casgevy™
(exagamglogene autotemcel)
suspension for IV infusion

CODING AND BILLING GUIDE

A resource for coding, billing, coverage, and reimbursement information for CASGEVY™

Across the patient journey, various procedures are rendered in the hospital inpatient setting based on the pre-treatment regimens and timing of services. This guide is intended to provide information on the inpatient coding and billing process for CASGEVY. The guide is not meant to capture all individual payer-specific requirements, and providers must confirm eligibility and coverage with each prospective patient's payer.

The coding information in this guide is general in nature and subject to change without notice. Vertex cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and patient status. It is the sole responsibility of the healthcare provider to select the appropriate codes and modifiers and to confirm payer policies on coverage, prior authorization, coding, and claims billing.

This coding and billing guide is intended for informational purposes only.

VERTEX

Please see Important Safety Information on pages 2 and 16 and full Prescribing Information for CASGEVY™.

ENTER

Introduction

INDICATION

CASGEVY is indicated for the treatment of patients aged 12 years and older with:

- sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs)
- transfusion-dependent ß-thalassemia (TDT)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neutrophil Engraftment Failure

There is potential risk of neutrophil engraftment failure after treatment with CASGEVY. In the clinical trials, all treated patients achieved neutrophil engraftment and no patients received rescue CD34$^+$ cells.

Monitor absolute neutrophil counts (ANC) and manage infections according to standard guidelines and medical judgement. In the event of neutrophil engraftment failure, patients should be infused with rescue CD34$^+$ cells.

Delayed Platelet Engraftment

Delayed platelet engraftment has been observed with CASGEVY treatment. There is an increased risk of bleeding until platelet engraftment is achieved. In the clinical trials, there was no association observed between incidence of bleeding events and time to platelet engraftment.

Monitor patients for bleeding according to standard guidelines and medical judgement. 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.

CUSTOMER SUPPORT RESOURCES

Vertex understands that gene therapy treatment for SCD or TDT is a complex journey that encompasses many steps and stakeholders. Our Access and Reimbursement Leads (ARLs) have knowledge of hospital administration and payer reimbursement with respect to CASGEVY.

Please call your ARL directly with questions about access and reimbursement.

Vertex Connects™ is a program that provides educational resources, communications, and support to help navigate the treatment journey for patients who have been prescribed a Vertex cell and genetic therapy and their loved ones.

VERTEX Connects™

Vertex Connects offers support through a small team of dedicated care managers who will

- Share educational resources to help patients prepare for each step
- Provide information and help answer questions along the treatment journey
- Work with Authorized Treatment Centers (ATCs) delivering gene therapy to help manage logistics for each patient's treatment journey

Please visit www.VertexConnects.com to learn about the support available.

Confirmation of eligibility and a completed enrollment form are required to enroll in Vertex Connects Patient Support. Enrollment in Vertex Connects Patient Support is not required for Vertex cell and genetic therapy.

Please see Important Safety Information on pages 2 and 16 and full Prescribing Information for CASGEVY™.

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CASGEVY™ Administrative Treatment Journey Overview[a]

Process involves multiple steps to ensure quality of care. Patient status is at the sole discretion of the healthcare provider.[1-4]

Patient Journey	Patient Identification and Evaluation	Pre-mobilization[b]	Mobilization and Apheresis[b]	Manufacturing and Quality	Myeloablative Conditioning, Infusion, and Engraftment[b]	Follow-up
Estimated Timing[a]	Timing varies per patient	SCD: ≥8 weeks TDT: ongoing	SCD: ~3-4 days per cycle[c] TDT: ~7 days per cycle[c]	~24 weeks	SCD: Median 41 days (range 29-62)[d] TDT: Median 47 days (range 31-117)[d]	Up to 15 years post infusion
What Is Involved Clinically	Patient is screened and prescribed	SCD: Red blood cell transfusions and exchanges TDT: Red blood cell transfusions	Mobilization of stem cells Apheresis of stem cells Cryopreservation of backup cells	Manufacturing and quality process	Myeloablative conditioning[e] CASGEVY infusion Engraftment and monitoring	Follow-up visits and supportive care
Patient Status	Outpatient	Outpatient	SCD: Inpatient (~3-4 days) TDT: Variable (4 days)[f]; Inpatient (~3 days)	N/A	Inpatient	Outpatient
Administrative Process and Claims Submission	Eligibility and coverage verification Submission of CASGEVY purchase order Standard claim processing	Claim processing as determined by payer	May require multiple separate cycles and separate claims as determined by payer requirements	N/A	Single admission and claim processing as determined by payer requirements	Standard claim processing

Please see full Prescribing Information for CASGEVY for additional information. The accurate completion of claims is the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

[a]The time frame for each step of the CASGEVY treatment journey is approximate and will vary per patient. The entire CASGEVY treatment journey could take up to a year.
[b]Timing and patient status are based on clinical trials (Trial 1 and Trial 2).
[c]The median (min, max) number of collection cycles for SCD and TDT was 2 (1, 6) and 1 (1, 4), respectively. Timing is reflective of a hospital admission on Day 0 for SCD and Day 4 for TDT.[1,3]
[d]The median total length of hospitalization for myeloablative conditioning and CASGEVY infusion through discharge for SCD and TDT was approximately 6 weeks and 7 weeks, respectively.[2,4]
[e]It is recommended that patients with SCD or TDT be transfused for at least 8 weeks or for 60 days, respectively, prior to the initiation of myeloablative conditioning.[1]
[f]Subcutaneously administered mobilizing agents can be self-administered at home, but due to certain circumstances and payer requirements, inpatient administration of the injection may be required.

N/A, not applicable; SCD, sickle cell disease; TDT, transfusion-dependent β-thalassemia.

