lyfgenia™
(lovotibeglogene autotemcel)
suspension for IV infusion

BILLING & CODING GUIDE

A Resource for Coding, Billing, and Reimbursement Information for LYFGENIA™

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.

PLEASE NOTE:
This Billing & Coding Guide is intended to help healthcare professionals understand key billing and coding considerations for LYFGENIA and its related services when using LYFGENIA for its FDA-approved use.

The information provided in this guide is for informational and reference purposes only. The information provided in this guide 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 selecting codes and submitting claims to accurately reflect the services rendered to individual patients. Coding and coverage policies can change, often without warning. It is the responsibility of the provider to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure and to submit accurate claims. The information in this guide 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 coding for a specific plan.

For reimbursement 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 mybluebirdsupport.com.

Please see Important Safety Information on pages 17-19 and full Prescribing Information, including **Boxed WARNING**.

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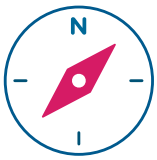
Please see Important Safety Information on pages 17-19 and full Prescribing Information, including **Boxed WARNING**.

We're committed to supporting your patients

my bluebird support is here to help your patients and their caregivers navigate access to bluebird bio gene therapies with resources designed to support their unique treatment paths. Examples of support range from helping to identify Qualified Treatment Center options for consultation to understanding their insurance benefits and the process for prior authorization.

With **my bluebird support**, your patient or their loved ones have a dedicated copilot to help at any point in the treatment journey. Their Patient Navigator will be available to help navigate, educate, and elevate their experience.



Navigate

Guiding your patient and their loved ones through the treatment journey while connecting them with helpful people and organizations

Educate

Sharing important resources about gene therapy and the benefits information your patient needs to access treatment with insurance

Elevate

Collaborating with your patient to help reach personal health goals

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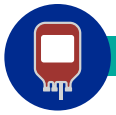
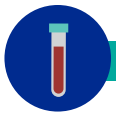
6 Important Steps to Treatment With LYFGENIA



STEP 1: Pre-Treatment

Pre-treatment involves coordinating with an individual's care team and confirming that autologous HSC transplantation is a good fit for the patient prior to mobilization and apheresis. Patients are prepared for mobilization with at least 2 cycles of scheduled transfusions (1 each month), with erythrocytapheresis being preferred.



STEP 2: Stem Cell Collection (~7+ days)[1]

Patients are required to undergo HSC mobilization* followed by apheresis to obtain CD34+ cells for LYFGENIA manufacturing. One mobilization cycle typically includes 2 consecutive days, with plerixafor mobilization and subsequent apheresis occurring on each of these days. In clinical studies, most patients collected the minimum number of CD34+ cells to manufacture LYFGENIA with 1 or 2 cycles of mobilization and apheresis, but additional cycles may be required.†

STEP 3: Production (70-105 days)[1]

The patient's cells are sent to a manufacturing site to produce LYFGENIA. LYFGENIA is then supplied in 1 to 4 infusion bags.

STEP 4: Conditioning and Washout (~6+ Days)[1]

Full myeloablative conditioning (4 days) is followed by a washout period of at least 48 hours prior to infusion of LYFGENIA.

STEP 5: Infusion (~30 Minutes per Bag)[1]

Each infusion bag of LYFGENIA is administered via intravenous infusion over a period of less than 30 minutes per bag. LYFGENIA is supplied in 1 or more infusion bags.

STEP 6: Post-Infusion Monitoring (21-42 days)[1]

Patients should be prepared to remain hospitalized and monitored for an additional 3-6 weeks after infusion.

After treatment with LYFGENIA, patients require long-term monitoring[1]

Post-Treatment: Long-Term Follow-Up

Hematologic malignancy has occurred in patients treated with LYFGENIA; therefore, patients should be monitored lifelong. 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.

If a malignancy is detected, contact bluebird bio at 1-833-999-NEST (6378) for reporting and to obtain instructions on collection of samples for testing.

*There is a risk of sickle cell crisis during stem cell mobilization.[1]

†After manufacture, if the minimum dose of 3.0×10^6 CD34+ cells/kg is not met, the patient may undergo additional cycles of mobilization and apheresis, separated by at least 14 days, in order to obtain more cells for additional manufacture. Multiple drug product lots may be administered to comprise the final dose.[1]

Time frames are approximate and may vary per patient.

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Access & Reimbursement Considerations

PLANNED READMISSION

If the initial cell collection is conducted during an inpatient hospital admission and patient is discharged prior to subsequent admission for administration of LYFGENIA, it may be necessary to confirm with each payer that the subsequent admission is a planned admission for gene therapy administration.

