include, but is not limited to, chart notes, laboratory test results, claims records, and/or other information.

Initials:

_____ I verify that the patient will be closely followed and monitored for progression of disease

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- **ZYNTEGLO™ (betibeglogene autotemcel)**

_____ I agree to submit clinical outcomes data and information

_____ **For Zynteglo only:** I agree to submit documentation of any packed Red Blood Cell transfusions the individual receives

Provider (or designee) Signature: _____

Date: _____

Description:

Beta thalassemia is a rare autosomal recessive blood disorder with potential for high morbidity and mortality. It is caused by a genetic mutation in the *HBB* gene that leads to reduced or absent β-globin proteins of hemoglobin, which causes clinically significant anemia. Severity can range from asymptomatic or mild for individuals that carry only one mutation to the most severe in individuals with two copies of the mutation with completely absent β-globin (β/0β0).

Transfusion-dependent thalassemia (TDT) is the most severe form and is manage with lifelong blood transfusions which generally causes iron overload. Excess iron accumulation has leads to pulmonary hypertension, livery dysfunction and cardiac failure. It is managed with iron chelation therapy. Historically, the only curative treatment option has been allogenic hematopoietic stem cell transplantation from a matched donor, preferably a sibling. Fewer than 25% of patients have access to a matched donor.

Sickle Cell Disease (SCD) refers a group of inherited disorders carried by the beta (β) allele of the hemoglobin (Hb) gene. It is characterized by abnormal hemoglobin polymerization during the deoxygenation resulting in sickle-shaped erythrocytes. Vaso-occlusive crisis (VOC), a recurrent acute pain crisis, is the most prevalent manifestation of SCD. Individuals also experience significant acute complications such as acute chest syndrome, serious infections, stroke, renal necrosis and priapism.

Hydroxyurea is the mainstay of treatment as it has been shown to reduce the incidence of acute vaso-occlusive pain episodes, other vaso-occlusive events, including acute chest syndrome and stroke, decreases hospitalization and prolongs survival. It may take three to six months to see the full effects of hydroxyurea benefit. Secondary treatment options include l-glutamine, voxelotor, crizanlizumab or prophylactic blood transfusions.

Allogeneic hematopoietic stem cell transplants (HSCTs) may offer a cure for SCD, but less than 20 percent of eligible individuals have a related matched donor. Gene therapy for SCD may be potentially curative, but study results are needed to determine longer-term outcomes. Unlike allogenic HCSTs, the two current gene therapies are autologous HSCTs in that stem cells are harvested, with manipulations to

add a new gene or alter the sequence of an endogenous gene, and then reinfused back into the individual. This eliminates the risk of graft versus host disease. However, all HSCTs, including these gene therapies, have potential risks for serious complications and morbidities.

Casgevy (exagamglogene autotemcel) is an autologous genome edited hematopoietic stem cell-based gene therapy indicated for the treatment of sickle cell disease (SCD) in patients 12 years and older with recurrent VOCs. Casgevy consists of autologous CD34+ HSCs edited by CRISPR/Cas9-technology at the erythroid specific enhancer region of the BCL11A gene to reduce BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) protein production. The edited CD34+ cells engraft in the bone marrow and differentiate to erythroid lineage cells with reduced BCL11A expression. Reduced BCL11A expression results in an increase in γ-globin expression and HbF protein production in erythroid cells. In patients with SCD, HbF expression reduces intracellular hemoglobin S (HbS) concentration, preventing the red blood cells from sickling and addressing the underlying cause of disease, thereby eliminating VOCs.

Casgevy will be administered at Authorized Treatment Center (ATC) in the United States and requires an intensive multi-step process with additional monitoring after administration. Due to the complexity of stem-cell based gene therapy only available at ATCs, care coordination should be considered to assist the member when needed.