1. CASGEVY [prescribing information]. Vertex Pharmaceuticals Incorporated. Boston, MA; January 2024. **2.** Data on file. Vertex Pharmaceuticals Incorporated. Boston, MA. REF-23044 (v2.0); 2023. **3.** Data on file. Vertex Pharmaceuticals Incorporated. Boston, MA. REF-15461 (v3.0); 2023. **4.** Data on file. Vertex Pharmaceuticals Incorporated. Boston, MA. REF-22852 (v3.0); 2023.

Coverage and Reimbursement Considerations

Coverage and reimbursement may vary significantly by payer, plan, patient, and patient status. If you have questions and/or concerns regarding patient coverage and payer reimbursement policies, please contact your Vertex ARL.

MEDICAID

Medicaid coverage and reimbursement varies on a state-by-state basis[1]

- Check the specific requirements of the state Medicaid FFS program and Medicaid managed care plan in which the patient is enrolled

The type of inpatient reimbursement methodology used by Medicaid FFS and Medicaid managed care programs varies and may include the following[1,2]:

- MS-DRGs
- APR-DRGs
- Per diems
- Carve-outs
- Episodes of care

Programs may also require specialized billing of the CASGEVY™ biological product

For patients who have both Medicare and Medicaid (ie, "dual-eligible"), Medicare pays first[3]

- See Medicare column for more information on reimbursement methodologies

COMMERCIAL

CASGEVY may be subject to payer-specific coverage requirements

- Payers may have medical policies that include patient eligibility limitations in addition to the FDA label

Commercial payers will reimburse based on the terms of a contract or single case agreement with a particular hospital/provider

- May use a range and combination of reimbursement methodologies for CASGEVY and its administration, including the following[4,5]:
  - Case rates
  - Per diems
  - Average sales price/WAC/invoice-based rates
  - Percentage of billed charges

If a provider is not contracted with the patient's payer, a single case agreement will likely be needed

- Contact the managed care contracting department to initiate negotiations of a single case agreement that encompasses each step of treatment with CASGEVY

MEDICARE

For Medicare FFS, FDA-approved drugs and biologics are generally covered when reasonable and medically necessary for the treatment of a Medicare patient[6]

- May be subject to additional restrictions or requirements at the national or local level

Reimbursement for inpatient administration of CASGEVY to Medicare FFS patients is set nationally by CMS via an annual process

- A Medicare FFS inpatient stay is reimbursed using an MS-DRG and may be eligible to receive NTAP and an outlier payment, if applicable[7,8]

Medicare Advantage plans may administer their own prior authorization processes and requirements to approve a particular treatment

- Plans must abide by Medicare coverage requirements[9]
- Providers negotiate with Medicare Advantage plans for reimbursement

The accurate completion of claims is the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

APR-DRG, All Patient Refined-Diagnosis Related Group; ARL, Access and Reimbursement Lead; CMS, Centers for Medicare & Medicaid Services; FDA, US Food and Drug Administration; FFS, fee-for-service; MS-DRG, Medicare Severity-Diagnosis Related Group; NTAP, New Technology Add-on Payment; WAC, wholesale acquisition cost.

1. Medicaid and CHIP Payment and Access Commission (MACPAC). Medicaid inpatient hospital services fee-for-service payment policy. MACPAC website. Published December 2018. Accessed January 10, 2024. https://www.macpac.gov/wp-content/uploads/2016/03/Medicaid-Inpatient-Hospital-Services-Fee-for-Service-Payment-Policy.pdf **2.** MACPAC. Medicaid inpatient hospital fee-for-service payment policies. MACPAC.gov website. Published March 2018. Accessed January 10, 2024. https://www.macpac.gov/wp-content/uploads/2018/12/State-Medicaid-Fee-for-Service-Inpatient-Hospital-Payment-Policies.xlsx **3.** Medicare.gov. Medicaid. Medicare website. Accessed January 10, 2024. https://www.medicare.gov/basics/costs/help/medicaid **4.** Congressional Budget Office (CBO). The prices that commercial health insurers and Medicare pay for hospitals' and physicians' services. CBO website. Published January 2022. Accessed January 10, 2024. https://www.cbo.gov/system/files/2022-01/57422-medical-prices.pdf **5.** Bruen B, Docteur E, Lopert R, et al; US Department of Health and Human Services (HHS). The impact of reimbursement policies and practices on healthcare technology innovation. HHS website. Published February 2016. Accessed January 10, 2024. https://aspe.hhs.gov/sites/default/files/private/pdf/188741/ImpactofReimbursementonInnovation.pdf **6.** Social Security Act sec. 1862(a)(1)(A). Accessed January 10, 2024. https://www.ssa.gov/OP_Home/ssact/title18/1862.htm **7.** Medicare Payment Advisory Commission (MedPAC). Hospital acute inpatient services payment system. MedPAC website. Updated November 2021. Accessed January 10, 2024. https://www.medpac.gov/wp-content/uploads/2021/11/medpac_payment_basics_21_hospital_final_sec.pdf **8.** CMS. New medical services and new technologies. CMS website. Updated December 14, 2023. Accessed January 10, 2024. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/newtech **9.** Medicare Managed Care Manual, ch. 4, sec. 10.2. Accessed January 10, 2024. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/reports/jun18_ch10_medpacreport_sec.pdf

Coding and Billing for CASGEVY™

DIAGNOSIS CODING

CASGEVY is FDA-approved for the treatment of patients aged 12 years and older with sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs) and transfusion-dependent ß-thalassemia (TDT). Diagnosis coding is necessary and important to demonstrate the medical necessity of a service such as a gene-editing stem cell transplant. Complete and comprehensive diagnosis coding is important, including coding for the specific diagnosis treated by CASGEVY, any complication arising from the transfusion of CASGEVY, and any comorbidities of the patient.

