Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Lyfgenia

Professional / Institutional
Original Effective Date: August 1, 2024
Latest Review Date:
Current Effective Date: August 1, 2024

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

Indication	Dose
Sickle-Cell Disease	Lyfgenia is provided as a single dose for infusion containing a suspension of CD34+ cells in one to four infusion bags. • The minimum recommended dose of Lyfgenia is 3×10^6 CD34+ cells/kg.
- Mobilization should occur using a CXCR4 (e.g., plerixafor) in the absence of G-CSF *- Myeloablative conditioning (e.g., busulfan) should not occur until Lyfgenia (and back-up cell collection) are received. Prophylaxis for hepatic veno-occlusive disease (VOD)/hepatic sinusoidal obstruction syndrome should be considered.* *- Lyfgenia must be administered at least 48 hours after the last dose of the myeloablative conditioning.* *- Lyfgenia is for autologous use only. Before infusion, confirm that the patient's identity matches the unique patient identifiers on the Lyfgenia bag(s). Do not infuse if the information on the patient-specific label does not match the intended patient.*	

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

I. Length of Authorization

Coverage will be provided for one treatment course (1 dose of Lyfgenia) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- A single dose of Lyfgenia containing a minimum of 3.0×10^6 CD34+ cells/kg of body weight, in one or more infusion bags

B. Max Units (per dose and over time) [HCPS Unit]:

- A single dose of Lyfgenia containing a minimum of 3.0×10^6 CD34+ cells/kg of body weight, in one or more infusion bags

III. Initial Approval Criteria [1]

o Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

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

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

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

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

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

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**

Patient will not receive therapy concomitantly with any of the following:

- 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**
- Myelosuppressive iron chelators (e.g., deferiprone, etc.) for 7-days prior to mobilization, conditioning, and 6 months post-treatment; **AND**
- Disease-modifying agents (e.g., L-glutamine, voxelotor, crizanlizumab) for at least 2 months prior to mobilization; **AND**
- 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**
- Mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF); **AND**
- Erythropoietin for at least 2 months prior to mobilization; **AND**

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

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

Sickle Cell Disease [1-3] † Φ

- Patient has a confirmed diagnosis of sickle-cell disease with one of the following βS/βS or βS/β0 or βS/β+ *(Note: additional genotypes will be considered on a case-by-case basis based on disease severity)* as determined by one of the following:
  - Identification of significant quantities of HbS with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
  - Identification of biallelic *HBB* pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**
- Patient does NOT have disease with more than two α-globin gene deletions; **AND**
- Patient experienced at least two vaso-occlusive events/crises (VOE/VOC)* in the previous 12 months *(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.*

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

† FDA Approved Indication(s); ǂ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,3]

- Coverage cannot be renewed.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CLINICAL RATIONALE

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

HCPCS:

- J3590 – Unclassified biologics

NDC:

- Lyfgenia is supplied in one to four infusion bags containing a frozen suspension of genetically modified autologous cells, enriched for CD34+ cells, 20 mL infusion bag, overwrap, and metal cassette: 73554- 1111-xx

REFERENCES

1. Lyfgenia [package insert]. Somerville, MA; Bluebird Bio, Inc., December 2023. Accessed December 2023.
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3. Bender MA, Carlberg K. Sickle Cell Disease. 2003 Sep 15 [Updated 2022 Nov 17]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1377/.
4. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA. 2014 Sep 10;312(10):1033-48.
5. Tisdale JF, Pierciey FJ, Bonner M, et al. (2020) Safety and feasibility of hematopoietic progenitor stem cell collection by mobilization with plerixafor followed by apheresis vs bone marrow harvest in patients with sickle cell disease in the multi-center HGB-206 trial. Am J Hematol E239–E242. https://doi.org/10.1002/ajh.25867.
6. Palmer J, McCune JS, Perales M-A, et al. (2016) Personalizing Busulfan-Based Conditioning: Considerations from the American Society for Blood and Marrow

Transplantation Practice Guidelines Committee. Biol Blood Marrow Transplant 1915–1925. https://doi.org/10.1016/j.bbmt.2016.07.013

7. Brunson A, Keegan THM, Bang H, et al. (2017) Increased risk of leukemia among sickle cell disease patients in California. Blood 130:1597–1599. doi: 10.1182/blood-2017-05-783233.
8. Seminog OO, Ogunlaja OI, Yeates D, Goldacre MJ (2016) Risk of individual malignant neoplasms in patients with sickle cell disease: English national record linkage study. J R Soc Med 109:303–309. doi: 10.1177/0141076816651037.

REVISIONS	
Posted 07-01-2024 Effective 08-01-2024	New medical policy added to the bcbsks.com web site. Policy maintained by Prime Therapeutics LLC.