- Step 1: Patient identification and evaluation at an ATC
- Step 2: Pre-mobilization (minimum of 8 weeks on an outpatient basis)
  - Red blood cell (RBC) exchanges or infusions are recommended
- Step 3: Mobilization and apheresis (up to 3-7 days per cycle, inpatient at an ATC) and may need to be repeated.
  - Collection of blood stem cells through mobilization and apheresis. This process takes approximately one week and may need to be repeated
  - Plerixafor is used for mobilization
- Step 4: Manufacturing and quality (5-6 months at a manufacturing facility)
  - Patients typically remain at home during this process
  - CRISPR/Cas9 technology used to edit stem cell at the erythroid-specific enhancer region of the BCL11A gene.
  - Quality release testing confirm product meets release criteria, including viability, purity, content, potency, sterility, and other safety tests
- Step 5: Myeloablative conditioning, infusion, and engraftment (approximately 6-7 weeks admitted at an ATC)
  - The median time for neutrophil engraftment was 27 days (SCD) and 29 days (TDT)
  - The median time for platelet engraftment was 35 days (SCD) and 44 days (TDT)

Lyfgenia (lovotibeglogene autotemcel) is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events (VOE).

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- **ZYNTEGLO™ (betibeglogene autotemcel)**

Limitations of Use: Following treatment with Lyfgenia, patients with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell transfusions. Lyfgenia has not been studied in patients with more than two α-globin gene deletions.

Lyfgenia is intended for one-time administration to add functional copies of a modified form of the β-globin gene (βA-T87Q-globin gene) into the patient's own stem cells. The transduced CD34+ HSCs engraft in the bone marrow and differentiate to produce red blood cells containing biologically active βA-T87Q-globin that will combine with α-globin to produce functional Hb containing βA-T87Q-globin (HbAT87Q). HbAT87Q has similar oxygen-binding affinity and oxygen hemoglobin dissociation curve to wild type HbA, reduces intracellular and total hemoglobin S (HbS) levels, and is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells.

Lyfgenia will be administered at Qualified Treatment Center (QTC) in the United States and requires an intensive multi-step process with additional monitoring after administration. Due to the complexity of stem-cell based gene therapy only available at QTCs, care coordination should be considered to assist the member when needed.

- Step 1: Pre-treatment
  - Individual is prepared for mobilization with at least 2 cycles of scheduled transfusions (1 each month), with erythrocytapheresis being preferred
- Step 2: Mobilization and apheresis (7+ days)
  - Plerixafor is used for mobilization
- Step 3: Production (70-105 days)
  - Stem cells sent to manufacturing site to produce Lyfgenia
- Step 4: Myeloablative conditioning (4 days) with washout of at least 48 hours (6+days total)
- Step 5: Infusion (approximately 30 days)
- Step 6: Post-infusion monitoring (21-42 days)
  - Individual will remain hospitalized and monitored for 3-6 weeks after infusion

Post-treatment: long-term follow up: Hematologic malignancy has occurred in patients treated with Lyfgenia; therefore, patients should be monitored lifelong. Complete blood count (with differential) should be done every 6 months for 15 years and integration site analysis at 6 and 12 months and as warranted Zynteglo (betibeglogene autotemcel) is indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions. It is a potentially curative gene therapy for beta thalassemia. Betibeglogene autotemcel adds functional copies of a modified β-globin gene into the individuals own hematopoietic stem cells through transduction of autologous CD34+ cells with BB305 LVV, a lentiviral vector. After infusion, the transduced stem cells engraft in the bone marrow and differentiate to produce red blood cells containing the functional β-globin. Studies showed almost 90% of individuals in the clinical trials achieved transfusion independence.

Zynteglo will be administered at qualified treatment centers (QTC) in the United States and requires an intensive four step process with additional monitoring after administration. Due to the complexity of stem-

cell based gene therapy only available at QTCs, care coordination should be considered to assist the member when needed.

