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BILLING & CODING GUIDE

A Resource For Coding, Billing, and Reimbursement Information for ZYNTEGLO™

INDICATION

ZYNTEGLO is indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.

IMPORTANT SAFETY INFORMATION

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with ZYNTEGLO treatment. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia; 15% of patients had ≥ Grade 3 decreased platelets on or after Day 100.

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 NOTE:

This Billing & Coding Guide is intended to help healthcare professionals understand key billing and coding considerations for ZYNTEGLO and its related services when using ZYNTEGLO for its FDA-approved use during a hospital admission.

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, 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 Genetix CARES for additional resources regarding coding for a specific plan.

For reimbursement questions or appeals support, talk with a Patient Navigator at Genetix CARES by calling 1-833-888-6378, emailing support@genetixcares.com, or visiting genetixcares.com.

Please see additional Important Safety Information on pages 16-18 and full Prescribing Information.

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We're committed to supporting your patients

GENETIX CARES™

Genetix CARES is here to help your patients and their caregivers navigate access to Genetix Biotherapeutics 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.

From the moment your patient decides to explore transformative treatment, **Genetix CARES** is available to them at no cost. Enrollment gives you and your patient the information and guidance needed to **navigate treatment with confidence**.

Coordination of care services and logistics, including assistance with travel and lodging

Access to financial assistance and insurance coverage

Resources tailored for every treatment stage, including support for fertility preservation

Education that empowers informed treatment decisions

Support from a dedicated, single point of contact and from other people and families who experienced treatment firsthand

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6 Important Steps to Treatment

STEP 1: Pre-Treatment

Before mobilization, apheresis, and myeloablative conditioning are initiated, confirm that hematopoietic stem cell (HSC) transplantation is appropriate for the patient.

It is recommended that patients be maintained at a hemoglobin (Hb) ≥11 g/dL for at least 30 days prior to mobilization and 30 days prior to myeloablative conditioning.

STEP 2: Stem Cell Collection ~1 week[1]

Patients are required to undergo hematopoietic stem cell mobilization (5–6 days) followed by apheresis (apheresis generally occurred on day 5 and 6 of mobilization) to obtain CD34+ cells for ZYNTEGLO manufacturing. If the minimum number of CD34+ cells to manufacture ZYNTEGLO is not met, additional cycles of mobilization and apheresis, separated by at least 14 days, may be required.

STEP 3: Production ~70-90 days[1]

The patient's cells are sent to a manufacturing site to produce ZYNTEGLO. ZYNTEGLO is then supplied in one or more infusion bags.

STEP 4: Conditioning and Washout 4 days + at least 48 hours washout[1]

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

STEP 5: Infusion ~30 minutes per bag[1]

Each infusion bag of ZYNTEGLO is administered via intravenous infusion over a period of less than 30 minutes per bag. ZYNTEGLO is supplied in up to four infusion bags containing a frozen suspension of genetically modified autologous cells, enriched for CD34+ cells.

STEP 6: Post-Infusion Monitoring ~3-6 weeks[1]

Patients should be prepared to remain hospitalized and monitored for an additional 3–6 weeks after infusion. Times may vary by patient.

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

Post-infusion monitoring/Long-term follow-up

Patients treated with ZYNTEGLO may develop hematologic malignancies and should be monitored lifelong. Monitor for hematologic malignancies with a complete blood count (with differential) at Month 6 and Month 12 and then at least annually for at least 15 years after treatment with ZYNTEGLO, and integration site analysis at Months 6, 12, and as warranted. If a hematologic malignancy is detected, contact Genetix Biotherapeutics at 1-833-999-6378 for reporting and to obtain instructions on collection of samples for testing.

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 ZYNTEGLO, it may be necessary to confirm with each payer that the subsequent admission is a planned admission for gene therapy administration.

ZYNTEGLO

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[1]

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.

The target number of CD34+ cells to be collected is $\geq 12 \times 10^6$ CD34+ cells/kg. If the minimum dose of 5.0×10^6 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. Up to two drug product lots may be administered to meet the target dose.