LYFGENIA

Payers 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.

PRIOR AUTHORIZATION CONSIDERATIONS

Testing results will be required as part of the prior authorization request. Payers may require the following tests, eg, HIV-1/2, hepatitis B core antibody, hepatitis B surface antigen, hepatitis C virus antibody, HTLV-1/2.

In addition, before collection of cells for manufacturing, screening for infectious diseases, specifically HIV-1/2 in accordance with clinical guidelines will be required. Payers may vary on the required testing, imaging, and biopsies for authorization; healthcare professionals should confirm with each payer prior to submission.

One mobilization cycle typically includes 2 consecutive days, with plerixafor mobilization and subsequent apheresis occurring on each of these days. The patient may undergo additional cycles of mobilization and apheresis, separated by at least 14 days, in order to obtain more cells for additional manufacture to meet minimum cell dose (3.0×10^6 CD34+ cells/kg). A collection of CD34+ cells of $\geq16.5\times10^6$ CD34+ cells/kg is required for manufacturing and back-up, including $\geq1.5\times10^6$ CD34+ cells/kg for back up. The back up collection may be needed for rescue treatment if there is: 1) compromise of hematopoietic stem cells or LYFGENIA before infusion, 2) primary engraftment failure, or 3) loss of engraftment after infusion with LYFGENIA.

Payers may require multiple prior authorizations for coverage of both LYFGENIA and all other ancillary services to be provided for treatment.

