DR.021.A Lyfgenia™ (lovotibeglogene autotemcel)

Original Implementation Date : 8/21/2024
Version [A] Date : 8/21/2024
Last Reviewed Date: 8/21/2024

PRODUCT VARIATIONS

This policy applies to all Medicaid, CHIP and Medicare product lines.

Gene therapy is a benefit exclusion for Individual and Family (ACA) product lines and therefore, non-covered.

POLICY STATEMENT

We consider Lyfgenia™ (lovotibeglogene autotemcel) medically necessary for its FDA approved indications when the prior authorization listed in this policy are met.

FDA APPROVED INDICATIONS

Gene Therapy is the introduction, removal, or change in the content of a person's genetic code with the goal of treating or curing a disease. It includes therapies such as gene transfer, gene modified cell therapy, and gene editing.

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

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

Prior authorization is required for Lyfgenia™ (lovotibeglogene autotemcel). Requests for prior authorization of Lyfegnia® (lovotibeglogene autotemcel) will be approved for 18 months for 1 infusion.

Lyfgenia™(lovotibeglogene autotemcel) may be considered medically necessary when **ALL** of the following apply:

1. Is prescribed Lyfgenia™ (lovotibeglogene autotemcel) for an indication that is included in the U.S. Food and Drug Administration (FDA)-approved package labeling; AND

2. Is age-appropriate according to FDA-approved package labeling; AND

3. Is prescribed a dose and number of treatments that are consistent with FDA-approved package labeling; AND

4. Is prescribed Lyfgenia™ (lovotibeglogene autotemcel) by a specialist at a qualified treatment center for Lyfgenia™ (lovotibeglogene autotemcel); AND

5. Does not have a contraindication to the prescribed medication; AND

6. Is not a prior recipient of gene therapy or an allogeneic hematopoietic stem cell transplant; AND

7. For treatment of sickle cell disease, both of the following:

    a. Has sickle cell disease with a βS/βS, βS/β0, or βS/β+ genotype.

    b. One of the following:

        i. Has a history of vaso-occlusive episodes (e.g., pain crises, acute chest syndrome, splenic sequestration, priapism) that required a medical facility visit (e.g., emergency department, hospital).
        ii. Is currently receiving chronic transfusion therapy for recurrent vaso-occlusive episodes.

DOSAGE AND ADMINISTRATION

Administration:

- Administer within 4 hours after thawing.
- Patients are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for manufacturing.
- Myeloablative conditioning must be administered before infusion.

    - Following myeloablative conditioning, allow a minimum of 48 hours of washout before infusion.
- Do not sample, alter, irradiate, or refreeze.
- Do not use an in-line blood filter or an infusion pump.

Dosing:

- Based on the number of CD34+ cells in the infusion bag(s) per kg of body weight.
- The minimum recommended dose is 3×10^6 CD34+ cells/kg.

RISK FACTORS/SIDE EFFECTS

Most common adverse reactions ≥ Grade 3 (incidence ≥ 20%) were stomatitis, thrombocytopenia, neutropenia, febrile neutropenia, anemia, and leukopenia.

Drug Interactions:

- Anti-retrovirals: Discontinue anti-retroviral medications at least one month prior to mobilization and until all cycles of apheresis are completed. There are some long-acting anti-retroviral medications that may require a longer duration of discontinuation for elimination of the medication.

- Hydroxyurea: Discontinue 2 months prior to mobilization and 2 days prior to conditioning.

- Iron chelation: Discontinue at least 7 days prior to mobilization and conditioning.

MONITORING

1. **Neutrophil Engraftment Failure**: Monitor absolute neutrophil counts (ANC) after infusion. Administer rescue cells in the event of neutrophil engraftment failure. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) ≥ 0.5×10^9 cells/L obtained on different days by Day 43 after infusion.

2. **Delayed Platelet Engraftment:** Monitor platelet counts until platelet engraftment and recovery are achieved.