A back-up collection of CD34+ cells of $\geq 1.5 \times 10^6$ CD34+ cells/kg (if collected by apheresis) or $> 1.0 \times 10^8$ TNC/kg (Total Nucleated Cells, if collected by bone marrow harvest) is required. These cells must be collected from the patient and be cryopreserved prior to myeloablative conditioning. The back-up collection may be needed for rescue treatment if there is: 1) compromise of hematopoietic stem cells or ZYNTEGLO before infusion, 2) primary engraftment failure, or 3) loss of engraftment after infusion with ZYNTEGLO.

Additional apheresis cycles may be necessary to meet the drug product dose, and these additional cycles would require additional prior authorization and approval.

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

POST TESTING[1]

Patients treated with ZYNTEGLO 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 ZYNTEGLO, and integration site analysis at Months 6, 12, and as warranted.

For reimbursement questions or appeals support, talk with a Patient Navigator at Genetix CARES by calling 1-833-888-6378, emailing support@genetixcares.com, or visiting genetixcares.com.

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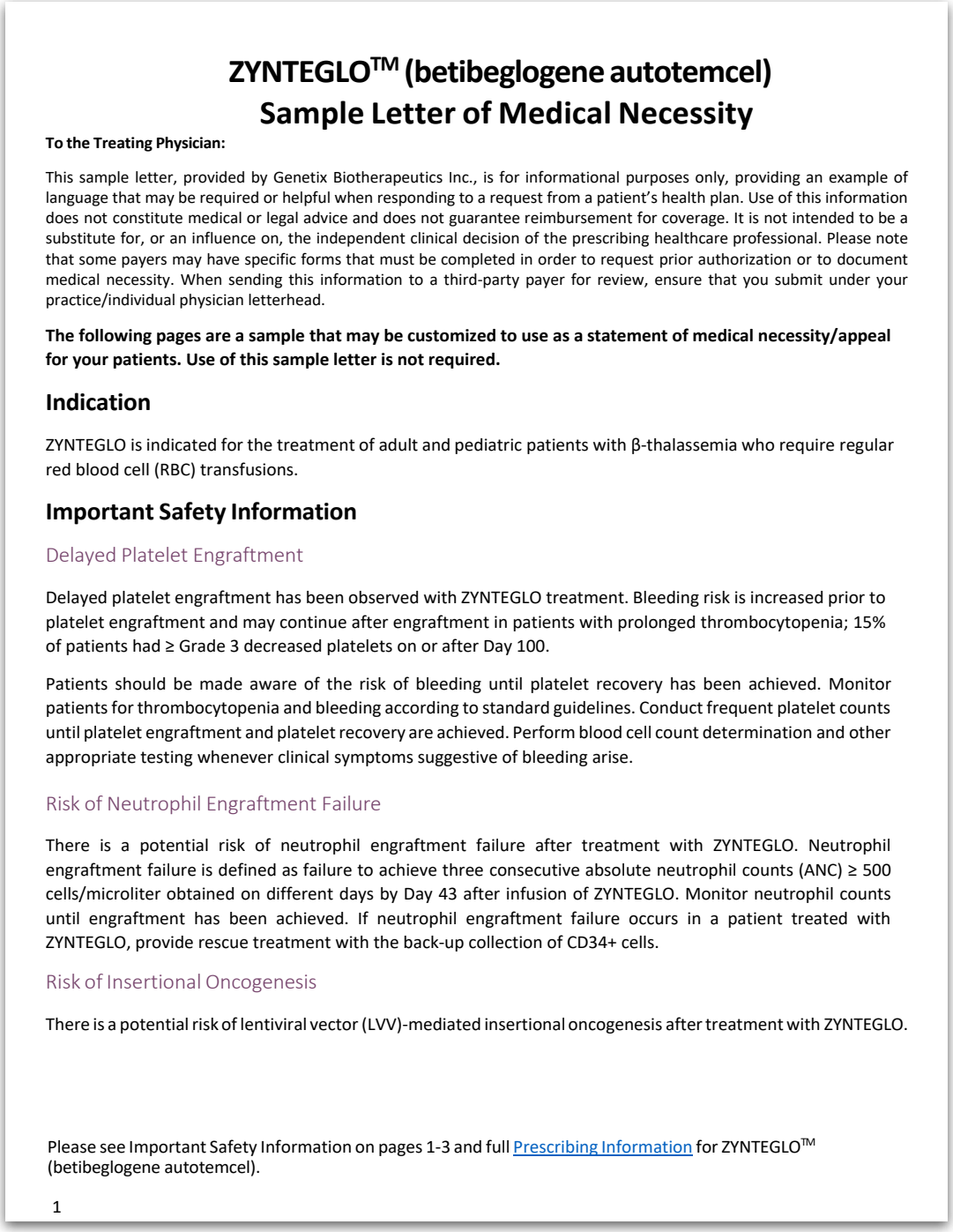
Sample Letter of Medical Necessity