The list of the most common diagnoses for CASGEVY are provided on the next 2 pages. The clinician's documentation must support a particular diagnosis and its specificity within the medical record. For the code ranges represented herein, it is necessary to code to the greatest level of specificity.

The selection of codes and modifiers and the accurate completion of claims are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

D56	THALASSEMIA[1]
D56.1	**Beta thalassemia**
D56.5	**Hemoglobin E-beta thalassemia**

D57	SICKLE-CELL DISORDERS[1]
D57.0	**Hb-SS disease with crisis**
D57.00	Hb-SS disease with crisis, unspecified
D57.01	Hb-SS disease with acute chest syndrome
D57.02	Hb-SS disease with splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.04	Hb-SS disease with dactylitis
D57.09	Hb-SS disease with crisis with other specified complication
D57.1	**Sickle-cell disease without crisis**
D57.2	**Sickle-cell/Hb-C disease**
D57.20	Sickle-cell/Hb-C disease without crisis
D57.21	Sickle-cell/Hb-C disease with crisis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement
D57.214	Sickle-cell/Hb-C disease with dactylitis
D57.218	Sickle-cell/Hb-C disease with crisis with other specified complication
D57.219	Sickle-cell/Hb-C disease with crisis, unspecified

(continued on next page)

FDA, US Food and Drug Administration; Hb, hemoglobin.

1. Centers for Medicare & Medicaid Services (CMS). ICD-10-CM tabular list of diseases and injuries. CMS website. Updated June 29, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-code-tables-tabular-and-index-updated-06/29/2023.zip

DIAGNOSIS CODING (continued)

D57	SICKLE-CELL DISORDERS[1] (continued)
D57.4	**Sickle-cell thalassemia**
D57.40	Sickle-cell thalassemia without crisis
D57.41	Sickle-cell thalassemia, unspecified, with crisis
D57.411	Sickle-cell thalassemia, unspecified, with acute chest syndrome
D57.412	Sickle-cell thalassemia, unspecified, with splenic sequestration
D57.413	Sickle-cell thalassemia, unspecified, with cerebral vascular involvement
D57.414	Sickle-cell thalassemia, unspecified, with dactylitis
D57.418	Sickle-cell thalassemia, unspecified, with crisis with other specified complication
D57.419	Sickle-cell thalassemia, unspecified, with crisis
D57.42	Sickle-cell thalassemia beta zero without crisis
D57.43	Sickle-cell thalassemia beta zero with crisis
D57.431	Sickle-cell thalassemia beta zero with acute chest syndrome
D57.432	Sickle-cell thalassemia beta zero with splenic sequestration
D57.433	Sickle-cell thalassemia beta zero with cerebral vascular involvement
D57.434	Sickle-cell thalassemia beta zero with dactylitis
D57.438	Sickle-cell thalassemia beta zero with crisis with other specified complication
D57.439	Sickle-cell thalassemia beta zero with crisis, unspecified

D57	SICKLE-CELL DISORDERS[1] (continued)
D57.44	Sickle-cell thalassemia beta plus without crisis
D57.45	Sickle-cell thalassemia beta plus with crisis
D57.451	Sickle-cell thalassemia beta plus with acute chest syndrome
D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
D57.453	Sickle-cell thalassemia beta plus with cerebral vascular involvement
D57.454	Sickle-cell thalassemia beta plus with dactylitis
D57.458	Sickle-cell thalassemia beta plus with crisis with other specified complication
D57.459	Sickle-cell thalassemia beta plus with crisis, unspecified
D57.8	**Other sickle-cell disorders**
D57.80	Other sickle-cell disorders without crisis
D57.81	Other sickle-cell disorders with crisis
D57.811	Other sickle-cell disorders with acute chest syndrome
D57.812	Other sickle-cell disorders with splenic sequestration
D57.813	Other sickle-cell disorders with cerebral vascular involvement
D57.814	Other sickle-cell disorders with dactylitis
D57.818	Other sickle-cell disorders with crisis with other specified complication
D57.819	Other sickle-cell disorders with crisis, unspecified

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1. Centers for Medicare & Medicaid Services (CMS). ICD-10-CM tabular list of diseases and injuries. CMS website. Updated June 29, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-code-tables-tabular-and-index-updated-06/29/2023.zip

ICD-10-PCS PROCEDURE CODING

CASGEVY™ is genetically modified from each patient's hematopoietic stem cells. Stem cells must be collected from the patient after stem cell mobilization, which is necessary to ensure adequate numbers of stem cells will be collected to produce CASGEVY and to store unmodified cells as backup for potential rescue treatment. Prior to infusion of CASGEVY, the patient receives myeloablative conditioning.

ICD-10-PCS procedure codes are used to report services provided to hospital inpatients during their stay. The codes in the following table may be used to describe each of these services: cell mobilization, cell collection, conditioning, and the administration of CASGEVY.

The selection of codes and modifiers and the accurate completion of claims are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

TYPE OF SERVICE	ICD-10-PCS CODE	DESCRIPTION
Cell Mobilization[1]	**3E033GC**	Introduction of Other Therapeutic Substance into Peripheral Vein, Percutaneous Approach
	3E043GC	Introduction of Other Therapeutic Substance into Central Vein, Percutaneous Approach
Cell Collection[1]	**6A550ZV**	Pheresis of Hematopoietic Stem Cells, Single
	6A551ZV	Pheresis of Hematopoietic Stem Cells, Multiple
Conditioning[1]	**3E03305**	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
	3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
CASGEVY Administration[1]	**XW133J8**	Transfusion of Exagamglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 8
	XW143J8	Transfusion of Exagamglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8

ICD-10-PCS, International Classification of Diseases, Tenth Revision, Procedure Coding System.

