Medical Policy:

Lyfgenia (lovotibeglogene autotemcel) intravenous infusion

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.410	June 20, 2025	May 9, 2024

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

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Definitions

Lyfgenia is an autologous hematopoietic stem cell (HSC)-based gene therapy indicated for the treatment of sickle cell disease in patients ≥ 12 years of age with a history of vaso-occlusive events (VOEs).

Length of Authorization

Lyfgenia is given as a one-time dose (once per lifetime) by IV infusion.

Dosing Limits [Medical Benefit]

A single dose of Lyfgenia containing a minimum of 3 x 10^6 $CD34^+$ cells/kg of body weight, in one or more infusion bags

Guideline

I. INITIAL APPROVAL CRITERIA

Coverage is provided in the following conditions:

1. Patient is at least 12 years of age; **AND**

2. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning; **AND**
3. Patient will be monitored for hematologic malignancies periodically after treatment; **AND**
4. Must not be administered concurrently with live vaccines while immunosuppressed; **AND**
5. Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; **AND**
6. Patient is HIV negative as confirmed by a negative HIV test prior to mobilization (Note: Patients who have received Lyfgenia are likely to test positive by polymerase chain reaction (PCR) assays for HIV due to integrated BB305 LVV proviral DNA, resulting in a possible false-positive PCR assay test result for HIV. Therefore, patients who have received Lyfgenia should not be screened for HIV infection using a PCR-based assay.); **AND**
7. Patient will not receive therapy concomitantly with any of the following:
   A. Hydroxyurea for at least 2 months prior to mobilization and until all cycles of apheresis are completed *(Note: If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning);* **AND**
   B. Myelosuppressive iron chelators (e.g., deferiprone, etc.) for 7-days prior to mobilization, conditioning, and 6 months post-treatment; OR 3-months post-treatment for non-myelosuppressive iron chelators; **AND**
   C. Disease-modifying agents (e.g., L-glutamine, crizanlizumab) for at least 2 months prior to mobilization; **AND**
   D. Prophylactic HIV anti-retroviral therapy (Note: Patients receiving prophylactic ART should stop therapy for at least one month prior to mobilization and until all cycles of apheresis are completed); **AND**
   E. Mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF); **AND**
   F. Erythropoietin for at least 2 months prior to mobilization; **AND**
8. Patient has not received other gene therapy [e.g., Casgevy™ (exagamglogene autotemcel)] *; **AND**
9. Patient is a candidate for autologous hematopoietic stem cell transplant (HSCT); **AND**
10. Patient does not have a known clinically suitable 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic HSCT; **AND**
11. Patient will be transfused at least twice (once each month) prior to mobilization to reach a target Hb of 8-10 g/dL (less than 12 g/dL) and <30% HbS; **AND**

*Requests for subsequent use of lovotibeglogene after receipt of exagamglogene autotemcel will be evaluated on a case-by-case basis

1. **<u>Sickle Cell Disease</u>**
   A. Patient has a confirmed diagnosis of sickle-cell disease (includes genotypes βS/βS or βS/β0 or βS/β+) as determined by one of the following:
      i. Identification of significant quantities of HbS with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
      ii. Identification of biallelic HBB pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**
   B. Patient does NOT have disease with more than two α-globin gene deletions; **AND**
   C. Patient has symptomatic disease despite treatment with hydroxyurea or add-on therapy (e.g., crizanlizumab, etc.); **AND**
   D. Patient experienced four or more vaso-occlusive events/crises (VOE/VOC)* in the previous two year

*VOE/VOC is defined as an event requiring a visit to a medical facility for evaluation which results in a diagnosis of such being

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documented due to one (or more) of the following: acute pain, acute chest syndrome, acute splenic sequestration, acute hepatic sequestration, priapism lasting > 2 hours AND necessitating subsequent interventions such as opioid pain management, non-steroidal anti-inflammatory drugs, RBC transfusion, etc.