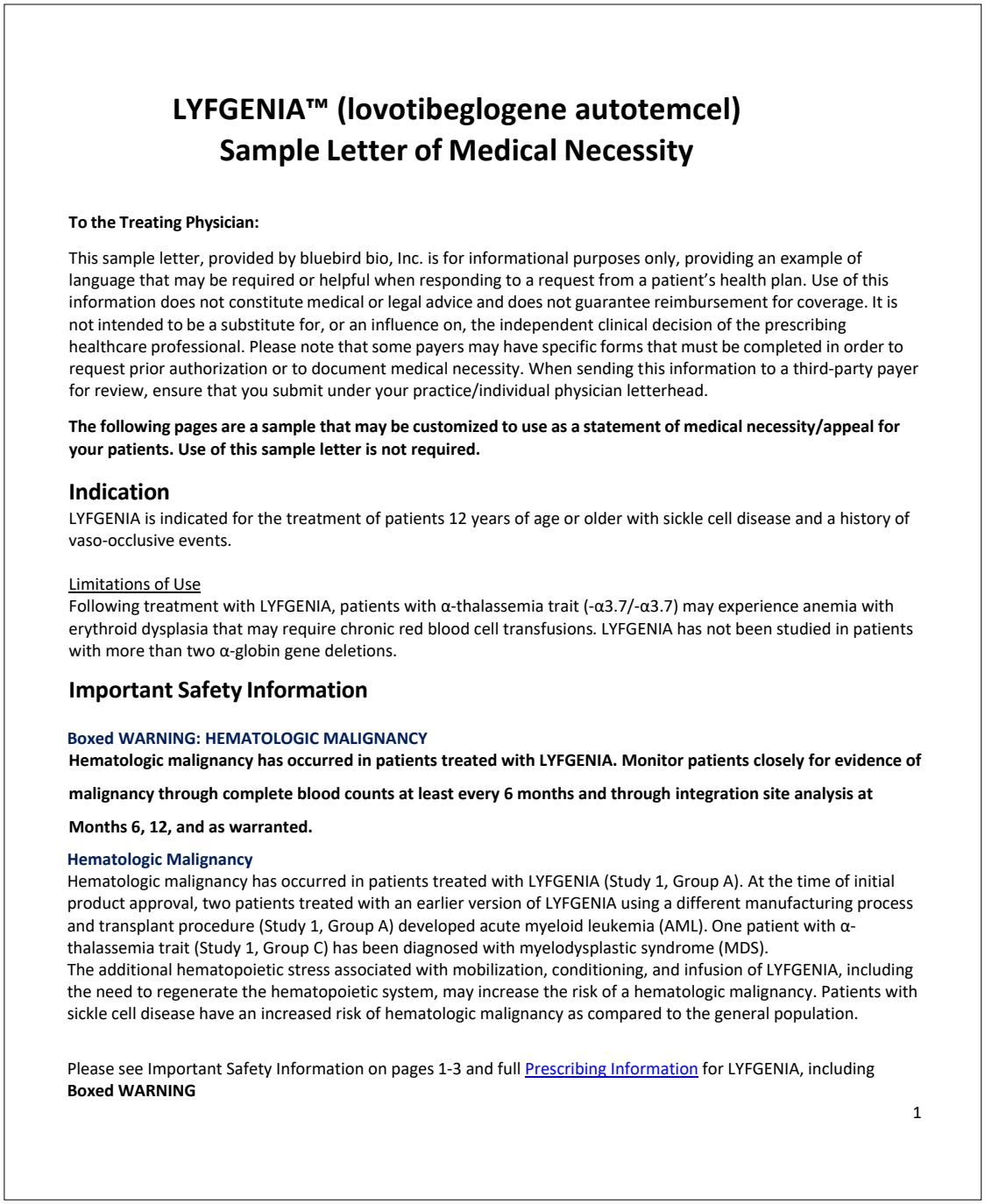
POST TESTING

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.

Sample Letter of Medical Necessity

LYFGENIA

Clicking on the image below will open the Sample Letter of Medical Necessity in a new window.



LYFGENIA™ (lovotibeglogene autotemcel)
Sample Letter of Medical Necessity

To the Treating Physician:

This sample letter, provided by bluebird bio, Inc. is for informational purposes only, providing an example of language that may be required or helpful when responding to a request from a patient's health plan. Use of this information does not constitute medical or legal advice and does not guarantee reimbursement for coverage. It is not intended to be a substitute for, or an influence on, the independent clinical decision of the prescribing healthcare professional. Please note that some payers may have specific forms that must be completed in order to request prior authorization or to document medical necessity. When sending this information to a third-party payer for review, ensure that you submit under your practice/individual physician letterhead.

The following pages are a sample that may be customized to use as a statement of medical necessity/appeal for your patients. Use of this sample letter is not required.

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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.

Please see Important Safety Information on pages 1-3 and full Prescribing Information for LYFGENIA, including **Boxed WARNING**

1

Additional support for medical necessity may be required for new patients. Resources available through **my bluebird support** include a Letter of Medical Necessity sample, which can be downloaded and adapted to reflect your patient's prior treatment journey and clinical rationale for treatment with LYFGENIA.

lyfgenia™ (lovotibeglogene autotemcel) suspension for IV infusion

Diagnosis Coding

ICD-10-CM CODE	ICD-10-CM CODE DESCRIPTOR
D57.02	Hb-SS disease with splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.1	Sickle-cell disease without crisis
D57.20	Sickle-cell/Hb-C disease without crisis
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement
D57.40	Sickle-cell thalassemia without crisis
D57.412	Sickle-cell thalassemia, unspecified, with splenic sequestration
D57.413	Sickle-cell thalassemia, unspecified, with cerebral vascular involvement
D57.42	Sickle-cell thalassemia beta zero without crisis
D57.432	Sickle-cell thalassemia beta zero with splenic sequestration
D57.433	Sickle-cell thalassemia beta zero with cerebral vascular involvement
D57.44	Sickle-cell thalassemia beta plus without crisis
D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
D57.453	Sickle-cell thalassemia beta plus with cerebral vascular involvement

Cell Collection Coding

Mobilization and Apheresis

More than one collection session may be required to acquire the minimum dose needed for transplanting. Plerixafor should be dosed and documented based on Prescribing Information.

When apheresis is conducted during a hospital inpatient admission, the following ICD-10-PCS codes may apply:

ICD-10-PCS CODE[3]	DESCRIPTION
6A550ZV	Pheresis of Hematopoietic Stem Cells, Single
6A551ZV	Pheresis of Hematopoietic Stem Cells, Multiple

Although commonly applied for hospital outpatient mobilization and apheresis, the following CPT procedure codes may also be applicable for inpatient processes as well, based on payer-specific requirements:

CPT® CODE[4]	DESCRIPTION
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
38206*	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous

*Each code may be recorded only once per day, regardless of the quantity of bone marrow/stem cells manipulated.

HCPCS CODE[5]	DESCRIPTION
J2562	Injection, plerixafor, 1 mg

Revenue codes are provided for informational purposes only and may vary by hospital:

REVENUE CODE[6,10]	DESCRIPTION
0250	Pharmacy
0636	Drugs requiring detailed coding
0871	Cell/Gene Therapy Cell Collection

Payers may vary on the required coding to appropriately reflect mobilization and apheresis for the collection of cells. Providers should confirm with each payer prior to submitting claims. If collecting cells on behalf of another institution, please confirm coding requirements with that institution as it may differ.

Conditioning Regimen Coding

Busulfan was used for conditioning in clinical trials prior to administration of LYFGENIA.[1]

Due to high gonadotoxicity associated with conditioning agents, refer to the Fertility Preservation section of this guide.

