Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 319.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Lyfgenia (lovotibeglogene autotemcel)

I. Policy:
Lyfgenia (lovotibeglogene autotemcel)

II. Purpose/Objective:
To provide a policy of coverage regarding Lyfgenia (lovotibeglogene autotemcel)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
Lyfgenia (lovotibeglogene autotemcel) is a cellular gene therapy consisting of autologous CD34+ cells containing hematopoietic cells (HCs) transduced ex-vivo with a BB305 lentiviral vector encoding a modified β-globin gene. Following lovotibeglogene autotemcel infusion, the transduced CD34+ hematopoietic cells engraft in the bone marrow and differentiate to produce RBCs that combine with α-globin to produce HbAT87Q (a modified adult hemoglobin with an amino acid substitution [threonine to glutamine at position 87]), which then reduces intracellular and total hemoglobin S (HbS) levels, and sterically inhibits HbS polymerization, thereby limiting the sickling of RBCs. HbAT87Q maintains 99.9% identity to adult hemoglobin, has a similar oxygen-binding affinity and oxygen-hemoglobin dissociation curve (to wild type hemoglobin A), and can be differentiated from transfused adult hemoglobin.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

Lyfgenia (lovotibeglogene autotemcel) will be considered medically necessary for the Commercial, Exchange, and CHIP lines of business when ALL of the following criteria are met:

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years **AND**
    - Documentation of therapeutic failure, contraindication, or intolerance to hydroxyurea

  AND
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Casgevy) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

*Note to reviewer: The package insert recommends confirming that hematopoietic stem cell transplantation (HSCT) is appropriate prior to Lyfgenia since patients will be going through similar steps (mobilization, apheresis, and myeloablative) required for a HSCT. However, the clinical trials excluded patients who had a known and available HLA-matched related donor. Considering that HSCT has been available for longer and has more evidence supporting its use, it may be appropriate to require HSCT as an alternate to Lyfgenia. While it is possible for patients to have a matched unrelated donor, outcomes are best with matched related donors.

**Note to reviewer: In clinical trials, VOCs were defined as:
an event with no medically determined cause other than a vaso-occlusion, requiring a ≥ 24-hour hospital or Emergency Room (ER) observation unit visit OR
at least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment OR
4 priapism episodes that require a visit to a medical facility (with or without inpatient admission)

AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Lyfgenia (lovotibeglogene autotemcel) will be considered medically necessary for the Medicare line of business when ALL of the following criteria are met:

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years

  AND
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Casgevy) **AND**

- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
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LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

REFERENCES:

1. Lyfgenia [Prescribing Information]. Somerville MA. bluebird bio, Inc. December 2023.
2. IPD Analytics. Lyfgenia for the Treatment of Sickle Cell Disease. New Drug Approval Review. January 05, 2024. Accessed January 29, 2024. https://www.ipdanalytics.com
3. A Study Evaluating the Safety and Efficacy of bb1111 in Severe Sickle Cell Disease [Internet]. Bethesda, MD: US National Library of Medicine. c2023. Available at https://clinicaltrials.gov/study/NCT02140554?term=NCT02140554&rank=1
4. Holmberg L, Deeg, HJ, Sandmaier, B. Determining Eligibility for autologous hematopoietic cell transplantation. UpToDate [database online]. Last updated Mar 07, 2022. Available at http://www.uptodate.com/home/index.html. Accessed May 9, 2024.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 5/21/24

Revised:

Reviewed:

MA UM Committee approval: Pending