Applicable Procedure Codes

Code	Description
J3590	Unclassified biologics

Applicable NDCs

Code	Description
73554-1111-01	Lyfgenia Intravenous Suspension 20 mL infusion bag

ICD-10 Diagnoses

Code	Description
D57.00	Hb-Ss Disease With Crisis, Unspecified
D57.01	Hb-Ss Disease With Acute Chest Syndrome
D57.02	Hb-Ss Disease With Splenic Sequestration
D57.03	Hb-Ss Disease With Cerebral Vascular Involvement
D57.04	Hb-Ss Disease With Dactylitis
D57.09	Hb-Ss Disease With Crisis With Other Specified Complication
D57.1	Sickle-Cell Disease Without Crisis
D57.20	Sickle-Cell/Hb-C Disease Without Crisis
D57.211	Sickle-Cell/Hb-C Disease With Acute Chest Syndrome
D57.212	Sickle-Cell/Hb-C Disease With Splenic Sequestration
D57.213	Sickle-Cell/Hb-C Disease With Cerebral Vascular Involvement
D57.214	Sickle-Cell/Hb-C Disease With Dactylitis
D57.218	Sickle-Cell/Hb-C Disease With Crisis With Other Specified Complication
D57.219	Sickle-Cell/Hb-C Disease With Crisis, Unspecified
D57.40	Sickle-Cell Thalassemia Without Crisis
D57.411	Sickle-Cell Thalassemia, Unspecified, With Acute Chest Syndrome
D57.412	Sickle-Cell Thalassemia, Unspecified, With Splenic Sequestration
D57.413	Sickle-Cell Thalassemia, Unspecified, With Cerebral Vascular Involvement
D57.414	Sickle-Cell Thalassemia, Unspecified, With Dactylitis
D57.418	Sickle-Cell Thalassemia, Unspecified, With Crisis With Other Specified Complication
D57.419	Sickle-Cell Thalassemia, Unspecified, With Crisis
D57.42	Sickle-Cell Thalassemia Beta Zero Without Crisis
D57.431	Sickle-Cell Thalassemia Beta Zero With Acute Chest Syndrome
D57.432	Sickle-Cell Thalassemia Beta Zero With Splenic Sequestration
D57.433	Sickle-Cell Thalassemia Beta Zero With Cerebral Vascular Involvement
D57.434	Sickle-Cell Thalassemia Beta Zero With Dactylitis
D57.438	Sickle-Cell Thalassemia Beta Zero With Crisis With Other Specified Complication
D57.439	Sickle-Cell Thalassemia Beta Zero With Crisis, Unspecified
D57.44	Sickle-Cell Thalassemia Beta Plus Without Crisis
D57.451	Sickle-Cell Thalassemia Beta Plus With Acute Chest Syndrome

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D57.452	Sickle-Cell Thalassemia Beta Plus With Splenic Sequestration
D57.453	Sickle-Cell Thalassemia Beta Plus With Cerebral Vascular Involvement
D57.454	Sickle-Cell Thalassemia Beta Plus With Dactylitis
D57.458	Sickle-Cell Thalassemia Beta Plus With Crisis With Other Specified Complication
D57.459	Sickle-Cell Thalassemia Beta Plus With Crisis, Unspecified
D57.80	Other Sickle-Cell Disorders Without Crisis
D57.811	Other Sickle-Cell Disorders With Acute Chest Syndrome
D57.812	Other Sickle-Cell Disorders With Splenic Sequestration
D57.813	Other Sickle-Cell Disorders With Cerebral Vascular Involvement
D57.814	Other Sickle-Cell Disorders With Dactylitis
D57.818	Other Sickle-Cell Disorders With Crisis With Other Specified Complication
D57.819	Other Sickle-Cell Disorders With Crisis, Unspecified

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	6/20/2025	Update: Removal from policy: • Vexelotor from disease modifying agents • From sickle cell disease removed two vaso-occlusive events and replaced it with four. Updated from one year to two years and removed “while adhering to the above therapy” Addition to policy: • Addition of “clinically suitable” to 10/10 human leukocyte antigen
EmblemHealth & ConnectiCare	2/27/2025	Annual Review: Addition of OR 3-months post-treatment for non-myelosuppressive iron chelators to myelosuppressive iron chelators requirement.
EmblemHealth & ConnectiCare	05/09/2024	New Policy

References

1. Lyfgenia® intravenous infusion [prescribing information]. Somerville, MA: bluebird bio; December 2023.

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