1. Centers for Medicare & Medicaid Services (CMS). ICD-10-PCS code tables. CMS website. Updated December 19, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-icd-10-pcs-code-tables-and-index-updated-12/19/2023.zip

NATIONAL DRUG CODE (NDC) CODING

NDCs are unique codes that identify a drug's or biologic's labeler, the product, and the package size. For hospitals, NDCs and HCPCS codes for drugs and biologics, in addition to charges linked to the Charge Description Master (CDM), may be included within a hospital's or provider's pharmacy information system. HCPCS codes and charges for drugs and biologics may be included in the pharmacy system and/or the CDM. Certain payers may require reporting NDC numbers on claims for hospital-administered therapies.[1,2] Specific requirements for reporting may vary by payer, and certain payers may require additional information beyond the code itself, such as the qualifier, basis of measure, and quantity.

Several NDC numbers are associated with important components involved in treating a patient with CASGEVY™, such as those for the drugs and biologics used in cell mobilization and myeloablative conditioning of the patient. CASGEVY is a cell suspension for intravenous infusion. A single dose of CASGEVY is composed of 1 or more vials. Each vial contains 4 to 13 × 10^6 $CD34^+$ cells/mL suspended in 1.5 to 20 mL cryopreservative medium. The minimum recommended dose of CASGEVY is 3 × 10^6 $CD34^+$ cells per kilogram of body weight.

See the Lot Information Sheet for actual strength and dose. The Lot Information Sheet is included inside the lid of the liquid nitrogen dry shipper used to transport CASGEVY.[3]

The table below shows certain drugs and biologics used in the process of the CASGEVY treatment and for CASGEVY itself. It is important to confirm with a payer what NDCs are needed and what format is required (eg, 11 digits in 5-4-2 format).

TYPE OF DRUG/ BIOLOGIC	10-DIGIT NDC	11-DIGIT NDC (5-4-2 FORMAT)	DESCRIPTION
Cell Mobilization - Plerixafor[4]	**0024-5862-01[a]**	**00024-5862-01[a]**	24 mg/1.2 mL in 1 vial, single-use in 1 carton for subcutaneous injection
Cell Mobilization - G-CSF (eg, filgrastim)[5]	**XXXX-XXXX-XX[a]**	**XXXXX-XXXX-XX[a]**	Various strengths for intravenous or subcutaneous use
Conditioning - Busulfan[6]	**XXXX-XXXX-XX[a]**	**XXXXX-XXXX-XX[a]**	6.0 mg/mL in various packages for intravenous infusion
CASGEVY[3]	**51167-290-09**	**51167-0290-09[b]**	Provided as a single dose in 1 or more vials for intravenous infusion

[a]Multiple NDCs may be available for plerixafor, G-CSF, and busulfan due to different manufacturers and packages.[4-6] Please check what NDC was used for appropriate submission of the claim.
[b]The NDC for CASGEVY has been adjusted from the way it appears in the Prescribing Information (51167-290-09) to comply with the 11-digit format (5-4-2) for claim processing.

The selection of codes and modifiers and the accurate completion of claims are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

G-CSF, granulocyte-colony stimulating factor; HCPCS, Healthcare Common Procedure Coding System.
1. UnitedHealthcare. National drug code (NDC) requirement policy, professional and facility. UHCprovider.com website. Accessed January 11, 2024. https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-reimbursement/COMM-National-Drug-Code-Requirement-Policy.pdf **2.** Centers for Medicare & Medicaid Services. Medicare claims processing manual: chapter 25 - completing and processing the Form CMS-1450 data set. CMS website. Revised August 6, 2021. Accessed January 11, 2024. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c25.pdf **3.** CASGEVY [prescribing information]. Vertex Pharmaceuticals Incorporated. Boston, MA; January 2024. **4.** National Cancer Institute. CanMED: NDC–plerixafor. SEER website. Accessed January 11, 2024. https://seer.cancer.gov/oncologytoolbox/canmed/ndconc/00024-5862/ **5.** National Cancer Institute. CanMED: NDC-filgrastim. SEER website. Accessed January 11, 2024. https://seer.cancer.gov/oncologytoolbox/canmed/ndconc/?q=filgrastim&effective_date=&effective_date=&paginate_by=25 **6.** National Cancer Institute. CanMED: NDC-busulfan. SEER website. Accessed January 11, 2024. https://seer.cancer.gov/oncologytoolbox/canmed/ndconc/?q=busulfan&effective_date=&effective_date=&paginate_by=25

REVENUE CODING

National Uniform Billing Committee (NUBC) hospital revenue codes are required to bill for hospital services, biologics, items, and supplies. Each line item on a CMS-1450 (UB-04) claim or its electronic equivalent (837I) must have an assigned revenue code.

NUBC and the Centers for Medicare & Medicaid Services (CMS) issue guidance and instructions on appropriate standards and billing of revenue codes.[1] Hospitals follow NUBC revenue code definitions and report their charges under the revenue code that will result in the charges being assigned to the same cost center to which the cost of those services is assigned in the hospital's cost report.[2] For some services, this means a variety of revenue codes may be applicable to charges for services and items for the treatment of a patient with CASGEVY™.

The following revenue codes may be applicable to claims for CASGEVY and the services provided to a patient being treated with the therapy, such as cell mobilization, cell collection, cell processing, conditioning, the administration of CASGEVY, and the biological CASGEVY itself.