ICD-10-PCS CODE[3]	DESCRIPTION
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach

CPT CODE[4]	DESCRIPTION
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour

HCPCS CODE[5]	DESCRIPTION
J0594	Injection, busulfan, 1 mg

REVENUE CODE[6]	DESCRIPTION
0250	General Pharmacy
0251	General Pharmacy
0260	General IV Therapy
0636	Drug Requiring Detailed Coding

10-digit NDC[7]	DESCRIPTION
Varies	Several manufacturers produce busulfan. Therefore, providers should reference and apply the appropriate NDC code, if required by payers.

Payers may vary on their requirements for detailed coding on the delivery of any conditioning regimen associated with subsequent LYFGENIA administration. These requirements can vary based on the setting of care as well as for the patient's specific plan. Providers should confirm requirements with individual payers.

Administration Coding

HCPCS CODES[5]	DESCRIPTION
J3490	Unclassified drugs
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

ICD-10-PCS codes are applied to define specific procedures during a hospital inpatient admission. LYFGENIA-specific ICD-10-PCS codes have been created and became effective 10/01/2023.

ICD-10-PCS CODES[3]	DESCRIPTION
XW133H9†	Transfusion of Lovotibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 9
XW143H9†	Transfusion of Lovotibeglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 9

MS-DRG alignment—Medicare only. Applying the appropriate ICD-10-PCS code and ICD-10-CM diagnosis codes will align inpatient admissions to MS-DRG 016 or 017 for payment. It is the provider's responsibility to contact each payer for payer-specific coding requirements before submitting any claims.

MS-DRG[12]	DESCRIPTION
016	Autologous bone marrow transplant with cc/mcc
017	Autologous bone marrow transplant without cc/mcc

CPT CODE[4]	DESCRIPTION
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour

Administration Coding (cont'd)

REVENUE CODES[6,10]	DESCRIPTION
0872	Cell/Gene Therapy Specialized Biologic Processing and Storage—Prior to Transport
0873	Cell/Gene Therapy Storage and Processing after Receipt of Cells from Manufacturer
0874	Cell/Gene Therapy Infusion of Modified Cells
0892	Special Processed Drugs–FDA Approved Gene Therapy—Charges for Modified Gene Therapy

Many payers require that the LYFGENIA NDC code be reported on the claim using an 11-digit format (5-4-2) to comply with the electronic claims transaction provisions of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).[8]

10-DIGIT NDC[7]	11-DIGIT NDC[8]	CLAIM REPORTING REQUIREMENTS[9]
73554-1111-1	73554-1111-01	N473554111101UN

One-Page Coding Summary

HOSPITAL REVENUE CODES

One or more of the following revenue codes may apply to services associated with LYFGENIA. Each payer's acceptance of and associated claim documentation for these codes should be verified.

REVENUE CODES[6]	DESCRIPTION
0871	Cell/Gene Therapy Cell Collection
0872	Cell/Gene Therapy Specialized Biologic Processing and Storage—Prior to Transport
0873	Cell/Gene Therapy Storage and Processing after Receipt of Cells from Manufacturer
0874	Cell/Gene Therapy Infusion of Modified Cells
0892	Special Processed Drugs—FDA Approved Gene Therapy—Charges for Modified gene therapy

NDC INFORMATION

Payers may require that either a 10-digit or 11-digit format NDC code be documented on claims for LYFGENIA. The table below outlines the format options, including potential requirement of an NDC qualifier (N4).

10-DIGIT NDC[7]	11-DIGIT NDC[8]	DESCRIPTION
73554-1111-1	73554-1111-01	N473554 111101UN

VALUE CODE

Select payers may require a Value Code to document the invoice price for LYFGENIA.

VALUE CODE[10]	DESCRIPTION
87	Invoice/acquisition cost of modified biologics. For use with Revenue Category 0892

CPT® CODES

Currently, there is no gene therapy-specific infusion code. Therefore, the following CPT® codes may be applicable for LYFGENIA administration.

CPT® CODE[4]	DESCRIPTION
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug

HCPCS LEVEL II PRODUCT CODES

LYFGENIA does not currently have a unique HCPCS code. Until a unique HCPCS code is assigned by CMS, LYFGENIA may be reported by using one of the following unclassified HCPCS codes per payer requirements.

HCPCS CODES[5]	DESCRIPTION
J3490	Unclassified drugs
J3590	Unclassified biologics
C9399*	Unclassified drugs or biologicals

ICD-10-PCS INPATIENT PROCEDURE CODES

LYFGENIA-specific ICD-10-PCS code became effective 10/01/2023.

