DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

CENTER FOR MEDICARE

ICD-10 Coordination and Maintenance Committee Meeting
ICD-10-PCS Therapeutic Agent Topics

Consistent with the requirements of section 1886(d)(5)(K)(iii) of the Social Security Act, applicants submitted requests to create a unique procedure code to describe the administration of a therapeutic agent, such as the option to create a new code in Section X within the International Classification of Diseases, 10th Revision, Procedure Coding System (ICD-10-PCS). CMS is soliciting public comments on the proposed coding options and any clinical questions for two procedure code topics associated with new technology add-on payment (NTAP)-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent. The deadline to submit comments for topics being considered for an April 1, 2023 implementation is October 14, 2022 and the deadline to submit comments for topics being considered for an October 1, 2023 implementation is November 14, 2022. Members of the public should send any questions or comments to the CMS mailbox at: ICDProcedureCodeRequest@cms.hhs.gov.

Prior to the meeting, CMS will post a question and answer document on our website at https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials to address clinical or coding questions that members of the public have submitted related to the two therapeutic agents, as discussed in the following pages. At a later date, CMS will post an updated question and answer document to address any additional clinical or coding questions that members of the public may have submitted by the October 14, 2022 or November 14, 2022 deadline, respectively.

CMS will not be presenting the NTAP-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent at the upcoming virtual meeting on September 13-14, 2022. CMS will present the NTAP-related ICD-10-PCS procedure code requests that do not involve the administration of a therapeutic agent and all non-NTAP-related procedure code requests during the virtual meeting on September 13, 2022.

Comments on these procedure code proposals should be sent to the following email address: ICDProcedureCodeRequest@cms.hhs.gov

Instructions for Joining the ICD-10 Coordination and Maintenance Committee Meetings Govdelivery Subscriber List

To sign up go to CMS website:
https://public.govdelivery.com/accounts/USCMS/subscriber/new?topic_id=USCMS_124 20

To sign up for updates or to access your subscriber preferences, please enter your contact information below.

1. Email Address

Submit

2. A new subscriber screen will appear. Confirm your primary email address.
3. Select an Email delivery preference.
4. Enter an optional password to add password protection to your subscriber preferences.
5. Check privacy box confirming your consent to our data privacy. Additional information on our data privacy policy can be found at www.cms.gov/privacy.
6. You should receive a SUCCESS message that states (your email address) has been successfully subscribed to ICD-10 Coordination and Maintenance
7. Click on the Finish button at bottom of screen.
8. You should now be on the Welcome Quick subscribe page. You can subscribe to receive information from a list of topics of your choice from our partner organizations by checking the boxes; unsubscribe by unchecking the boxes.
9. Scroll down to the bottom of the page. Check the data privacy policy box and click on Submit. Additional information on our data privacy policy can be found at www.cms.gov/privacy.
10. You should have now reached the SUCCESS page confirming that you have been successfully subscribed. Click on Finish.

NTAP-Related ICD-10-PCS Procedure Code Requests That Involve Administration of a Therapeutic Agent

**Requestor intends to submit an NTAP application for FY 2024 consideration.*
***Request is for an April 1, 2023 implementation date. The requestor intends to submit an NTAP application.*

The slide presentations for these procedure code topics are available at: https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.

ICD-10 TIMELINE

A timeline of important dates in the ICD-10 process is described below:

September 13-14, 2022	The September 2022 ICD-10 Coordination and Maintenance Committee Meeting.
September 2022	Recordings and slide presentations of the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
October 1, 2022	New and revised ICD-10-CM and ICD-10-PCS codes go into effect along with MS-DRG changes. Final addendum available on web pages as follows: **Diagnosis addendum –** https://www.cdc.gov/nchs/icd/icd10cm.htm **Procedure addendum –** https://www.cms.gov/medicare/coding/icd10
October 14, 2022	**Deadline for receipt of public comments on proposed new codes discussed at the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2023.**
November 2022	Any new ICD-10 codes required to capture new diseases or technology that will be implemented on the following April 1 will be announced. Information on any new codes to be implemented April 1, 2023 will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd10cm.htm https://www.cms.gov/medicare/coding/icd10
November 14, 2022	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2023.**