The selection of codes and modifiers and the accurate completion of claims are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

DESCRIPTION OF SERVICE/ITEM	REVENUE CODE	CODE DESCRIPTION
Cell Mobilization[3]	**0250**	Pharmacy - General
	0636	Pharmacy - Drugs requiring detailed coding
	0260	IV Therapy - General
Cell Collection[3]	**0871**	Cell/Gene Therapy - Cell Collection
	0761	Specialty Services - Treatment Room
Cell Processing[3]	**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
	0305	Laboratory - Hematology
	0310	Laboratory Pathology - General
Conditioning[3]	**0250**	Pharmacy - General
	0636	Pharmacy - Drugs requiring detailed coding
	0335	Radiology/Therapeutic - Chemotherapy IV
CASGEVY Administration[3]	**0874**	Cell/Gene Therapy - Infusion of Modified Cells
	0761	Specialty Services - Treatment Room
	0940	Other Therapeutic Services - General
CASGEVY Biological[3]	**0892**	Special Processed Drugs - FDA Approved Gene Therapy
	0250	Pharmacy - General
	0636	Pharmacy - Drugs requiring detailed coding

FDA, US Food and Drug Administration; IV, intravenous.

1. Centers for Medicare & Medicaid Services (CMS). Medicare claims processing manual: chapter 25 - completing and processing the Form CMS-1450 data set. CMS website. Revised August 6, 2021. Accessed January 11, 2024. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c25.pdf **2.** CMS. Medicare claims processing manual: chapter 4 - Part B hospital (including inpatient hospital Part B and OPPS). CMS website. Revised December 21, 2023. Accessed January 11, 2024. https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c04.pdf **3.** Noridian Healthcare Solutions. Medicare Part A revenue codes. NoridianMedicare website. Updated December 9, 2023. Accessed January 16, 2024. https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes

SAMPLE CMS 1450 (UB-04) CLAIM FORM

Requirements for specific fields may vary by payer; review payer-specific policies for claims billing.

These sample claims are for informational purposes only and should not be relied upon to complete claims. The accurate completion of claims is the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

Fields 42 and 43: Enter the appropriate revenue code for each reported line and its corresponding description. For example[1]:

0892	Special Processed Drugs - FDA Approved Gene Therapy

For field **43**, NDC reporting requirements may vary by payer. Other revenue codes may apply; see page 10 for additional examples

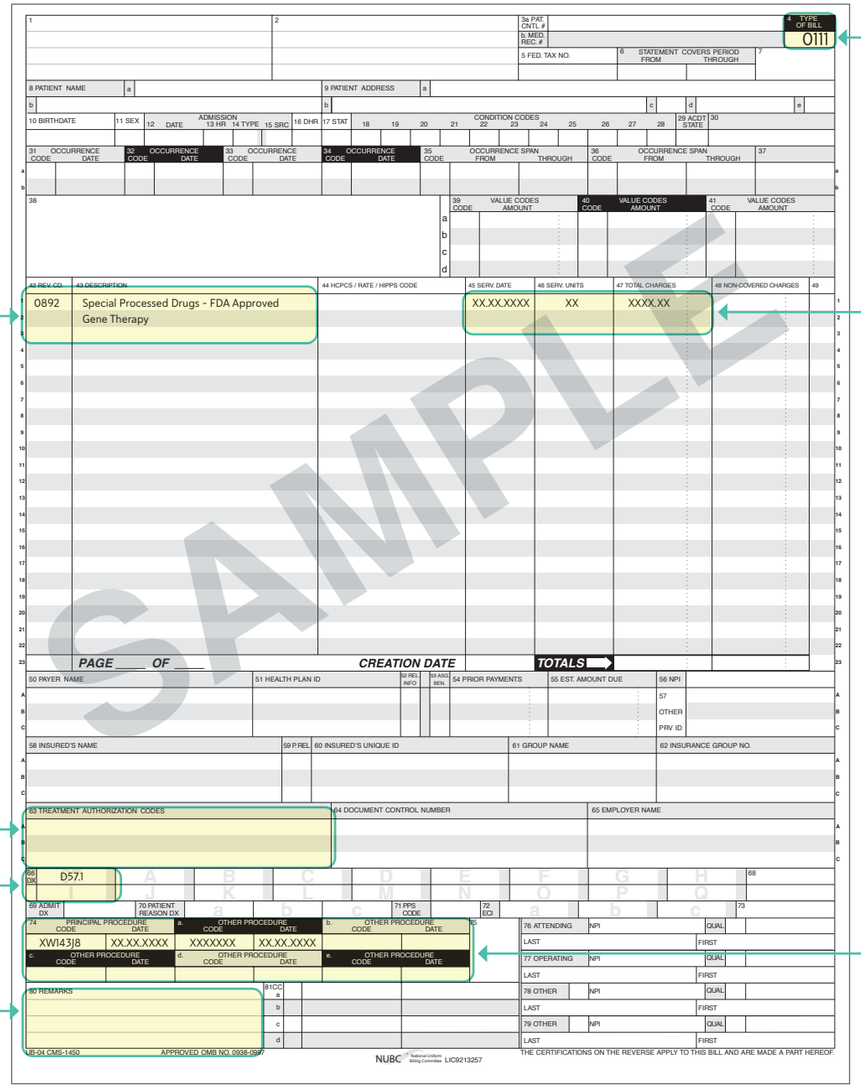
Field 63: Enter the treatment authorization code, if applicable

Fields 66 and 67: Enter the appropriate primary ICD-10-CM diagnosis code. For example[2]:

D57.1	Sickle-cell disease without crisis

For additional examples, see pages 6-7

Field 80: Enter any additional remarks or information required by the payer



Field 4: Enter the type of bill code. For example[1]:

011X	Hospital inpatient

"X" represents a placeholder for the fourth digit, which indicates the sequence of this bill in the particular episode of care

Fields 45, 46, and 47: Enter the corresponding date(s) of service, units of service, and the total charges for each reported line

Fields 74-74E: Enter the appropriate principal and secondary procedure codes (along with the corresponding dates). For example[3]:

XW143J8	Transfusion of Exagamglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8

Other procedure codes may apply; see page 8 for additional examples

FDA, US Food and Drug Administration; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NDC, National Drug Code.