ICD-10-PCS CODES[3]	DESCRIPTION
XW133H9	Transfusion of Lovotibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 9
XW143H9	Transfusion of Lovotibeglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 9

In all cases, providers should verify claims coding requirements by payer.

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Fertility Preservation

The myeloablative conditioning regimen associated with LYFGENIA treatment can increase risk of infertility. Therefore, consideration may be appropriate for pursuing fertility preservation.

The American Society of Clinical Oncology (ASCO)[10] and the National Comprehensive Cancer Network (NCCN)[11] have guidance on the need for fertility preservation in patients receiving gonadotoxic therapy. This guidance may provide support in discussions with payers when pursuing coverage of preservation services. These guidelines may be found at the following links:

These links will take you to sites that are outside the control of bluebird bio, Inc. Links are provided for informational purposes only. We do not make or imply any endorsement of external websites.

https://ascopubs.org/doi/full/10.1200/JCO.2018.78.1914

https://nccn.org

Fertility preservation for iatrogenic infertility may be covered by payers. Providers should confirm covered benefits and can reference the pending treatment with myeloblative conditioning agent(s) as a conditioning regimen for subsequent LYFGENIA treatment.

Covered services may include the following procedures when provided by or under the care or supervision of a physician:

- Collection of sperm
- Cryo-preservation of sperm
- Ovarian stimulation, retrieval of eggs and fertilization
- Oocyte cryo-preservation
- Embryo cryo-preservation

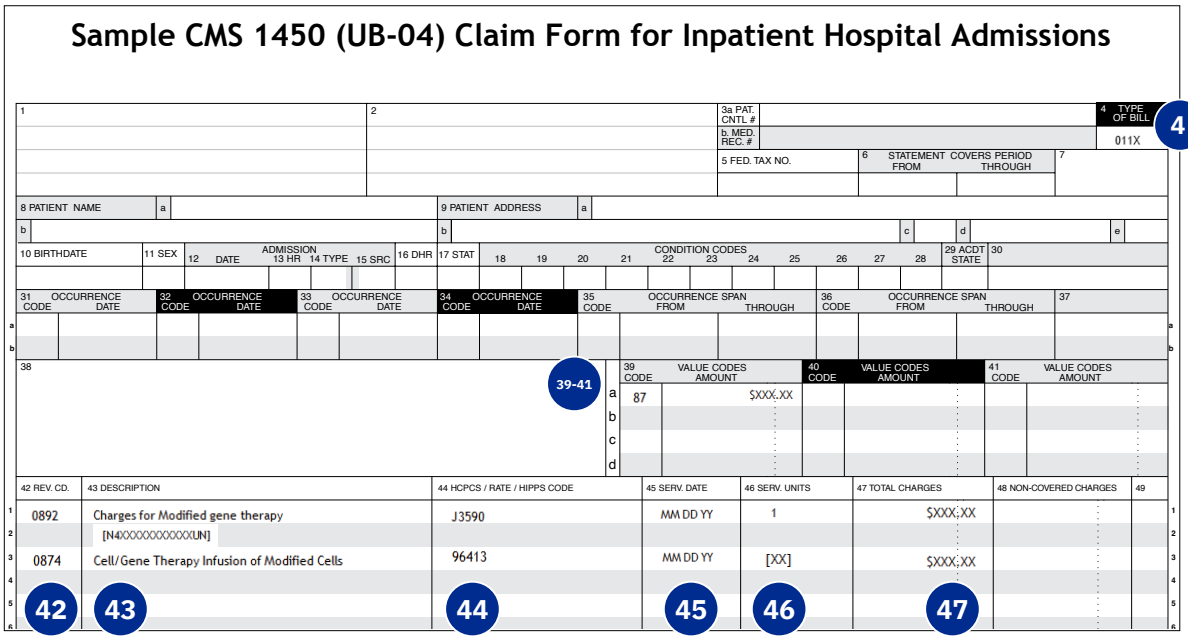
Fertility Preservation (cont'd)

CPT CODE[4]	CPT CODE DESCRIPTOR
58321	Artificial insemination; intra-cervical
58970	Follicle puncture for oocyte retrieval, any method
89250	Culture of oocyte(s)/embryo(s), less than 4 days
89251	Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
89253	Assisted embryo hatching, microtechniques (any method)
89254	Oocyte identification from follicular fluid
89258	Cryopreservation; embryo(s)
89259	Cryopreservation; sperm
89260	Sperm isolation; simple prep (eg, sperm wash and swim-up) for insemination or diagnosis with semen analysis
89261	Sperm isolation; complex prep (eg, Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
89264	Sperm identification from testis tissue, fresh or cryopreserved
89268	Insemination of oocytes
89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
89320	Semen analysis; volume, count, motility, and differential
89337	Cryopreservation, mature oocyte(s)
89342	Storage (per year); embryo(s)
89343	Storage (per year); sperm/semen
89346	Storage (per year); oocyte(s)

Payers may vary on their requirements for detailed coding on the delivery of any fertility preservation regimen associated with subsequent LYFGENIA administration. These requirements can vary based on the setting of care as well as for the patient's specific plan. Providers should confirm requirements with individual payers.