December 2, 2022	**Deadline for requestors: Those members of the public requesting that topics be discussed at the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting must have their requests submitted to CMS for procedures and to NCHS for diagnoses by this date.** Procedure code requests should be directed to CMS at https://mearis.cms.gov. Diagnosis code requests should be directed to NCHS at nchsicd10cm@cdc.gov. Requestors should indicate if they are submitting their code request for consideration for an October 1, 2023 implementation date or an April 1, 2024 implementation date.
January 2023	The ICD-10 Coordination and Maintenance Committee will make efforts to accommodate the requested implementation date for each request submitted, however, the Committee will determine which requests will be presented for consideration for an October 1, 2023 implementation date or an April 1, 2024 implementation date. Federal Register notice for the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
February 2023	Tentative agenda for the Procedure portion of the March 7, 2023 ICD-10 Coordination and Maintenance Committee Meeting posted on CMS webpage as follows: https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html Tentative agenda for the Diagnosis portion of the March 8, 2023 ICD-10 Coordination and Maintenance Committee Meeting posted on NCHS homepage as follows: https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm
February 1, 2023	ICD-10 MS-DRG Grouper software and related materials posted on CMS webpage at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/MS-DRG-Classifications-and-Software
February 1, 2023	Any updates to the ICD-10-CM and ICD-10-PCS Coding Guidelines will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd10cm.htm https://www.cms.gov/medicare/coding/icd10

February 1, 2023	All ICD-10-CM and ICD-10-PCS code update files (includes April 1 update and full files from prior October 1) will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd10cm.htm https://www.cms.gov/medicare/coding/icd10
March 7-8, 2023	ICD-10 Coordination and Maintenance Committee Meeting.
March 2023	Recordings and slide presentations of the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
April 1, 2023	Any new ICD-10 codes will be implemented on April 1, 2023.
April 7, 2023	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2023**.
April 2023	Notice of Proposed Rulemaking to be published in the Federal Register as mandated by Public Law 99-509. This notice will include references to the FY 2024 ICD-10-CM diagnosis and ICD-10-PCS procedure codes finalized to date. It will also include proposed revisions to the MS-DRG system based on ICD-10-CM/PCS codes on which the public may comment. The proposed rule can be accessed at: https://www.cms.gov/medicare/medicare-fee-for-service-payment/acuteinpatientpps
May 5, 2023	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2024.** **Deadline for receipt of public comments on proposed new diagnosis codes and revisions discussed at the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2024**.

May/June 2023	Final addendum posted on web pages as follows: **Diagnosis addendum -** https://www.cdc.gov/nchs/icd/icd10cm.htm **Procedure addendum -** https://www.cms.gov/medicare/coding/icd10
June 9, 2023	**Deadline for requestors: Those members of the public requesting that topics be discussed at the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting, must have their requests submitted to CMS for procedures and NCHS for diagnoses.** Requestors should indicate if they are submitting their code request for consideration for an April 1, 2024 implementation date or an October 1, 2024 implementation date.
July 2023	Federal Register notice for the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
August 1, 2023	Hospital Inpatient Prospective Payment System final rule expected to be published in the Federal Register as mandated by Public Law 99-509. This rule will also include links to all the final codes to be implemented on October 1, 2023. This rule can be accessed at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/index.html
August 2023	Tentative agenda for the Procedure portion of the September 12, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the CMS webpage at – https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html Tentative agenda for the Diagnosis portion of the September 13, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the NCHS webpage at - https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm
September 12-13, 2023	The September 2023 ICD-10 Coordination and Maintenance Committee Meeting is anticipated to be fully virtual by zoom and dial-in. Those who wish to attend must participate via Zoom Webinar or by dialing in.

September 2023	Recordings and slide presentations of the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
October 1, 2023	New and revised ICD-10-CM and ICD-10-PCS codes go into effect along with MS-DRG changes. Final addendum available on web pages as follows: **Diagnosis addendum –** https://www.cdc.gov/nchs/icd/icd10cm.htm **Procedure addendum –** https://www.cms.gov/medicare/coding/icd10
October 13, 2023	**Deadline for receipt of public comments on proposed new codes discussed at the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2024.**
November 2023	Any new ICD-10 codes that will be implemented on the following April 1 will be announced. Information on any new codes to be implemented April 1, 2024 will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd10cm.htm https://www.cms.gov/medicare/coding/icd10
November 15, 2023	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2024.**

Medicare Electronic Application Request Information System™ (MEARIS™)

Effective January 5, 2022, the new electronic application request intake system, Medicare Electronic Application Request Information System™ (MEARIS™), became available as an initial release for users to begin gaining familiarity with a new approach and process to submit ICD-10-PCS procedure code requests. The ICD-10-PCS code request application can be accessed at: https://mearis.cms.gov. We encouraged users to register and begin using this system to provide feedback on their experience with this initial version.