ZYNTEGLO

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



ZYNTEGLO™ (betibeglogene autotemcel)
Sample Letter of Medical Necessity

To the Treating Physician:

This sample letter, provided by Genetix Biotherapeutics 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.

Indication

ZYNTEGLO is indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.

Important Safety Information

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with ZYNTEGLO treatment. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia; 15% of patients had ≥ Grade 3 decreased platelets on or after Day 100.

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.

Risk of Neutrophil Engraftment Failure

There is a potential risk of neutrophil engraftment failure after treatment with ZYNTEGLO. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) ≥ 500 cells/microliter obtained on different days by Day 43 after infusion of ZYNTEGLO. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with ZYNTEGLO, provide rescue treatment with the back-up collection of CD34+ cells.

Risk of Insertional Oncogenesis

There is a potential risk of lentiviral vector (LVV)-mediated insertional oncogenesis after treatment with ZYNTEGLO.

Please see Important Safety Information on pages 1-3 and full Prescribing Information for ZYNTEGLO™ (betibeglogene autotemcel).

1

Additional support for medical necessity may be required for new patients. Resources available through **Genetix CARES** include the above 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 ZYNTEGLO

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Cell Collection Coding

MOBILIZATION AND APHERESIS

ICD-10-CM CODE[2]	DESCRIPTION
D56.1	Beta-thalassemia

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

Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein.

CPT is a registered trademark of the American Medical Association.

U.S. Government End Users. CPT is commercial technical data, which was developed exclusively at private expense by the American Medical Association (AMA), 330 North Wabash Avenue, Chicago, Illinois 60611. Use of CPT in connection with this product shall not be construed to grant the Federal Government a direct license to use CPT based on FAR 52.227-14 (Data Rights - General) and DFARS 252.227-7015 (Technical Data - Commercial Items).

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

*Report the code for each collection encounter.

HCPCS CODE[5]	DESCRIPTION
J2562	Injection, plerixafor, 1 mg
J1442	Injection, filgrastim (G-CSF), excludes biosimilar, 1 mcg
J1447	Injection, tbo-filgrastim, 1 mcg
Q5101	Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 mcg
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg
Q5125	Injection, filgrastim-ayow, biosimilar, (Releuko), 1 mcg

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

REVENUE CODE[6]	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.

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Conditioning Regimen Coding

All patients received full myeloablative conditioning with busulfan prior to administration of ZYNTEGLO.[1]

There are risks associated with myeloablative conditioning agents on pregnancy and fertility. Refer to the Fertility Preservation section of this guide.

ICD-10-CM CODE[2]	DESCRIPTION
D56.1	Beta-thalassemia

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	Generic Pharmacy
0260	General IV Therapy
0636	Drug Requiring Detailed Coding

10-DIGIT NDC[7]	NOTES
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 ZYNTEGLO 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.

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Administration Coding

ICD-10-CM CODE[3]	DESCRIPTION
D56.1	Beta-thalassemia

ICD-10-PCS codes are applied to define specific procedures during a hospital inpatient admission.

ICD-10-PCS CODE[3]	DESCRIPTION
XW133B8	Transfusion of betibeglogene autotemcel into peripheral vein, percutaneous approach, New Technology Group 8
XW143B8	Transfusion of betibeglogene autotemcel into central vein, percutaneous approach, New Technology Group 8

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-DRG1[3]	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

Effective July 1, 2024, ZYNTEGLO has been granted pass-through status and a product-specific HCPCS code (J-code).

