LYFGENIA™ (lovotibeglogene autotemcel)
Prior Authorization Checklist

Considerations for Completing a LYFGENIA PA Request Form for Your Patients

- Review the PA guidelines on the insurer's website or contact the insurer's provider relations for process information, including forms and contacts. In the absence of a published coverage policy, PA submissions might be reviewed on a case-by-case basis.
- When a PA is required, the prescribing healthcare provider should submit it directly to the payer and/or specialty pharmacy, if applicable.
- Clarify with the payer if one PA will cover LYFGENIA and all of the ancillary services for treatment or if/when additional requests will be necessary. Ensure timing & duration of prior authorization(s) is appropriate for treatment scheduling & anticipated journey length. This may include pre-treatment regimen, screening, cell collection(s), conditioning, post-infusion stay, etc.
- Provide complete and accurate information on any required PA forms and attach any requested supplemental information.
- Align patient eligibility with payer criteria, including any applicable codes such as ICD-10-CM diagnosis codes, HCPCS product code, NDC, and others.
- Identify preferred procurement methodology (e.g., specialty pharmacy or specialty distributor) and authorized SP or SD. If using an SP, it may be helpful to indicate name of SP in the PA request.

Available Access Support Resources:

- LYFGENIA Billing & Coding Guide
- LYFGENIA full Prescribing Information
- Sample Letter of Medical Necessity
- Sample Letter of Appeal for Denial of Coverage
- PA assistance offered by **my bluebird support**, if enrolled

For questions regarding individual payer-level coverage of LYFGENIA, reach out to your local bluebird bio Account Executive.

Important Safety Information

WARNING: HEMATOLOGIC MALIGNANCY

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.

PLEASE NOTE: This Prior Authorization Checklist is intended to help healthcare professionals understand key prior authorization steps & considerations for LYFGENIA and its related services when using LYFGENIA for its FDA-approved use. The information provided in this document is for informational and reference purposes only. The information provided in this document should not be construed as medical or legal advice. All medical decisions should be made at the discretion of the provider. Healthcare professionals should exercise independent clinical judgment when submitting prior authorizations. Coding and coverage policies can change, often without warning. The information in this document is not a guarantee of coverage or reimbursement for any product or service. Please contact your patient's health plan or work with **my bluebird support** for additional resources regarding prior authorization for a specific plan.

HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; NDC=National Drug Code; SD = specialty distributor; SP = specialty pharmacy; PA=prior authorization.

Please see additional Important Safety Information on pages 3-5 and full Prescribing Information, including **Boxed WARNING** for LYFGENIA

Key Clinical Criteria to Consider When Drafting a LYFGENIA PA Request Form

The following criteria (not exhaustive) are commonly found in payer prior authorization criteria and may be required to support your decision to treat with LYFGENIA. Payers may vary on the required criteria for authorization, and some may establish prior authorizations based on clinical trial inclusion and exclusion criteria, which may require documentation or physician attestation for specific diagnostic testing and clinical history. Healthcare professionals should confirm with each payer prior to submission.

☑ Patient diagnosis information:

- Current age (12 or older)
- Patient's diagnosis and current condition
- Genetic testing information (e.g., genotype, fewer than two α-globin deletions)
- History of vaso-occlusive events

☑ Intended treatment information:

- Prescription by or in consultation with a hematologist, stem cell transplant physician, and/or expert in sickle cell disease
- Projected date of apheresis and/or pre-treatment initiation

☑ Potential assessments for specific coverage criteria:

- Prior treatments and responses to those treatments (including history of hydroxyurea usage at any point in the past, lack of prior gene therapy for SCD)
- Appropriateness for HSCT
- Lack of a clinically suitable, willing, fully matched sibling donor
- Performance status measures (Karnofsky for ≥ 16 years of age & Lansky for ≤ 16 years of age)
- Screening for infectious diseases, specifically HIV-1/2 (may also include hepatitis B/C, HTLV-1/2)

☑ Documents that outline a patient's medical necessity, including but not limited to:

- A Letter of Medical Necessity
- Relevant medical history documentation
- Prescribing physician notes
- LYFGENIA full Prescribing Information
- All of the documents listed or referenced in the payer's PA request form

For PA questions or appeals support, talk with a Patient Navigator at my bluebird support by calling 1-833-888-6378, emailing mybluebirdsupport@bluebirdbio.com, or visiting www.mybluebirdsupport.com**.**

Indication

LYFGENIA is indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events.

Limitations of Use

Following treatment with LYFGENIA, patients with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell transfusions. LYFGENIA has not been studied in patients with more than two α-globin gene deletions.

Important Safety Information

Boxed WARNING: HEMATOLOGIC MALIGNANCY

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.