Effective March 1, 2022, the full release of MEARIS™ became active for ICD-10-PCS code request submissions.

CMS will only accept ICD-10-PCS code request applications submitted via MEARIS™. Requests submitted through the ICDProcedureCodeRequest mailbox will no longer be considered. Within MEARIS™, we have built in several resources to support requestors:

- Please refer to the "Resources" section for guidance regarding the request submission process at: https://mearis.cms.gov/public/resources.
- Technical support is available under "Useful Links" at the bottom of the MEARIS™ site
- Request related questions can be submitted to CMS using the form available under "Contact" at: https://mearis.cms.gov/public/resources?app=icd-10-pcs
- The time required for application request submission, including the time needed to gather relevant information as well as to complete the form may be extensive depending on the nature of the code request. Requestors are, therefore, encouraged to start in advance of the due date to ensure adequate time for submission.

Requests submitted through MEARIS™ will not only help CMS track requests and streamline the review process, but it will also create efficiencies for requestors when compared to the previous submission process.

ICD-10-PCS code request submissions are due no later than December 2, 2022 to be considered for the March 7-8, 2023 ICD-10 Coordination and Maintenance Committee Meeting.

Introductions and Overview

- ICD-10 Coordination & Maintenance (C&M) Committee meeting is a public forum on ICD-10-CM & ICD-10-PCS code updates
- CMS & CDC Co-chair the meetings
  - CMS has lead responsibility on procedure issues
  - CDC has lead responsibility on diagnosis issues
- Coding proposals requested by the public are presented and public given opportunity to comment

Code Proposals

- ICD-10-PCS code proposals being considered for implementation on April 1, 2023 and October 1, 2023
- No final decisions are made at the meeting
- CMS will describe options and recommendations to facilitate discussion
- Public can comment during the meeting and send written comments

Comments on Code Proposals

- Submit written comments by
  - October 14, 2022 for codes being considered for April 1, 2023 implementation
  - November 14, 2022 for codes being considered for October 1, 2023 implementation
- Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
- Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

Proposed and Final Rules

- April 2022 – Notice of Proposed Rulemaking, IPPS
  - Includes ICD-10-CM/PCS diagnosis and procedure updates approved prior to March 2022 C&M meeting
- August 2022 – Final rule with links to final codes to be implemented October 1, 2022
  - Includes any additional codes approved from March 8-9, 2022 C&M meeting
  - https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS

Addendum

- May/June 2022 – Final code updates and addendum posted
  - FY 2023 ICD-10-PCS (Procedures) https://www.cms.gov/medicare/coding/icd10
  - FY 2023 ICD-10-CM (Diagnoses) http://www.cdc.gov/nchs/icd/icd10cm.htm

Public Participation

- For the virtual meeting, the public may participate in the following ways:
  - Participate via Zoom Webinar
  - Listen to proceedings through free conference lines
  - Listen to recordings and view slide presentations

- CMS & CDC hope this provides greater opportunity for public participation

Written Comments

- No matter how you participate – please send written comments by
  - October 14, 2022 for codes being considered for April 1, 2023 implementation
  - November 14, 2022 for codes being considered for October 1, 2023 implementation
  - Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
  - Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

ICD-10-PCS Codes Implementation

- ICD-10-PCS codes are under consideration for April 1, 2023 or October 1, 2023 implementation

March 7-8, 2023 C&M Code Requests

- December 2, 2022 – Deadline for submitting topics for March 7-8, 2023 C&M meeting
  - Procedure requests to CMS: https://mearis.cms.gov
  - Diagnosis requests to NCHS: nchsicd10cm@cdc.gov

    Requestors should indicate if they are submitting their code request for consideration for an October 1, 2023 implementation date or an April 1, 2024 implementation date.

