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
March 7, 2023
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 the nine 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 October 1, 2023 implementation is April 7, 2023. Members of the public should send any questions or comments to CMS' ICD-10-PCS 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 nine therapeutic agents. 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 April 7, 2023 deadline.

CMS will not be presenting the nine NTAP-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent at the March 7, 2023 virtual meeting. 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 March 7, 2023.

Comments on all 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 the 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.

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2. A new subscriber screen will appear. Confirm your primary email address.
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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.
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NTAP-Related ICD-10-PCS Procedure Code Requests That Involve Administration of a Therapeutic Agent

** Requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2024.*
***Requestor intends to submit a NTAP application for FY 2026 consideration.*

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

Note: References may appear in either a topic background paper, the accompanying slide deck, or both.

ICD-10 TIMELINE

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

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	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/Comprehensive-Listing-of-ICD-10-CM-Files.htm **Procedure addendum -** https://www.cms.gov/Medicare/Coding/ICD10/index.html
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 to 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 will 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/Comprehensive-Listing-of-ICD-10-CM-Files.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/Comprehensive-Listing-of-ICD-10-CM-Files.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.

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 June 9, 2023 to be considered for the September 12-13, 2023 ICD-10 Coordination and Maintenance Committee Meeting.

An updated release for MEARIS™ was made publicly available in mid-October 2022 for users to continue submitting ICD-10-PCS code requests. The updated release provides additional resources including templates and sample background papers for submitting a code request for either the administration of a drug/therapeutic agent or for a device/technology/service or procedure.

Requests for new procedure codes must include both a background paper utilizing the format of the sample template provided and an accompanying 508 compliant presentation slide deck. Requestors must also indicate if the code request is for consideration for an October 1 implementation date or an April 1 implementation date at the time of submission to be considered complete.

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 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
  - April 7, 2023 for code updates being considered for October 1, 2023 implementation
  - May 5, 2023 for code updates being considered for April 1, 2024 or October 1, 2024 implementation
- Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
- Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

Proposed and Final Rules

- April 2023 – Notice of Proposed Rulemaking, IPPS
  - Includes ICD-10-CM/PCS diagnosis and procedure updates approved prior to March 2023 C&M meeting
- August 2023 – Final rule with links to final codes to be implemented October 1, 2023
  - Includes any additional codes approved from March 7-8, 2023 C&M meeting
  - https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS

Addenda

- May/June 2023 – Final code updates and addendum posted
  - FY 2024 ICD-10-PCS (Procedures) http://www.cms.gov/Medicare/Coding/ICD10/index.html
  - FY 2024 ICD-10-CM (Diagnoses) https://www.cdc.gov/nchs/icd/Comprehensive-Listing-of-ICD-10-CM-Files.htm

Public Participation

- For this 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
  - April 7, 2023 for updates being considered for October 1, 2023 implementation
  - May 5, 2023 for updates being considered for April 1, 2024 or October 1, 2024 implementation
  - Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
  - Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

September 12-13, 2023 C&M Code Requests

- June 9, 2023 – Deadline for submitting topics for September 12-13, 2023 C&M meeting
  - Procedure requests to CMS: https://mearis.cms.gov
  - Diagnosis requests to NCHS: nchsicd10cm@cdc.gov

Topic # 01 - Fluorescence-guided surgery using CYTALUX® (Pafolacianine)

Issue: There are currently no unique ICD-10-PCS codes to describe fluorescence-guided surgery using CYTALUX® (pafolacianine), an optical imaging agent used as an adjunct for intraoperative identification of ovarian cancer or lung cancer.

New Technology Application? Yes. The requestor has submitted two New Technology Add-on Payment (NTAP) applications for FY 2024 consideration. One is specific to ovarian cancer and the other is specific to known or suspected non-malignant or malignant cancer of the lung.

Food & Drug Administration (FDA) Approval? Yes. The requestor received FDA approval for CYTALUX® in the intraoperative identification of ovarian cancer (November 29, 2021) and for lung cancer (December 16, 2022). The FDA approved ovarian cancer indication is: CYTALUX® is indicated as an adjunct for intraoperative identification of malignant lesions in adult patients with ovarian cancer. The FDA approved lung cancer indication is: CYTALUX® is indicated as an adjunct for intraoperative identification of malignant and non-malignant pulmonary lesions in adult patients with known or suspected cancer in the lung.

Ovarian Cancer

Background: Approximately 22,000 women are diagnosed with ovarian cancer per year in the U.S. and 70% of patients diagnosed with ovarian cancer will have a recurrence. Ovarian cancer remains the leading cause of death from gynecologic malignancies and ranks fifth as a cause of cancer-related deaths among women.

The 5-year survival rate for extensive-stage disease remains low at 30% to 40%, with limited therapeutic options; and overall survival (OS) of patients with advanced-stage ovarian cancer showed little improvement in the last 30 years despite progress in surgery and therapy. Recurrent ovarian cancer remains a major challenge, and it is associated with > 80% patient mortality within 5 years.

Standard treatment of patients with ovarian cancer is debulking cytoreductive surgery and chemotherapy. The goal of a debulking operation is localization and accurate delineation of malignant and benign tissue to maximize removal of cancer, while minimizing removal of noncancerous tissue. The standard surgical approach is open surgery, although in selected cases, minimally invasive surgery has been shown to be safe regarding postoperative complications and short-term mortality. Tumor prognosis depends on the effectiveness of cytoreductive surgery in removing cancerous tissue. Debulking surgery followed by chemotherapy in most cases ends in recurrent chemo resistant disease. The amount of residual disease is an independent prognostic factor of survival, and the absence of macroscopic residual disease is associated with a significantly lower risk of recurrence. In a retrospective study of 496 eligible patients, those with residual disease of 1 to 10 mm had better progression-free survival and overall survival than patients left with residual disease greater than 10 mm. Studies have shown that complete resection of all macroscopic gynecologic disease (at primary or interval surgery) was the strongest independent variable in predicting overall survival.