Sample CMS 1450 (UB-04) Claim Form for Inpatient Hospital Admissions

Clicking on the image below will open the Sample Claims Form in a new window.



4 TYPE OF BILL[11]

Enter the appropriate type of bill code. For example, 011X for an inpatient hospital facility.

39-41 VALUE CODES[10]

Payers may require a Value Code to document acquisition cost for LYFGENIA. Enter the appropriate value code(s). For example, Value Code 87 is defined as: Invoice/acquisition cost of modified biologics. For use with Revenue Category 0892

42 REVENUE CODE[6,10]

Enter the appropriate revenue code for each reported line. For example, 0892 Charges for Gene Therapy.

43 DESCRIPTION

Enter the 11-digit NDC[8] with an appended N4 qualifier (electronic equivalent Loop 2410, LIN02). Enter the appropriate description for corresponding revenue codes.[6,10]

44 HCPCS[5]

Enter the appropriate HCPCS Level II code, along with the applicable modifier. For example, J3590 or J3490. In lieu of a gene therapy-specific code for the infusion, the 96413 CPT[4] code may be required.

45 SERVICE DATE

Enter the corresponding date(s) of service.

46 SERVICE UNITS

Enter appropriate units of service. For unclassified codes, such as J3490 and J3590, 1 unit of service may be required.

47 TOTAL CHARGES

Enter total charges for each reported line.

Sample forms are for informational purposes only. The accurate completion of a claim is the responsibility of the healthcare provider. There is no guarantee regarding reimbursement for any service or item. Since requirements may vary, providers should refer to specific payer policy.

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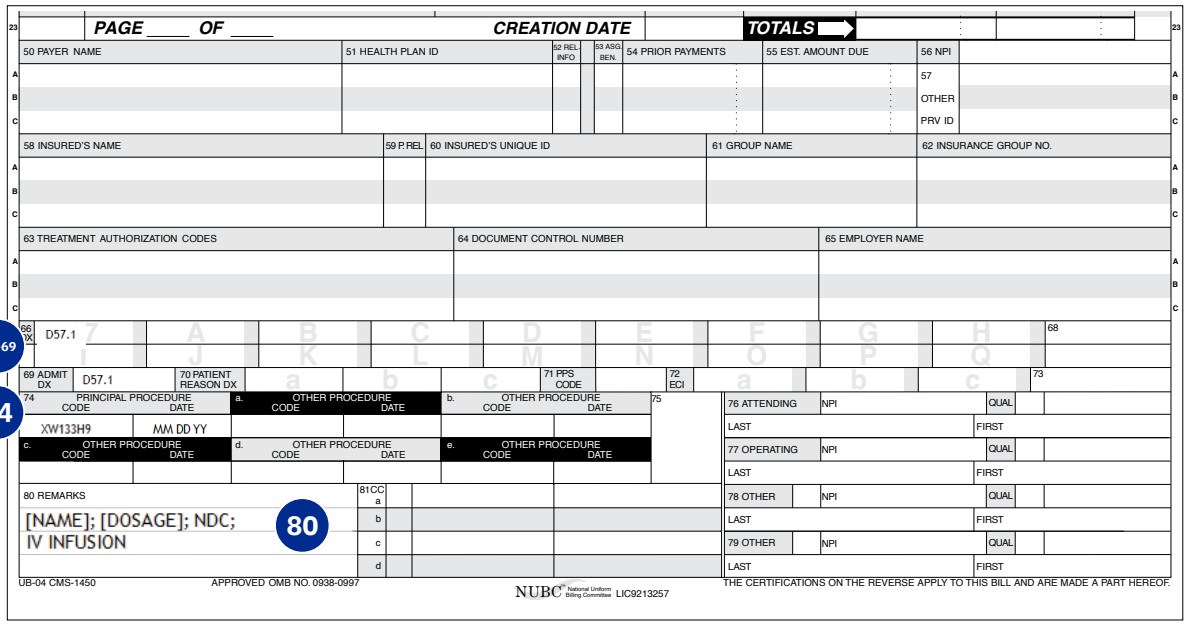