Topic # 01 - Administration of Lovotibeglogene autotemcel (lovo-cel)

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of lovotibeglogene autotemcel (lovo-cel), an autologous ex vivo gene addition therapy.

New Technology Application? Yes. The requestor intends to submit a New Technology Add-on Payment (NTAP) application for FY 2024 consideration.

Food & Drug Administration (FDA) Approval? No. A Biologics License Application (BLA) is projected to be submitted to the FDA in the first quarter of 2023, with a request for Priority Review.

Background: Sickle cell disease (SCD)[1] is a serious, progressive and debilitating genetic disease caused by a single mutation in the Beta (β)-globin gene that leads to the production of abnormal sickle hemoglobin (HbS).[2,3,4] In low oxygen conditions, high HbS concentrations cause red blood cells (RBCs) to become sickled, sticky and rigid with a shorter lifespan, which manifests acutely as hemolytic anemia, vasculopathy and vaso-occlusion.[2-4] Repeated, painful vaso-occlusive events (VOEs), progressive vasculopathy and prolonged hemolytic anemia can result in chronic complications leading to disease progression and end-organ damage.[2,3] Chronic complications of SCD increase in prevalence and severity with age.[5,6] The median age of survival of patients with SCD is estimated to be in the fifth or sixth decade of life, which is about 20-30 years shorter than the general population.[7]

Current management of SCD relies on the lifelong use of acute and chronic therapies with suboptimal clinical benefits. Despite these therapies, patients continue to experience clinical symptoms, progressive organ damage, and other substantial morbidities, which contribute to decreased quality of life, sociopsychological challenges, significant healthcare resource utilization, and early mortality.[2,8,9] Allogeneic hematopoietic-cell transplantation with matched sibling donor (MSD) remains the sole potentially curative treatment, though its use is limited by donor availability and the risk of graft-versus-host disease and graft rejection.[2,10]

Lovotibeglogene autotemcel (lovo-cel) is an investigational one-time ex vivo gene addition therapy product being evaluated for the treatment of sickle cell disease (SCD).[1] According to the requestor, lovo-cel has the potential to treat the pathophysiological basis of the disease, reducing or eliminating downstream complications. A recent publication in the *New England Journal of Medicine*[11] reported interim analyses of efficacy and safety for patients with SCD treated with lovo-cel in the ongoing open label non-randomized Phase 1/2 study HGB-206.[1] As reported by Kanter et al,[9] as of the February 17, 2021 data cutoff, there had been no reports of graft versus host

[1] https://clinicaltrials.gov/ct2/show/NCT02140554?term=lentiglobin&cond=sickle+cell&draw=2&rank=2
[2] Kato GJ, et al. Nat Rev Dis Primers. 2018;4:18010.
[3] Sundd P, et al. Annu Rev Pathol. 2019;14:263-292.
[4] Ware RE, et al. Lancet. 2017;390:311–323
[5] Kanter, et al. Blood Rev. 2013;27(6):279- 287.
[6] Serjeant, GR. Cold Spring Harb Perspect Med. 2013;3(10):a011783.
[7] Elmariah H, et al. Am J Hematol. 2014;89(5):530-535.
[8] Buchanan GR, et al. 2014. Available at https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf.
[9] Brousseau DC, et al. JAMA. 2010;303(13) :1288-1294.
[10]Shenoy S. Hematology Am Soc Hematol Educ Program. 2011;2011:273-279.
[11] Kanter J, et al. N Engl J Med. 2022;386:617-628.

disease (GvHD), graft failure, replication-competent lentivirus, or vector-mediated insertional oncogenesis in subjects from Group C or any subject treated in HGB-206. The safety data from Group C patients in HGB-206 remain generally consistent with the known side effects of autologous hematopoietic stem cell collection and myeloablative single-agent busulfan conditioning, as well as underlying SCD.