- Step 1: Collection of blood stem cells through mobilization and apheresis. This process takes approximately one week and may need to be repeated
- Step 2: Blood stem cells are sent to the manufacturing site and the functioning gene is attached to the stem cells to make Zynteglo. This step takes approximately 70-90 days.
- Step 3: The individual is hospitalized and myeloablative chemotherapy is administered
- Step 4: Zynteglo is administered intravenously. The individual remains hospitalized during administration and for monitoring afterward for approximately 3-6 weeks. During the clinical trials, patients spent median of 44 days (range 29-92) in the hospital.

Definitions:

Mobilization: first step in autologous stem cell transplants done to increase number of stem cells released in the blood; hematopoietic stem cell mobilization is done by administering granulocyte-colony stimulating factor (G-CSF) and plerixafor prior to autologous transplantations

Apheresis: process of removing peripheral blood mononuclear cells, specifically CD34+ cells for product manufacturing. For Zynteglo, these cells are sent to manufacturer to add functional copies of modified β-globin gene (HBB) to the stem cells to later be infused back into the patient

Myeloablative Conditioning: Administration of busulfan to destroy hematopoietic cells in the bone marrow which results in pancytopenia that is irreversible until administration of stem cells.

Advanced Liver Disease is defined as any of the following:

- Persistent aspartate transaminase (AST), alanine transaminase (ALT), or direct bilirubin > 3 x the upper limit of normal (ULN)
- Baseline prothrombin time or partial thromboplastin time > 1.5 x ULN
- MRI of liver demonstrating clear evidence of cirrhosis. Additional testing including liver biopsy is required if MRI suggests active hepatitis, significant fibrosis, inconclusive cirrhosis, or liver iron concentrations ≥ 15 mg/g.
- Liver biopsy demonstrating cirrhosis, bridging fibrosis or active hepatitis

Familial Cancer Syndrome: Cancers including but not limited to hereditary breast and ovarian cancer syndrome, hereditary non-polyposis colorectal cancer syndrome, and familial adenomatous polyposis

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History:	**Date:**	**Activity:**
Pharmacy and Therapeutics Committee	02/15/24	Revisions to guideline
Pharmacy and Therapeutics Committee	11/16/23	Review with revisions
Pharmacy and Therapeutics Committee	12/01/22	Approved Guideline
Clinical Pharmacist	10/01/22	Development

Coding:

HCPCS: C9399, J3590

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Resources:

Literature reviewed 11/16/23. We do not include marketing materials, poster boards and non-published literature in our review.

1. Beaudoin FL, Richardson M, Synnott PG, et al. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review, July 19, 2022. https://icer.org/beta-thalassemia-2022/#timelineICER. Accessed September 6, 2022.

2. Benz EJ, Angelucci E. Diagnosis of thalassemia (adults and children). In: UpToDate, Vichinsky EP, Tirnauer JS (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated November 08, 2022. Accessed September 22, 2023.

3. Benz EJ, Angelucci E. Management of thalassemia. In: UpToDate, Vichinsky EP, Tirnauer JS (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated May 03, 2023. Accessed September 22, 2023.

4. Casgevy (exagamglogene autotemcel) prescribing information, revised by Vertex Pharmaceuticals Incorporated 01/2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 5, 2024.

5. Field JJ, Vichinsky EP. Overview of the management and prognosis of sickle cell disease. In: UpToDate, DeBaun MR, Tirnauer JS (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated October 18, 2023. Accessed December 14, 2023.

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EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 12/01/22**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 11/16/23**
	CURRENT EFFECTIVE DATE: 02/15/24
	LAST CRITERIA REVISION DATE: 02/15/24
NEXT ANNUAL REVIEW DATE: 4TH QTR 2024	**ARCHIVE DATE:**

GENE THERAPY FOR BETA THALASSEMIA AND SICKLE CELL DISEASE:

- **CASGEVY™ (exagamglogene autotemcel)**
- **LYFGENIA™ (lovotibeglogene autotemcel)**
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