Hematologic Malignancy

Hematologic malignancy has occurred in patients treated with LYFGENIA (Study 1, Group A). At the time of initial product approval, two patients treated with an earlier version of LYFGENIA using a different manufacturing process and transplant procedure (Study 1, Group A) developed acute myeloid leukemia (AML). One patient with α-thalassemia trait (Study 1, Group C) has been diagnosed with myelodysplastic syndrome (MDS).

The additional hematopoietic stress associated with mobilization, conditioning, and infusion of LYFGENIA, including the need to regenerate the hematopoietic system, may increase the risk of a hematologic malignancy. Patients with sickle cell disease have an increased risk of hematologic malignancy as compared to the general population.

Patients treated with LYFGENIA may develop hematologic malignancies and should have lifelong monitoring. Monitor for hematologic malignancies with a complete blood count (with differential) at least every 6 months for at least 15 years after treatment with LYFGENIA, and integration site analysis at Months 6, 12, and as warranted.

In the event that a malignancy occurs, contact bluebird bio at 1-833-999-6378 for reporting and to obtain instructions on collection of samples for testing.

Post-Marketing Long Term Follow-Up Study: Patients who intend to receive treatment with LYFGENIA are encouraged to enroll in the study, as available, to assess the long-term safety of LYFGENIA and the risk of malignancies occurring after treatment with LYFGENIA by calling bluebird bio at 1-833-999-6378. The study includes monitoring (at pre-specified intervals) for clonal expansion.

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with LYFGENIA. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia. Two patients (4%) required more than 100 days post treatment with LYFGENIA to achieve platelet engraftment.

Patients should be made aware of the risk of bleeding until platelet recovery has been achieved. Monitor patients for thrombocytopenia and bleeding according to standard guidelines. Conduct frequent platelet counts until platelet engraftment and platelet recovery are achieved. Perform blood cell count determination and other appropriate testing whenever clinical symptoms suggestive of bleeding arise.

Please see additional Important Safety Information on pages 3-5 and full Prescribing Information, including **Boxed WARNING** for LYFGENIA

Important Safety Information (cont'd)

Neutrophil Engraftment Failure

There is a potential risk of neutrophil engraftment failure after treatment with LYFGENIA. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) $\geq 0.5 \times 10^9$ cells/L obtained on different days by Day 43 after infusion of LYFGENIA. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with LYFGENIA, provide rescue treatment with the back-up collection of CD34+ cells.

Insertional Oncogenesis

There is a potential risk of lentiviral vector-mediated insertional oncogenesis after treatment with LYFGENIA.

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of LYFGENIA. The dimethyl sulfoxide (DMSO) or dextran 40 in LYFGENIA may cause hypersensitivity reactions, including anaphylaxis.

Anti-retroviral Use

Patients should not take prophylactic HIV anti-retroviral medications for 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. If a patient is taking anti-retrovirals for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization and apheresis of CD34+ cells.

Hydroxyurea Use

Patients should not take hydroxyurea for at least 2 months prior to mobilization and until all cycles of apheresis are completed. If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning.

Iron Chelation

Drug-drug interactions between iron chelators and the mobilization process and myeloablative conditioning agent must be considered. Iron chelators should be discontinued at least 7 days prior to initiation of mobilization or conditioning. Do not administer myelosuppressive iron chelators (e.g., deferiprone) for 6 months post-treatment with LYFGENIA. Non-myelosuppressive iron chelation should be restarted no sooner than 3 months after LYFGENIA infusion. Phlebotomy can be used in lieu of iron chelation, when appropriate.

Interference with PCR-based Testing

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.

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Important Safety Information (cont'd)

Adverse Reactions

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

Three patients died during LYFGENIA clinical trials; one from sudden cardiac death due to underlying disease and two from acute myeloid leukemia who were treated with an earlier version of LYFGENIA using a different manufacturing process and transplant procedure (Study 1, Group A).

Pregnancy/Lactation

Advise patients of the risks associated with myeloablative conditioning agents, including on pregnancy and fertility.

LYFGENIA should not be administered to women who are pregnant, and pregnancy after LYFGENIA infusion should be discussed with the treating physician.

LYFGENIA is not recommended for women who are breastfeeding, and breastfeeding after LYFGENIA infusion should be discussed with the treating physician.

Females and Males of Reproductive Potential

A negative serum pregnancy test must be confirmed prior to the start of mobilization and re-confirmed prior to conditioning procedures and before LYFGENIA administration.

Women of childbearing potential and men capable of fathering a child should use an effective method of contraception (intra-uterine device or combination of hormonal and barrier contraception) from start of mobilization through at least 6 months after administration of LYFGENIA.

Advise patients of the options for fertility preservation.

Please see full Prescribing Information, including **Boxed WARNING** for LYFGENIA.