PAGE ____ OF ____ CREATION DATE TOTALS

50 PAYER NAME | 51 HEALTH PLAN ID | 52 REL. INFO | 53 ASG. BEN. | 54 PRIOR PAYMENTS | 55 EST. AMOUNT DUE | 56 NPI | 57 OTHER PRV ID

58 INSURED'S NAME | 59 P REL | 60 INSURED'S UNIQUE ID | 61 GROUP NAME | 62 INSURANCE GROUP NO.

63 TREATMENT AUTHORIZATION CODES | 64 DOCUMENT CONTROL NUMBER | 65 EMPLOYER NAME

66 ICD IX | D57.1 | 68

69 ADMIT DX | D57.1 | 70 PATIENT REASON DX | 71 PPS CODE | 72 ECI | 73

74 PRINCIPAL PROCEDURE CODE DATE: XW133H9 MM DD YY | a. OTHER PROCEDURE CODE DATE | b. OTHER PROCEDURE CODE DATE | c. OTHER PROCEDURE CODE DATE | d. OTHER PROCEDURE CODE DATE | e. OTHER PROCEDURE CODE DATE | 75

76 ATTENDING NPI QUAL LAST FIRST

77 OPERATING NPI QUAL LAST FIRST

78 OTHER NPI QUAL LAST FIRST

79 OTHER NPI QUAL LAST FIRST

80 REMARKS: [NAME]; [DOSAGE]; NDC; IV INFUSION

81CC a b c d

UB-04 CMS-1450 APPROVED OMB NO. 0938-0997 NUBC National Uniform Billing Committee LIC9213257 THE CERTIFICATIONS ON THE REVERSE APPLY TO THIS BILL AND ARE MADE A PART HEREOF.

66-69 **DIAGNOSIS CODE(S)[2]**

Enter the appropriate ICD-10-CM diagnosis code(s). For example, D57.1 Sickle-cell disease without crisis.

74 **PRINCIPAL PROCEDURE[3]**

Enter relevant ICD-10-PCS procedure code(s) with corresponding date(s) of service. For example, XW133H9: Transfusion of Lovotibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach.

80 **REMARKS**

Enter relevant product information when reporting a miscellaneous HCPCS code. For example, drug name, dosage, NDC number and route of administration, and bluebird Patient ID.

Sample forms are for informational purposes only. The accurate completion of a claim is the responsibility of the healthcare provider. There is no guarantee regarding reimbursement for any service or item. Since requirements may vary, providers should refer to specific payer policy.

For reimbursement 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 mybluebirdsupport.com.

lyfgenia™ (lovotibeglogene autotemcel) suspension for IV infusion

Please see Important Safety Information on pages 17-19 and full Prescribing Information, including **Boxed WARNING**.

Indication and Important Safety Information

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.

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) ≥ 0.5×10^9 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.

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).

Important Safety Information (cont'd)

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.

References

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12. Centers for Medicare & Medicaid Services. MS-DRG Classifications and Software. FY 2024 - Version 41. Accessed October 2023 at https://www.cms.gov/medicare/payment/prospective-payment-systems/acute-inpatient-pps/ms-drg-classifications-and-software. Open Zip folder ICD-10 MS-DRG Definitions Manual Files V41, then open text document mdcs_00_07.

Links to external third-party websites are outside the control of bluebird bio, Inc. and are provided for informational purposes only. bluebird bio does not make or imply any endorsement of external websites.

lyfgenia™ (lovotibeglogene autotemcel) suspension for IV infusion

bluebirdbio®

Sample CMS 1450 (UB-04) Claim Form for Inpatient Hospital Admissions

This sample form is provided by bluebird bio, Inc. for informational purposes only and is not intended to be directive or construed as medical or legal advice. Healthcare providers should exercise independent clinical judgment when selecting codes and submitting claims. The accurate completion of a claim is the responsibility of the healthcare provider. There is no guarantee regarding reimbursement for any service or item. Since requirements may vary, providers should refer to specific payer policies.

Please see Important Safety Information on pages 17-19 in the LYFGENIA™ (lovotibeglogene autotemcel) Billing and Coding Guide and full Prescribing Information, **including Boxed WARNING.**

Field 4: TYPE OF BILL[11]
Enter the appropriate type of bill code. For example, 011X for an inpatient hospital facility.