1. Noridian Healthcare Solutions. Medicare Part A revenue codes. NoridianMedicare website. Updated December 9, 2023. Accessed January 16 2024. https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes **2.** Centers for Medicare & Medicaid Services (CMS). ICD-10-CM tabular list of diseases and injuries. CMS website. Updated June 29 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-code-tables-tabular-and-index-updated-06/29/2023.zip **3.** CMS. ICD-10-PCS code tables. CMS website. Updated December 19, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-icd-10-pcs-code-tables-and-index-updated-12/19/2023.zip

SAMPLE CMS 1500 CLAIM FORM

Requirements for specific fields may vary by payer; review payer-specific policies for claims billing.

Field 21: Enter the appropriate primary ICD-10-CM diagnosis code. For example[1]:

D57.1	Sickle-cell disease without crisis

For additional examples, see pages 6-7

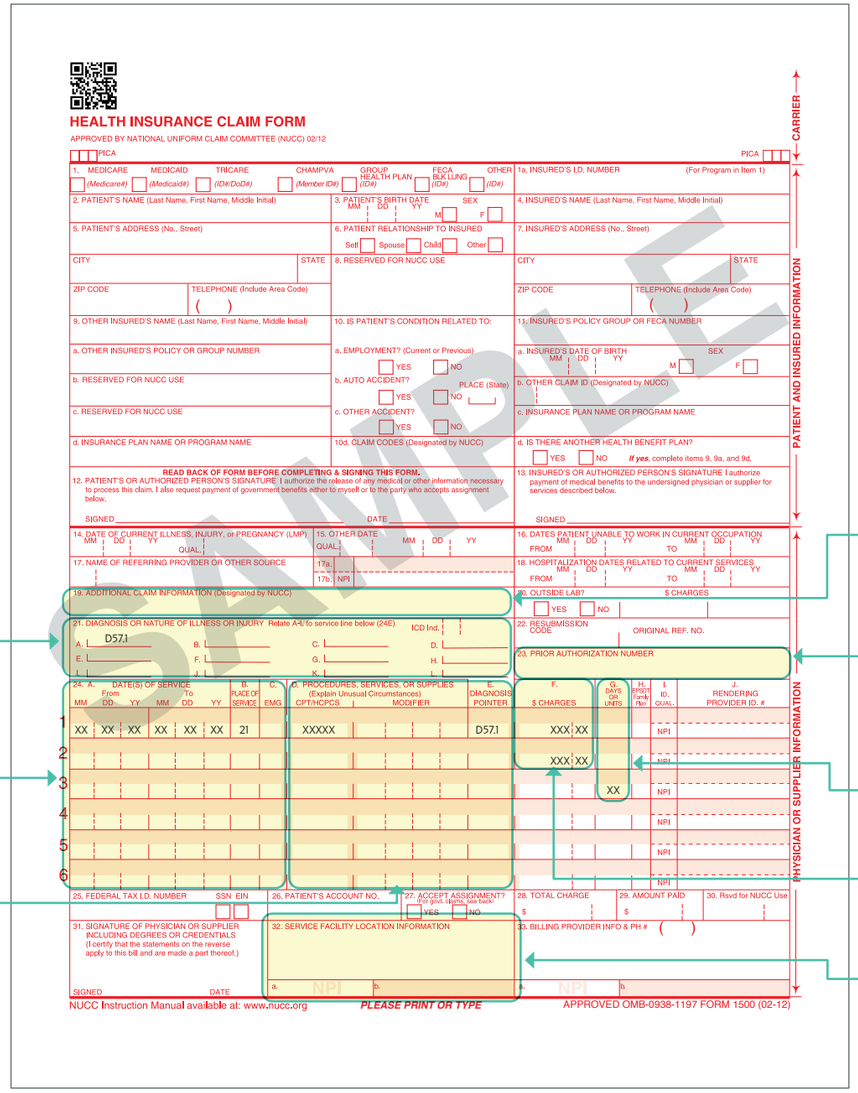
Fields 24A and 24B: Enter the appropriate dates for service for 24A and place of service, such as hospital inpatient, for 24B

Fields 24D and 24E: Enter the appropriate HCPCS Level I/CPT codes, along with applicable modifiers and date(s) of service, such as codes for cell mobilization, cell collection, cell processing, and stem cell infusion/transplantation. For example[2]:

38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous

For additional procedure codes, see appendix

For field **24E**, enter the corresponding diagnosis code reference from field 21



These sample claims are for informational purposes only and should not be relied upon to complete claims. The accurate completion of claims is the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

Field 19: Enter any additional information required by the payer when reporting physician professional services

Field 23: Enter the prior authorization number, if applicable

Field 24G: Enter the appropriate units of service

Field 24F: Enter the charges for each reported line

Field 32: Enter the service facility location

CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

1. Centers for Medicare & Medicaid Services (CMS). ICD-10-CM tabular list of diseases and injuries. CMS website. Updated June 29, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-code-tables-tabular-and-index-updated-06/29/2023.zip **2.** American Medical Association. CPT 2023 professional edition. Accessed January 11, 2024. https://ama.gilmoreglobal.com/en/product/ceb501e8-e3d4-4f09-a1af-76b4627b07db [subscription required]

CODING CONSIDERATIONS FOR SERVICES IN THE INPATIENT HOSPITAL SETTING RELATED TO CASGEVY™[1-4]

The table below provides a partial list of codes.