Mechanism of Action
Gene therapy with lovo-cel consists of the autologous transplantation of hematopoietic stem and progenitor cells (HSPCs) transduced with the BB305 lentiviral vector encoding a modified β-globin gene, which results in the production of antisickling hemoglobin HbA^{T87Q}. HbA^{T87Q} is a modified adult hemoglobin (Hb) with an amino-acid substitution (threonine to glutamine at position 87) designed to sterically inhibit polymerization of HbS.[11] Lovo-cel administration results in the engraftment of hematopoietic stem cells (HSCs) containing the $\beta^{A\text{-}T87Q}$-globin gene permanently integrated into their genomic DNA, enabling durable expression of $\beta^{A\text{-}T87Q}$-globin, which prevents the root cause of the disease burden of SCD (polymerization of HbS) by increasing total hemoglobin (Hb) concentration and therefore decreasing the concentration of HbS in the blood.[12,13,14]

Inpatient Administration of Lovotibeglogene autotemcel (lovo-cel)
Lovo-cel is a cell suspension for intravenous infusion. The minimum recommended dose is 3.0×10^6 CD34+ cells/kg, shipped to the hospital in one or more (up to four) patient-specific infusion bags, in metal cassette(s) in a cryoshipper.

The treatment regimen for SCD patients treated with lovo-cel comprises mobilization/apheresis to collect the patient's own stem cells, manufacturing of the gene therapy product utilizing those cells as the starting material (during which the patient remains out of the hospital), myeloablative conditioning, intravenous infusion of lovo-cel and recovery (during which the patient is in hospital). The lovo-cel infusion should be completed as soon as possible and no more than four hours after thawing. Each infusion bag will be administered via intravenous infusion over a period of less than 30 minutes. If there is more than one infusion bag, the entire volume of each must be infused consecutively. The myeloablative conditioning, lovo-cel infusion and monitoring through engraftment is expected to occur in the inpatient setting. In most cases, the mobilization and apheresis procedures also take place in the inpatient setting. Similar to an autologous or allogeneic stem cell transplant, following lovo-cel infusion the patient is expected to remain hospitalized for a period of time to allow for engraftment and reconstitution of the immune system. As reported by Kanter et al, 2022, in the interim analysis of Study HGB-206 Group C, the median (min, max) duration of hospitalization from admission for myeloablative conditioning to post-infusion discharge was 35 (26, 65) days (N=35).[9]

Current Coding: There are no unique ICD-10-PCS codes to describe the intravenous transfusion of lovotibeglogene autotemcel (lovo-cel). Facilities can report the intravenous transfusion of lovotibeglogene autotemcel (lovo-cel) with one of the following ICD-10-PCS codes:

[12] Kato GJ, et al. Blood Rev. 2007;21:37-47.
[13] Shaeffer JR, et al. Nature. 1978;276 :631-3.
[14] Ngo DA, et al. Br J Haematol. 2012;156 :259-64.

30233C0	Transfusion of autologous hematopoietic stem/progenitor cells, genetically modified into peripheral vein, percutaneous approach
30243C0	Transfusion of autologous hematopoietic stem/progenitor cells, genetically modified into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous transfusion of lovotibeglogene autotemcel (lovo-cel). Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous transfusion of lovotibeglogene autotemcel (lovo-cel).

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**1** Transfusion: Putting in blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD H** Lovotibeglogene Autotemcel	**ADD 9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

Interim Coding Advice: Continue using current codes as listed in current coding.

Topic # 02 - Administration of Exagamglogene autotemcel (exa-cel)

Issue: There are no unique ICD-10-PCS codes to describe the administration of exagamglogene autotemcel (exa-cel), an autologous ex vivo gene-edited biological product.

New Technology Application? Yes. The requestor intends to submit a New Technology Add-on Payment (NTAP) application. The requestor is seeking an April 1, 2023 implementation date.

Food & Drug Administration (FDA) Approval? No.

Background: The Beta (β)-hemoglobinopathies, which include β-thalassemia and sickle cell disease (SCD), are among the most prevalent monogenic (meaning caused by variation in a single gene) disorders worldwide. β-thalassemia is an autosomal recessive disease caused by a mutation in or near the beta-globin (HBB) gene that results in reduced or absent production of functional beta-globin. When beta-globin is absent, alpha-globin and its degradation products precipitate, which can cause intracellular hemichrome precipitation, ineffective erythropoiesis, chronic hemolysis, and profound anemia. In transfusion-dependent β-thalassemia (TDT), the most clinically severe form of the disease, patients require long-term red-cell transfusions for survival and the prevention of serious complications.

