LYFGENIA (PREAUTHORIZATION REQUIRED)

X.224

X.224 LYFGENIA (PREAUTHORIZATION REQUIRED)

POLICY

I. Target Agent(s) may be considered **medically necessary** when ALL of the following are met:

A. The patient is at least 12 years old **AND**

B. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning **AND**

C. Patient will be monitored for hematologic malignancies periodically after treatment **AND**

D. Must not be administered concurrently with live vaccines while immunosuppressed **AND**

E. Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40 **AND**

F. 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**

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1. 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**

2. Myelosuppressive iron chelators (e.g., deferiprone, etc.) for 7-days prior to mobilization, conditioning, and 6 months post-treatment **AND**

3. Disease-modifying agents (e.g., L-glutamine, vexelotor, crizanlizumab) for at least 2 months prior to mobilization **AND**

4. 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**

5. Mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF) **AND**

6. Erythropoietin for at least 2 months prior to mobilization **AND**

H. Patient has not received other gene therapy [e.g., Casgevy™ (exagamglogene autotemcel)] **AND**

I. Patient is a candidate for autologous hematopoietic stem cell transplant (HSCT) **AND**

J. 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

variant by hemoglobin assay **OR**

2. Identification of biallelic HBB pathogenic variants where at least one allele is the P.Glu6Val pathogenic variant on molecular genetic testing **AND**

K. Patient does NOT have disease with more than two α-globin gene deletions **AND**

L. Patient experienced at least two vaso-occlusive events/crises (VOE/VOC)* in the previous 12 months while adhering to the above therapy (Note: Patients experiencing four events/crises in the previous 24 months will also have met this requirement)

*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

Length of Approval: 1 per lifetime

Dates

Original Effective
03-01-2024
Last Review
11-06-2024
Next Review
11-06-2025

CLINICAL RATIONALE

LYFGENIA (lovotibeglogene autotemcel) is a βA-T87Q-globin gene therapy consisting of autologous CD34+ cells from patients with sickle cell disease

a modified form of the β-globin gene (βA-T87Q-globin gene) into the patient's own HSCs.

LYFGENIA is prepared using the patient's own HSCs, which are collected via apheresis procedure(s). The autologous cells are enriched for CD34+ cells, then transduced ex vivo with BB305 LVV. The promoter, a regulatory element that controls the expression of the transgene selected for BB305 LVV, is a cellular (non-viral) promoter that controls gene expression specific to the erythroid lineage cells (red blood cells and their precursors). BB305 LVV encodes βA-T87Q-globin.

The efficacy of LYFGENIA was studied in a single-arm, 24-month, open-label, multicenter Phase 1/2 study (Study 1-C) and continued on a long-term follow-up study. In Study 1-C, 43 subjects underwent apheresis after mobilization with plerixafor of which 36 patients received myeloablative busulfan conditioning. Seven patients did not proceed to conditioning; 2 patients discontinued due to apheresis-related issues and 5 discontinued at patient and/or physician discretion.

The transplant population for VOE efficacy outcomes included patients with a history of at least 4 VOEs in the 24 months prior to informed consent. The efficacy outcomes were complete resolution of VOEs (VOE-CR) and severe VOEs (sVOE-CR) between 6 months and 18 months after infusion of LYFGENIA. VOEs were defined as any of the following events requiring evaluation at a medical facility:

- an episode of acute pain with no medically determined cause other than vaso-occlusion, lasting more than 2 hours
- acute chest syndrome (ACS)
- acute hepatic sequestration
- acute splenic sequestration Severe VOE (sVOE) were defined as either of the following events: • VOE requiring a hospitalization or multiple visits to an emergency department/urgent care over 72 hours and receiving intravenous medications at each visit
- priapism requiring any level of medical attention

The median (min, max) duration of follow-up for the patients in Study 1-C (N = 36) is 38 (12, 61) months post LYFGENIA infusion. After the primary evaluation period to last follow-up, 4 of 32 patients who achieved VOE-CR experienced VOEs while maintaining GR. After the primary evaluation period up to 24 months, 17 of 35 (49%) patients were prescribed opioids for sickle cell and non-sickle cell-related pain.

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Added new 07/01/2024 HCPCS code: J3394

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