Service/ Item Description	ICD-10-PCS		Revenue[b]		MS-DRG	
	Code	Description	Code	Description	Group	Description
Mobilization[a]	3E033GC [OR] 3E043GC	Introduction of Other Therapeutic Substance into Peripheral Vein, Percutaneous Approach	0250	Pharmacy - General	951	Other factors influencing health status
			0636	Pharmacy - Drugs requiring detailed coding		
		Introduction of Other Therapeutic Substance into Central Vein, Percutaneous Approach	0260	IV Therapy - General		
Apheresis[a]	6A550ZV [OR] 6A551ZV	Pheresis of Hematopoietic Stem Cells, Single	0871	Cell/Gene Therapy - Cell Collection		
		Pheresis of Hematopoietic Stem Cells, Multiple	0761	Specialty Services - Treatment Room		
Myeloablative Conditioning	3E03305 [OR] 3E04305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach	0250	Pharmacy - General	016 [OR] 017	Autologous bone marrow transplant with [OR] without complication or comorbidity (CC)/major complication or comorbidity (MCC)
			0636	Pharmacy - Drugs requiring detailed coding		
		Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach	0335	Radiology/Therapeutic - Chemotherapy IV		
CASGEVY Administration	XW133J8 [OR] XW143J8	Transfusion of Exagamglogene Autotemcel into Peripheral Vein, Percutaneous Approach, New Technology Group 8	0874	Cell/Gene Therapy - Infusion of Modified Cells		
			0761	Specialty Services - Treatment Room		
		Transfusion of Exagamglogene Autotemcel into Central Vein, Percutaneous Approach, New Technology Group 8	0940	Other Therapeutic Services - General		

The time frame for each step of the CASGEVY treatment journey is approximate and will vary per patient. The entire CASGEVY treatment journey could take up to a year. The selection of codes and modifiers and the accurate completion of claims are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

[a]If the volume of cells collected and/or the manufactured cell dose is below the minimum requirement, steps will need to be repeated.[1]

[b]The revenue codes included here may be relevant for services related to CASGEVY. According to CMS guidance, hospitals should determine which department (ie, cost center) performs the service and select the revenue code that corresponds to that department in the hospital's cost report.[5]

CMS, Centers for Medicare & Medicaid Services; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS, International Classification of Diseases, Tenth Revision, Procedure Coding System; IV, intravenous; MS-DRG, Medicare Severity-Diagnosis Related Group.

1. CASGEVY [prescribing information]. Vertex Pharmaceuticals Incorporated. Boston, MA; January 2024. **2.** Centers for Medicare & Medicaid Services (CMS). ICD-10-PCS code tables. CMS website. Updated December 19, 2023. Accessed January 15, 2024. https://www.cms.gov/files/zip/2024-icd-10-pcs-code-tables-and-index-updated-12/19/2023.zip **3.** Noridian Healthcare Solutions. Medicare Part A revenue codes. NoridianMedicare website. Updated December 9, 2023. Accessed January 16, 2024. https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes **4.** CMS. ICD-10-CM/PCS MS-DRG v41. 0 Definitions Manual. CMS website. Updated March 1, 2023. Accessed January 16, 2024. https://www.cms.gov/icd10m/FY2024-nprmversion41.0-fullcode-cms/fullcode_cms/P0380.html **5.** CMS. Medicare Claims Processing Manual: Chapter 4 - Part B Hospital. CMS website. Published December 21, 2023. Accessed January 16, 2024. https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c04.pdf

Useful Access Practices

COORDINATION OF BENEFITS AND PRIOR AUTHORIZATION

Prior authorization is a common process required by payers that necessitates providers submitting clinical documentation and medical evidence to support why a therapy or service is medically necessary and appropriate for a patient. Prior authorization is a preliminary determination of coverage by the payer, but the payer always reserves the right to re-review the documentation either pre- or post-payment to make a final coverage determination. Some payers may have unique processes set up specifically for cell and genetic therapies such as CASGEVY™, so please check each patient's payer for requirements.

Navigating the prior authorization process requires a multistep approach. Review the following considerations in evaluating and completing the prior authorization process.

ELIGIBILITY

The patient's eligibility can be determined with each applicable insurance plan

- Consider checking whether or not the patient has a supplemental catastrophic insurance plan
- The coordination of benefits steps may be performed according to what is determined by the plan's eligibility criteria

COVERAGE AND BENEFIT IDENTIFICATION

Review the payer's published medical policies

- Check the patient's eligibility against all listed criteria, including the following:
  - Patient's diagnoses
  - Prior regimens and lines of therapy and patient's treatment response
  - Patient's overall fitness for the therapy

Confirm whether medical and hospital benefits exist for each component of treatment with CASGEVY

- May include the following components:
  - Cell mobilization and collection
  - Conditioning
  - Infusion of stem cells
  - Post-infusion care and monitoring
- Do this for each plan for which the patient is enrolled and has eligibility

Determine if inpatient hospital or maximum benefit limits may be reached during treatment

- If yes, apply coordination of benefits steps and any applicable financial assistance policies

PRIOR AUTHORIZATION PROCESSES

PREPARING THE REQUEST

Consider that multiple prior authorizations may be necessary during the treatment episode

- May include the following instances:
  - Clinical evaluation of patient
  - CASGEVY™ product
  - Transplant episode of care
    - Cell mobilization
    - Collection and processing
    - Conditioning
    - Infusion of stem cells
  - Post-infusion care and monitoring

The accurate completion of claims is the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

SUBMITTING THE REQUEST

Review coverage and documentation requirements of the patient's payer

Organize the patient's information and applicable medical records in a way that facilitates the payer's review