PAT. TL. #		4 TYPE OF BILL
MED. C. #		011X
ED. TAX NO.		7

10 BIRTHDATE	11 SEX	12 ADMISSION DATE	13 HR	14 TYPE	15 SRC	16 DHR	17 STAT	18	19	20	21	22	23	24	25	26	27	28	29 ACDT STATE	30

31 OCCURRENCE CODE	DATE	32 OCCURRENCE CODE	DATE	33 OCCURRENCE CODE	DATE	34 OCCURRENCE CODE	DATE	35 OCCURRENCE SPAN CODE	FROM	THROUGH	36 OCCURRENCE SPAN CODE	FROM	THROUGH	37
a														a
b														b

Fields 39-41: VALUE CODES[10]
Payers may require a Value Code to document acquisition cost for LYFGENIA. Enter the appropriate value code(s). For example, Value Code 87 is defined as: Invoice/acquisition cost of modified biologics. For use with Revenue Category 0892.

38		39 VALUE CODES CODE	AMOUNT	40 VALUE CODES CODE	AMOUNT	41 VALUE CODES CODE	AMOUNT
	a	87	$XXX.XX				
	b						
	c						
	d						

	42 REV. CD.	43 DESCRIPTION	44 HCPCS / RATE / HIPPS CODE	45 SERV. DATE	46 SERV. UNITS	47 TOTAL CHARGES	48 NON-COVERED CHARGES	49
1	0892	Charges for Modified Gene Therapy	J3590	MM DD YY	1	$XXX.XX		1
2		[N4XXXXXXXXXXUN]						2
3	0874	Cell/Gene Therapy Infusion of Modified Cells	96413	MM DD YY	[XX]	$XXX.XX		3
4								4
5								5
6								6
7								7
8								8
9								9
10								10
11								11
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21								21
22								22
23		***PAGE ____ OF ____***	***CREATION DATE***		**TOTALS**			23

Field 42: REVENUE CODE[6,10]
Enter the appropriate revenue code for each reported line. For example, 0892 Charges for Gene Therapy.

Field 43: DESCRIPTION
Enter the 11-digit NDC[8] with an appended N4 qualifier (electronic equivalent Loop 2410, LIN02). Enter the appropriate description for corresponding revenue code.[6,10]

Field 44: HCPCS[5]
Enter the appropriate HCPCS Level II code along with the applicable modifier. For example, J3590 or J3490. In lieu of a gene-therapy-specific code for the infusion, the 96413 CPT[4] code may be required.

Field 45: SERVICE DATE
Enter the corresponding date(s) of service.

Field 46: SERVICE UNITS
Enter appropriate units of service. For unclassified codes, such as J3490 and J3590, 1 unit of service may be required.

Field 47: TOTAL CHARGES
Enter total charges for each reported line.

	50 PAYER NAME	51 HEALTH PLAN ID	52 REL INFO	53 ASG. BEN.	54 PRIOR PAYMENTS	55 EST. AMOUNT DUE	56 NPI	
A							57	A
B							OTHER	B
C							PRV ID	C

	58 INSURED'S NAME	59 P REL	60 INSURED'S UNIQUE ID	61 GROUP NAME	62 INSURANCE GROUP NO.
A					
B					
C					

Fields 66 & 69: DIAGNOSIS CODES[2]
Enter the appropriate ICD-10-CM diagnosis codes. For example, D57.1 Sickle-cell disease without crisis.

	64 DOCUMENT CONTROL NUMBER	65 EMPLOYER NAME
A		
B		
C		

66 DX	D57.1	67	A	B	C	D	E	F	G	H	68
		I	J				N	O	P	Q	

69 ADMIT DX	D57.1	70 PATIENT REASON DX			72 ECI	a	b	c	73

Field 74: PRINCIPAL PROCEDURE[3]
Enter the relevant ICD-10-PCS procedure code(s) with corresponding date(s) of service. For example, XW133H9: Transfusion of Lovotibeglogene Autotemcel into Peripheral Vein, Percutaneous Approach.

74 PRINCIPAL PROCEDURE CODE	DATE	RE DATE	75
XW133H9	MM DD YY		
c. OTHER PROCEDURE CODE	DATE	RE DATE	

76 ATTENDING	NPI	QUAL	
LAST		FIRST	
77 OPERATING	NPI	QUAL	
LAST		FIRST	
78 OTHER	NPI	QUAL	
LAST		FIRST	
79 OTHER	NPI	QUAL	
LAST		FIRST	

Field 80: REMARKS
Enter relevant product information when reporting a miscellaneous HCPCS code. For example, drug name, dosage, NDC number and route of administration, and bluebird Patient ID.

80 REMARKS
[NAME]; [DOSAGE]; NDC;
IV INFUSION

UB-04 CMS-1450

NUBC® National Uniform Billing Committee LIC9213257

THE CERTIFICATIONS ON THE REVERSE APPLY TO THIS BILL AND ARE MADE A PART HEREOF.