SCD is an autosomal recessive disease caused by a specific mutation in the HBB gene that creates an amino acid substitution that produces hemoglobin S (Hb S). For the disease to manifest, there must be homozygosity for HB S or compound heterozygosity for Hb S and a pathogenic variant at the other HBB allele such as beta thalassemia or hemoglobin C. Sickle red blood can become misshapen and rigid, making it difficult to pass through small blood vessels and slowing or blocking blood flow. This in turn can compromise oxygen delivery to different tissues and organs, causing damage and inflammation. Blood vessel blockage also can result in episodes of sudden and severe pain known as vaso-occlusive crises (VOCs). Sickle red blood cells have a shorter lifespan and undergo intravascular and extravascular hemolysis causing a shortage of red blood cells, or anemia, the most common symptom of the disease.

The current standard of care for patients with TDT consists of lifelong, regular red-cell transfusions and iron chelation. The risks of serious complications from transfusion-related iron toxicity and viral infections persist despite improvements in care. In SCD, commonly used medications include antibiotics to prevent infections and painkillers to manage pain. Other treatments also are available to reduce the frequency of pain crises, including hydroxyurea and Adakveo (crizanlizumab). The only potentially curative option for both β-thalassemia and SCD is allogeneic hematopoietic-cell transplantation. Such transplants are complex, can require lifelong immunosuppression, and carry risks such as graft rejection, graft-versus-host disease, and other treatment-related toxic effects.

Exa-cel, also known as CTX001™, is an investigational, autologous, ex-vivo gene-edited therapy based on the clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated protein 9 (Cas9) gene-editing tool. CRISPR/Cas9 edits genes by precisely cutting DNA and then letting natural DNA repair processes take over. Exa-cel is designed to modify a patient's blood cell precursors to produce high levels of fetal hemoglobin (HbF). HbF is a form of oxygen-carrying hemoglobin found in newborn red blood cells that transports oxygen more efficiently than

its adult equivalent (Hb). HbF can substitute for the diseased hemoglobin in TDT and SCD patients, reducing or eliminating symptoms.

Mechanism of Action
As a therapy, exa-cel involves isolating a patient's own hematopoietic stem cells (HSCs), editing them with CRISPR/Cas9 to increase HbF in the red blood cells, and then returning the edited cells to the patient through a stem cell transplant. The target of CRISPR/Cas9 editing is the erythroid-specific enhancer region of BCL11A. Reducing BCL11A expression increases fetal hemoglobin expression. According to the requestor, the elevation of HbF by exa-cel has the potential to alleviate or eliminate transfusion requirements for patients with TDT and reduce painful and debilitating sickle crises for patients with SCD. Exa-cel is being studied in clinical trials. The safety data reported to date for exa-cel has been consistent with an autologous stem cell transplant and myeloablative conditioning with busulfan.

Inpatient Administration of Exagamglogene autotemcel (exa-cel)
Exa-cel is prepared from a patient's own HSCs, which are collected from the peripheral blood. The cells are edited at a manufacturing facility, cryopreserved and shipped back to the authorized treatment center (e.g., hospital). Once the cells are received at the authorized treatment center, the patient undergoes myeloablative conditioning with busulfan before the cells are infused. Exa-cel is then administered via a stem cell transplant procedure as a single dose through a central venous catheter, at least 48 hours and within 7 days after the last busulfan dose. Monitoring for adverse events and engraftment occurs along with the administration of any supportive therapy that may be required. Once engraftment occurs, the cells begin production of red blood cells that express fetal hemoglobin.

Current Coding: There are no unique ICD-10-PCS codes to describe the intravenous transfusion of exagamglogene autotemcel (exa-cel). Facilities can report the intravenous transfusion of exagamglogene autotemcel (exa-cel) with one of the following ICD-10-PCS codes:

30233C0	Transfusion of autologous hematopoietic stem/progenitor cells, genetically modified into peripheral vein, percutaneous approach
30243C0	Transfusion of autologous hematopoietic stem/progenitor cells, genetically modified into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous transfusion of exagamglogene autotemcel (exa-cel). Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous transfusion of exagamglogene autotemcel (exa-cel).

Section	**X** New Technology		
Body System	**W** Anatomical Regions		
Operation	**1** Transfusion: Putting in blood or blood products		
Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD J** Exagamglogene Autotemcel	**ADD 8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

Interim Coding Advice: Continue using current codes as listed in current coding.