- Provide the payer with a concise summary of the treatment and why it is medically necessary for the patient, including relevant peer-reviewed journal publication references
- If necessary, include a summary of the most pertinent information and its location in the records
  - A submission of prior medical records may not be sufficient to help the payer understand the necessity of the treatment
- If the patient's clinician will be involved in a peer-to-peer discussion with the payer, it is important to provide the submitted documentation to the clinician

Reconfirm patient eligibility and authorizations prior to treatment with CASGEVY

Note each prior authorization approval number in the patient's medical record for use during billing

APPEALING A DENIAL

If necessary, follow the payer's appeal process[a]

- Review the payer's notice of denial, which will contain information about the rationale for the denial and instructions for how to submit an appeal

Draft a letter of appeal that summarizes the payer's reason(s) for the denial and why those reasons are not valid

- Provide a concise rationale in response to each reason listed in the denial
- Include peer-reviewed journal publications/references that support the clinical rationale

Write a summary that includes why the therapy is medically necessary for the patient

- Include the following information:
  - The patient's relevant medical history
  - Previous lines of treatment and therapy response
  - Prognostic factors for the patient
  - Information on clinical fitness and how it relates to the patient's need for the treatment
  - Treatment guidelines and recognized compendia
- **It is not recommended to include copies of medical records without a written summary**

[a]There are typically several levels to advance an appeal of a denied authorization.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions
Hypersensitivity reactions, including anaphylaxis can occur due to dimethyl sulfoxide (DMSO) or dextran 40 in the cryopreservative solution. Monitor patients for hypersensitivity reactions during and after infusion.

Off-Target Genome Editing Risk
Although off-target genome editing was not observed in the edited CD34⁺ cells evaluated from healthy donors and patients, the risk of unintended, off-target editing in an individual's CD34⁺ cells cannot be ruled out due to genetic variants. The clinical significance of potential off-target editing is unknown.

ADVERSE REACTIONS

The most common Grade 3 or 4 non-laboratory adverse reactions (occurring in ≥ 25%) were mucositis and febrile neutropenia in patients with SCD and patients with TDT, and decreased appetite in patients with SCD.

All (100%) of the patients with TDT and SCD experienced Grade 3 or 4 neutropenia and thrombocytopenia. Other common Grade 3 or 4 laboratory abnormalities (≥ 50%) include leukopenia, anemia, and lymphopenia.

DRUG INTERACTIONS

No formal drug interaction studies have been performed. CASGEVY™ is not expected to interact with the hepatic cytochrome P450 family of enzymes or drug transporters.

Use of Granulocyte-Colony Stimulating Factor (G-CSF): G-CSF must not be used for CD34⁺ HSC mobilization of patients with SCD.

Use of Hydroxyurea: Discontinue the use of hydroxyurea at least 8 weeks prior to start of each mobilization cycle and conditioning. There is no experience of the use of hydroxyurea after CASGEVY infusion.

Use of Voxelotor and Crizanlizumab: Discontinue the use of voxelotor and crizanlizumab at least 8 weeks prior to start of mobilization and conditioning, as their interaction potential with mobilization and myeloablative conditioning agents is not known.

Use of Iron Chelators: Discontinue the use of iron chelators at least 7 days prior to initiation of myeloablative conditioning, due to potential interaction with the conditioning agent. Some iron chelators are myelosuppressive. If iron chelation is required, avoid the use of non-myelosuppressive iron chelators for at least 3 months and use of myelosuppressive iron chelators for at least 6 months after CASGEVY infusion. Phlebotomy can be used instead of iron chelation, when appropriate.

USE IN SPECIFIC POPULATIONS

Pregnancy/Lactation: CASGEVY must not be administered during pregnancy and breastfeeding should be discontinued during conditioning because of the risks associated with myeloablative conditioning. Pregnancy and breastfeeding after CASGEVY 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 each mobilization cycle and reconfirmed prior to myeloablative conditioning.

Women of childbearing potential and men capable of fathering a child should use effective methods of contraception from start of mobilization through at least 6 months after administration of CASGEVY. Advise patients of the risks associated with conditioning agents.

Infertility has been observed with myeloablative conditioning therefore, advise patients of fertility preservation options before treatment, if appropriate.

Please see full Prescribing Information for CASGEVY™.

Appendix

PHYSICIAN BILLING

CASGEVY™ is genetically modified from each patient's hematopoietic stem cells, which must be collected from the patient after stem cell mobilization. Physicians may bill for professional services that they render to hospital inpatients, such as for stem cell collection and the transplantation of CASGEVY, by using CPT codes in the CMS 1500 claim.

The codes in the following table may be used on professional claims to describe the collection, processing, and administration of CASGEVY. This table is not comprehensive. Other codes may be applicable for physician billing of services associated with CASGEVY.

The selection of procedure codes and applicable modifiers, as well as the accurate completion of supporting documentation and claims, are the sole responsibility of the healthcare provider. Vertex does not guarantee coverage or reimbursement for any service or item.

TYPE OF SERVICE	PROCEDURE CODE	DESCRIPTION
Cell Collection[1]	**38206**	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
Cell Processing[1]	**38207**	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
	38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
CASGEVY Administration[1]	**38241**	Hematopoietic progenitor cell (HPC); autologous transplantation

CMS, Centers for Medicare & Medicaid Services; CPT, Current Procedural Terminology.

1. American Medical Association. CPT 2023 professional edition. Accessed January 11, 2024. https://ama.gilmoreglobal.com/en/product/ceb501e8-e3d4-4f09-a1af-76b4627b07db [subscription required]

Please see Important Safety Information on pages 2 and 16 and full Prescribing Information for CASGEVY™.