3. **Hypersensitivity Reactions:** Monitor for hypersensitivity reactions during and after infusion. The dimethyl sulfoxide (DMSO) or dextran 40 in Lyfgenia™ may cause hypersensitivity reactions, including anaphylaxis.

4. **Insertional Oncogenesis**: There is a potential risk of lentiviral vector-mediated insertional oncogenesis after treatment.

BLACK BOX WARNING

Hematologic malignancy has occurred in patients treated with Lyfgenia™. Monitor patients closely for evidence of malignancy through complete blood counts at least every 6 months and through integration site analysis at Months 6, 12, and as warranted.

CLINICAL EVIDENCE

In a single-arm, 24-month, open-label, multicenter Phase 1/2 study and continued on a long-term follow-up study the efficacy of Lyfgenia was explored. 36 patients received intravenous infusion of V with a median (min, max) dose of 6.4 (3, 14) × 106 CD34+ cells/kg. 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 and/or priapism requiring any level of medical attention.

Efficacy outcomes were 28/32 in the VOE-CR group (95% CI 71,97) and 30/32 in the sVOE-CR group (95% CI 79,99). All 36 patients infused in Study 1-C (transplant population) were evaluated for globin response. 31/36 (86%) achieved GR. All patients maintained GR once it was achieved. 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.

BACKGROUND

Sickle cell disease is an inherited group of blood disorders caused by a hemglobin defect known as Hemglobin S that replaces both β-globin subunits in hemoglobin. This disease affects roughly 100,000 people in the US and is most commonly in black americans but also hispanic americans at a less prevalent rate. The mutation causes red blood cells to become rigid and have a sickle shape which makes it difficult and painful to pass through small blood vesels as they get stuck and clog blood flow. This blockage can results in many complications as it restricts blood supply to tissues preventing oxygenation. It could cause severe pain and damgage to oragans and joints. This is referred to vaso-occulsive events (VOEs) or vaso-occulsive crises (VOCs), which can be life-threatening if left unresolved. Sickle cell disases requires treatment in clinical settings that specialize

in preventing and managing complications from sickle cell diseases. Patients often require blood transfusions, pain management, and preventive measures for infections. Other treatments may be bone marrow transplant, monoclonal antibodies, and gene therapies.

Lyfgenia™ (lovotibeglogene autotemcel) is a $\beta^{A\text{-}T87Q}$-globin gene therapy consisting of autologous CD34+ cells from patients with sickle cell disease containing hematopoietic stem cells (HSCs) transduced with BB305 LVV encoding $\beta^{A\text{-}T87Q}$-globin, suspended in cryopreservation solution. LYFGENIA is intended for one-time administration to add functional copies of a modified form of the β-globin gene ($\beta^{A\text{-}T87Q}$-globin gene) into the patient's own HSCs. It is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
N/A	N/A

HCPCS Code	Description
J3394	Injection, lovotibeglogene autotemcel, per treatment

ICD-10 Codes	Description
N/A	N/A

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making.

Policy Bulletins are developed by us to assist in administering plan benefits and constitute neither offers of coverage nor medical advice.

This Policy Bulletin may be updated and therefore is subject to change.

For HealthChoices (Medicaid) and Children's Health Insurance Program (CHIP) products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
New policy.	A	8/21/2024

REFERENCES

1. Lyfgenia™ [prescribing information]. Somerville, MA: bluebird bio, Inc; December 2023.

2. The National Institutes of Health – National Heart, Lung, and Blood Institute Evidence-Based Management of Sickle Cell Disease, Expert Panel Report, 2014. Available at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed March 2024.

3. Connor RF, Fosmarin AG, Tirnauer JS. What's new in hematology. UpToDate [internet database]. Waltham, MA: UpToDate Inc. Updated February 29, 2024. Accessed March 18, 2024.

4. Fitzjugh C. Investigational therapies for sickle cell disease. UpToDate [internet database]. DeBaun MR, Tirnauer JS, eds. Waltham, MA: UpToDate Inc. Updated December 22, 2023. Accessed March 15, 2024.