HCPCS CODE[5]	DESCRIPTION
J3393	Injection, betibeglogene autotemcel, per treatment
J3490	Unclassified drugs
J3590	Unclassified biologics

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Administration Coding (cont'd)

CELL/GENE THERAPY REVENUE CODE[6]	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	Pharmacy—Special Processed Drugs—FDA Approved Gene Therapy

Many payers require that the ZYNTEGLO 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] Requirements may vary by payer. For example, certain payers may require the 10-digit NDC code; others may require the N4 format.

10-DIGIT NDC[7]	11-DIGIT NDC[8]	CLAIM REPORTING REQUIREMENTS[9]
73554-3111-1	73554-3111-01	N473554311101UN

Payers may vary on their requirements for detailed coding of ZYNTEGLO 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.

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Select Coding Summary

HOSPITAL REVENUE CODES

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

REVENUE CODE[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	Pharmacy—Special Processed Drugs —FDA Approved Gene Therapy

NDC INFORMATION

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

10-DIGIT NDC[7]	11-DIGIT NDC[8]	CLAIM REPORTING REQUIREMENT[9]
73554-3111-1	73554-3111-01	N473554311101UN

VALUE CODE

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

VALUE CODE[12]	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 ZYNTEGLO administration.

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

ICD-10-CM DIAGNOSIS CODES

Providers should code to the level of specificity documented in the patient's medical record, which could fall under the ICD-10-CM diagnosis code below.

ICD-10-CM CODE[2]	DESCRIPTION
D56.1	Beta-thalassemia

HCPCS LEVEL II PRODUCT CODES

Effective July 1, 2024, ZYNTEGLO has been granted pass-through status and a product-specific HCPCS code (J-code).

HCPCS CODE[5]	DESCRIPTION
J3393	Injection, betibeglogene autotemcel, per treatment
J3490	Unclassified drugs
J3590	Unclassified biologics

ICD-10-PCS INPATIENT PROCEDURE CODES

ZYNTEGLO-specific ICD-10-PCS codes became effective 10/01/2022.

ICD-10-PCS CODE[3]	DESCRIPTION
XW133B8	Transfusion betibeglogene autotemcel into peripheral vein, percutaneous approach, New Technology Group 8
XW143B8	Transfusion betibeglogene autotemcel into central vein, percutaneous approach, New Technology Group 8

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

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Fertility Preservation

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

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 Genetix Biotherapeutics Inc. Links are provided for informational purposes only. We do not make or imply any endorsement of external websites.

ASCO Publication - Fertility Preservation in Patients With Cancer

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 ZYNTEGLO 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

When using any of the referenced available CPT codes for fertility preservation, they may be billed with the following ICD-10-CM diagnosis code:

Z31.84: Encounter for fertility preservation procedure prior to cancer therapy[2]

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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 ZYNTEGLO 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.

When using any of the referenced available CPT codes for fertility preservation, they may be billed with the following ICD-10-CM diagnosis code:

Z31.84: Encounter for fertility preservation procedure prior to cancer therapy[2]

