Medical Policy:

Lyfgenia (lovotibeglogene autotemcel) intravenous infusion

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

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; **AND**
   C. Disease-modifying agents (e.g., L-glutamine, vexelotor, 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 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, voxelotor, etc.); **AND**
   D. Patient experienced two or more vaso-occlusive events/crises (VOE/VOC)* in the previous year while adhering to the above therapy

*VOE/VOC is defined as an event requiring a visit to a medical facility for evaluation which results in a diagnosis of such being 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
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	05/09/2024	New Policy

References

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