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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	April 12, 2024
Subject:	Lyfgenia	**Page:**	1 of 4

Last Review Date: September 6, 2024

Lyfgenia

Description

Lyfgenia (lovotibeglogene autotemcel)

Background
Lyfgenia (lovotibeglogene autotemcel) is a $\beta^{A\text{-}T87Q}$-globin gene therapy consisting of autologous $CD34^{+}$ cells from patients with sickle cell disease (SCD) containing hematopoietic stem cells (HSCs) transduced with BB305 LVV encoding $\beta^{A\text{-}T87Q}$-globin. Lyfgenia is intended for one-time administration to add functional copies of a modified form of the β-globin gene into the patient's own HSCs. After Lyfgenia infusion, the transduced CD34+ HSCs engraft in the bone marrow and differentiate to produce red blood cells containing biologically active $\beta^{A\text{-}T87Q}$-globin that will combine with α-globin to produce functional hemoglobin (Hb) containing $\beta^{A\text{-}T87Q}$-globin (HbA^{T87Q}). HbA^{T87Q} has similar oxygen-binding affinity and oxygen hemoglobin dissociation curve to wild type HbA, reduces intracellular total hemoglobin S (HbS) levels, and is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells (1).

Regulatory Status
FDA-approved indication: Lyfgenia 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 (1).

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 (1).

Lyfgenia has a boxed warning of hematologic malignancy. Complete blood counts should be monitored at least every 6 months and through integration site analysis at months 6, 12, and as warranted (1).

Lyfgenia has warnings for neutrophil engraftment failure, delayed platelet engraftment, hypersensitivity reactions and potential for insertional oncogenesis. The patient's absolute neutrophil count and platelet counts should be monitored. During and after infusion, the patient should be monitored for hypersensitivity reactions (1).

The safety and effectiveness of Lyfgenia in pediatric patients less than 12 years of age have not been established (1).

Related policies
Casgevy

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Lyfgenia may be considered **medically necessary** if the conditions indicated below are met.

Lyfgenia may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 12 years of age or older

Diagnoses

Patient must have the following:

Homozygous or heterozygous sickle cell disease (SCD)

AND ALL the following:

1. Diagnosis confirmed by genetic testing
2. Documented history of **ONE** of the following clinical signs or symptoms in the last 12 months:

a. Acute pain event requiring a visit to a medical facility and administration of pain medications (e.g., opioids (IV or oral) or intravenous non-steroidal anti-inflammatory drugs), hydration therapy, or red blood cell transfusion
b. Acute chest syndrome
c. Acute hepatic sequestration
d. Acute splenic sequestration
e. Priapism lasting > 2 hours and requiring a visit to a medical facility

3. Patient meets the institutional requirements for a stem cell transplant procedure including **ALL** of the following:
   a. Adequate Karnofsky performance status or Lansky performance status
   b. Absence of advanced liver disease
   c. Adequate estimated glomerular filtration rate (eGFR)
   d. Adequate diffusing capacity of the lungs for carbon monoxide (DLCO)
   e. Adequate left ventricular ejection fraction (LVEF)
   f. Absence of clinically significant active infection(s)

AND NONE of the following:

1. Prior gene therapy for sickle cell disease
2. Prior allogenic hematopoietic stem cell transplant

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity One infusion (only one PA approval for one infusion per lifetime)

Prior – Approval *Renewal* Limits

None

Rationale

Summary
Lyfgenia is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of sickle cell disease (SCD) and a history of vaso-occlusive events. Lyfgenia carries a boxed warning of hematologic malignancy. Patients should be monitored through complete blood counts and integration site analysis. The safety and effectiveness of Lyfgenia in pediatric patients less than 12 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Lyfgenia while maintaining optimal therapeutic outcomes.

References
1. Lyfgenia [Package Insert]. Somerville, MA: Bluebird bio, Inc.; December 2023.

Policy History

Date	Action
April 2024	Addition to PA
June 2024	Annual review
September 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.