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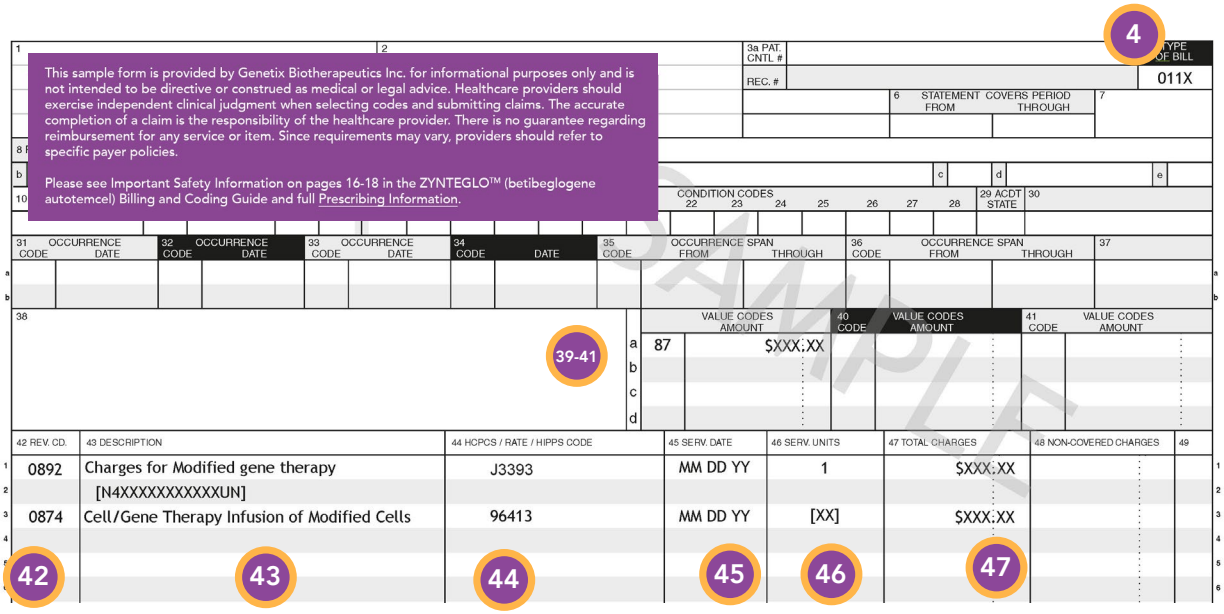
Sample CMS 1450 (UB-04) Claim Form for Inpatient Hospital Admissions

Clicking the image below will open the Sample Claims Form on page 20 of this document.



4 TYPE OF BILL[14]

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

39-41 VALUE CODES[12]

Payers may require a Value Code to document acquisition cost for ZYNTEGLO. 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]

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

43 DESCRIPTION[9]

Enter the 11-digit NDC with an appended N4 qualifier. Enter the appropriate description for corresponding revenue codes.

44 HCPCS[5]

Enter the appropriate HCPCS Level II code, J3393 (Injection, betibeglogene autotemcel, per treatment), along with the applicable modifier. In lieu of a gene therapy-specific code for the infusion, the 96413 CPT code may be required.

45 SERVICE DATE

Enter the corresponding date(s) of service.

46 SERVICE UNITS[5]

Enter appropriate units of service. For J3393, 1 unit of service is required as the code is per treatment.

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.

zynteglo™ (betibeglogene autotemcel) suspension for IV infusion

For reimbursement questions or appeals support, talk with a Patient Navigator at Genetix CARES by calling 1-833-888-6378, emailing support@genetixcares.com, or visiting genetixcares.com.

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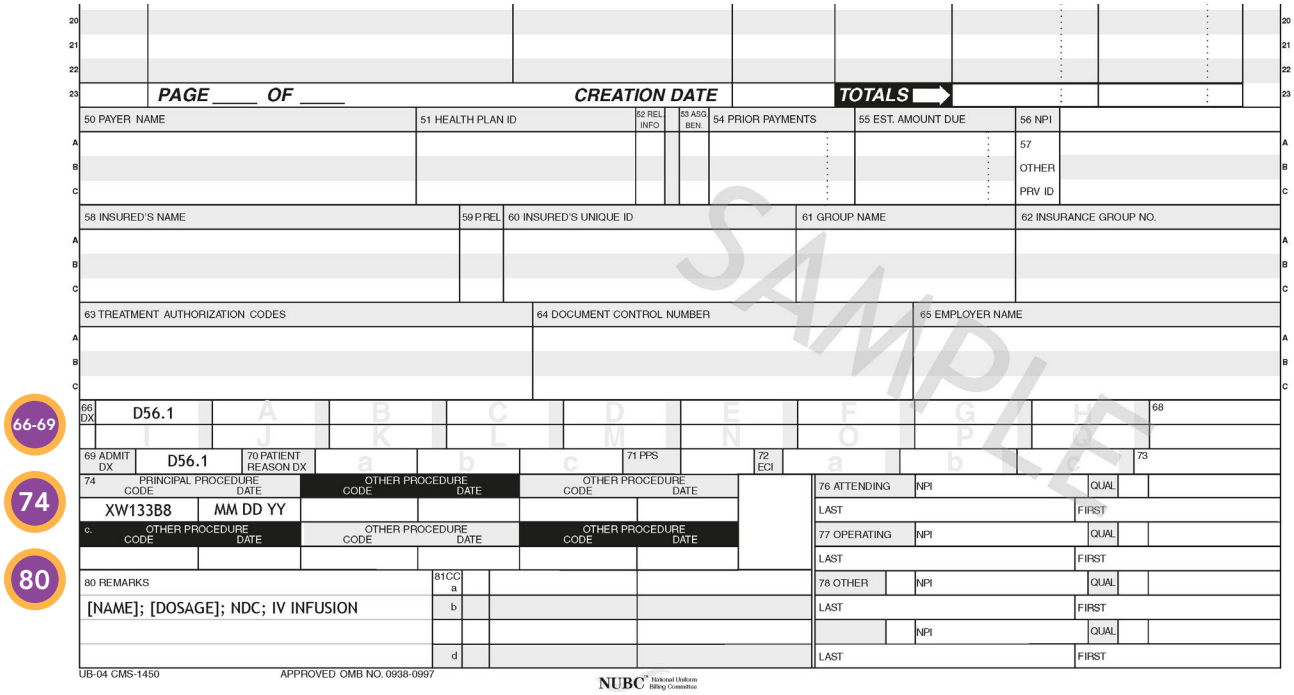
Sample CMS 1450 (UB-04) Claim Form for Inpatient Hospital Admissions (cont'd)

Clicking the image below will open the Sample Claims Form on page 20 of this document.



66-69 DIAGNOSIS CODE(S)[2]

Enter the appropriate ICD-10-CM diagnosis code(s) for patient condition(s). For example, D56.1 β-thalassemia. Field 69 is required for inpatient stay.

74 PRINCIPAL PROCEDURE[3]

Enter relevant ICD-10-PCS procedure code(s) with corresponding date(s) of service. CMS has assigned XW133B8 and XW143B8 for ZYNTEGLO™ effective 10/01/2022.

80 REMARKS[14]

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

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Indication and Important Safety Information[1]

INDICATION

ZYNTEGLO is indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.

IMPORTANT SAFETY INFORMATION

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with ZYNTEGLO treatment. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia; 15% of patients had ≥ Grade 3 decreased platelets on or after Day 100.

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.

Risk of Neutrophil Engraftment Failure

There is a potential risk of neutrophil engraftment failure after treatment with ZYNTEGLO. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) ≥ 500 cells/microliter obtained on different days by Day 43 after infusion of ZYNTEGLO. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with ZYNTEGLO, provide rescue treatment with the back-up collection of CD34+ cells.

Risk of Insertional Oncogenesis

There is a potential risk of lentiviral vector (LVV)-mediated insertional oncogenesis after treatment with ZYNTEGLO.

Patients treated with ZYNTEGLO may develop hematologic malignancies and should be monitored lifelong. Monitor for hematologic malignancies with a complete blood count (with differential) at Month 6 and Month 12 and then at least annually for at least 15 years after treatment with ZYNTEGLO, and integration site analysis at Months 6, 12, and as warranted.

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

Hypersensitivity Reactions

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

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Important Safety Information[1] (cont'd)

IMPORTANT SAFETY INFORMATION (CONT'D)

Anti-retroviral and Hydroxyurea Use

Patients should not take prophylactic HIV anti-retroviral medications or hydroxyurea for at least one month prior to mobilization, or for the expected duration for elimination of the medications, and until all cycles of apheresis are completed. If a patient requires anti-retrovirals for HIV prophylaxis, then confirm a negative test for HIV before beginning mobilization and apheresis of CD34+ cells.

Interference with Serology Testing

Patients who have received ZYNTEGLO are likely to test positive by polymerase chain reaction (PCR) assays for HIV due to integrated BB305 LVV proviral DNA, resulting in a false-positive test for HIV. Therefore, patients who have received ZYNTEGLO should not be screened for HIV infection using a PCR-based assay.

Adverse Reactions

The most common non-laboratory adverse reactions (≥20%) were mucositis, febrile neutropenia, vomiting, pyrexia, alopecia, epistaxis, abdominal pain, musculoskeletal pain, cough, headache, diarrhea, rash, constipation, nausea, decreased appetite, pigmentation disorder, and pruritus. The most common Grade 3 or 4 laboratory abnormalities (>50%) include neutropenia, thrombocytopenia, leukopenia, anemia, and lymphopenia.

Drug Interactions

Drug-drug interactions between iron chelators and the myeloablative conditioning agent must be considered. Iron chelators should be discontinued at least 7 days prior to initiation of conditioning. The prescribing information for the iron chelator(s) and the myeloablative conditioning agent should be consulted for the recommendations regarding co-administration with CYP3A substrates.

Some iron chelators are myelosuppressive. After ZYNTEGLO infusion, avoid use of these iron chelators for 6 months. If iron chelation is needed, consider administration of non-myelosuppressive iron chelators. Phlebotomy can be used in lieu of iron chelation, when appropriate.

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Important Safety Information[1] (cont'd)

IMPORTANT SAFETY INFORMATION (CONT'D)

Pregnancy/Lactation

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

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

ZYNTEGLO is not recommended for women who are breastfeeding, and breastfeeding after ZYNTEGLO 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 ZYNTEGLO 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 ZYNTEGLO.

Advise patients of the option to cryopreserve semen or ova before treatment if appropriate.

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Please see Important Safety Information on pages 16-18 and full Prescribing Information.

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ZYN-US-00061-v4 06/26

GENETIX™ Biotherapeutics

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

This sample form is provided by Genetix Biotherapeutics 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 16-18 in the ZYNTEGLO™ (betibeglogene autotemcel) Billing and Coding Guide and full Prescribing Information.

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

Fields 39-41: VALUE CODES[12]
Payers may require a Value Code to document acquisition cost of ZYNTEGLO™. 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.

4 TYPE OF BILL	REC. #	6 STATEMENT COVERS PERIOD FROM	THROUGH
011X			

39 CODE	VALUE CODES AMOUNT	40 CODE	VALUE CODES AMOUNT	41 CODE	VALUE CODES 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 [N4XXXXXXXXXXUN]	J3393	MM DD YYYY	1	$XXX.XX		
2								
3	0874	Cell/Gene Therapy Infusion of Modified Cells	96413	MM DD YYYY	[XX]	$XXX.XX		
4–22								
23		PAGE ____ OF ____	CREATION DATE		TOTALS			

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

Field 43: DESCRIPTION[9]
Enter the 11-digit NDC with an appended N4 qualifier (electronic equivalent: Loop 2410, LIN02). Enter the appropriate description for corresponding revenue code(s).[6,10]

Field 44: HCPCS[5]
Enter the appropriate HCPCS Level II code, J3393 (Injection, betibeglogene autotemcel, per treatment), along with the applicable modifier. In lieu of a gene therapy-specific code for the infusion, the 96413 CPT code may be required.

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

Field 46: SERVICE UNITS[5]
Enter appropriate units of service. For J3393, 1 unit of service is required per treatment.

Field 47: TOTAL CHARGES
Enter the 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 / 57 OTHER PRV ID
A						
B						
C						

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

63 TREATMENT	65 EMPLOYER NAME
A	
B	
C	

Fields 66-69: DIAGNOSIS CODE(S)[2]
Enter the appropriate diagnosis code(s) for patient condition(s). For example, D56.1 β-thalassemia. Field 69 is required for inpatient stay.

66 DX	67	A	B	C	D	E	F	G	H	68
D56.1										
		I	J	K	L	M	N	O	P	Q

69 ADMIT DX	70 PATIENT REASON DX	a	b	c	73
D56.1					

Field 74: PRINCIPAL PROCEDURE[3]
Enter the relevant ICD-10-PCS procedure code(s) with corresponding date(s) of service. CMS has assigned XW133B8 and XW143B8 for ZYNTEGLO™ effective 10/01/2022.

74 PRINCIPAL PROCEDURE CODE	DATE	a. OTH CODE	NPI	QUAL	
XW133B8	MM DD YYYY			FIRST	
c. OTHER PROCEDURE CODE	DATE	d. OTHI CODE	NPI	QUAL	
				FIRST	
				QUAL	
				FIRST	
				QUAL	
				FIRST	

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

80 REMARKS	81CC
[NAME]; [DOSAGE]; NDC; IV INFUSION	a
	b
	c
	d

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

SAMPLE

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