Although tumor debulking surgery is the cornerstone of current treatment in patients, the lesions can be diffuse and numerous, of various sizes, and often not readily visible in the surgical field, leading to varying rates of optimal cytoreduction among surgeons. Patient survival is greater

among patients who receive complete cytoreduction.

Lung Cancer
Background: Lung cancer is the third most common cancer in the United States. The American Cancer Society approximates 236,740 new cases of lung cancer per year (117,910 in men and 118,830 in women). It is the leading cause of cancer deaths. It is estimated that there are 130,180 deaths from lung cancer (68,820 in men and 61,360 in women).

Surgery remains the cornerstone of lung cancer treatment which may provide disease-free long-term survival or possible cures. Preoperative radiologic evaluation is essential to determine the appropriateness of surgical resection and the type of resection. The standard major pulmonary operative procedures include sublobar resection, lobectomy, bilobectomy, and pneumonectomy. Sublobar resections include wedge resection for peripheral lesions and segmentectomy. These surgical procedures can be performed by standard access (i.e., thoracotomy) or thoracoscopic access.

Five-year survival rate for lung cancer remains concerningly low at 61.2% for localized disease and 33.5% for regional disease. 30-55% of patients who undergo surgical resection develop a recurrence and do not survive, and up to 24% of patients recur locally following lung cancer surgery. The rates of local recurrence suggest that surgeons are unable to completely detect and remove primary tumor nodules. One study showed 8-9% of patients had malignant lesions that were not identified by preoperative CT imaging and thus could be left behind during surgery. Positive surgical resection margins also contribute to the recurrence rate. An increased margin distance has been shown to be associated with a lower risk of local recurrence, with a 10-mm margin distance having a 45% lower recurrence risk than a 5-mm distance. During minimally invasive thoracic surgery, smaller and deeper nodules are not always able to be located. Surgical oncologists continue to strive for greater effectiveness in achieving complete resection of lung tumors. Incomplete resection of non-small cell lung cancer negatively impacts survival rates. Survival time following local recurrence, including those patients who receive salvage treatment is less than one year on average.

Mechanism of Action
CYTALUX® is a small molecule that circulates quickly through the body. Most ovarian and lung cancers overexpress folate receptors on their surface. CYTALUX® binds to the folate receptors on these cancer cells and is endocytosed into folate receptor positive cancer cells. Using a near-infrared imaging system, CYTALUX® illuminates, making cancer visible within the surgical field.

Inpatient Administration of CYTALUX® (pafolacianine)
CYTALUX® would primarily be administered in the inpatient setting for both ovarian and lung cancer, however, it may also be administered as an outpatient for lung cancer. It is administered via IV infusion 1 to 9 hours prior to surgery for ovarian cancer and 1 to 24 hours prior to surgery for non-malignant or known or suspected lung cancer. The proposed dosing for CYTALUX® is a single intravenous infusion of 0.025 mg/kg diluted in 250 mL of 5% Dextrose Injection, administered over 60 minutes using a dedicated infusion line.

Current Coding: There are no unique ICD-10-PCS codes to describe fluorescence-guided surgery using CYTALUX® (pafolacianine). Code the procedure using the body region value W Trunk Region in table 8E0, Other Procedures, with the appropriate approach value and the method value E Fluorescence Guided Procedure for either the lung or ovarian indication. Facilities would also report the appropriate code(s) for any lesion(s) excised.

Section **8** Other Procedures *Body System* **E** Physiological Systems and Anatomical Regions *Operation* **0** Other Procedures: Methodologies which attempt to remediate or cure a disorder or disease			
Body Region	*Approach*	*Method*	*Qualifier*
W Trunk Region	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic **7** Via Natural or Artificial Opening **8** Via Natural or Artificial Opening Endoscopic	**C** Robotic Assisted Procedure **E** Fluorescence Guided Procedure	**Z** No Qualifier

Coding Options

Option 1. Do not create new ICD-10-PCS codes for fluorescence-guided surgery using pafolacianine. Continue coding as described in current coding.

Option 2. In table 8E0, Other Procedures, create new qualifier value N Pafolacianine applied to existing body region value W Trunk Region for the lung indication and add new body region value U Female Reproductive System for the ovarian indication, applied to existing method value E Fluorescence Guided Procedure and to all available approach values, to identify the fluorescence-guided surgery using pafolacianine. Facilities would also report the appropriate code(s) for any lesion(s) excised.

Section **8** Other Procedures *Body System* **E** Physiological Systems and Anatomical Regions *Operation* **0** Other Procedures: Methodologies which attempt to remediate or cure a disorder or disease			
Body Region	*Approach*	*Method*	*Qualifier*
W Trunk Region	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic **7** Via Natural or Artificial Opening **8** Via Natural or Artificial Opening Endoscopic	**E** Fluorescence Guided Procedure	**ADD N** Pafolacianine **Z** No Qualifier
ADD U Female Reproductive System	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic **7** Via Natural or Artificial Opening **8** Via Natural or Artificial Opening Endoscopic	**E** Fluorescence Guided Procedure	**ADD N** Pafolacianine **Z** No Qualifier

CMS Recommendation: Option 2, as described above.

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

Topic # 02 - Administration of Glofitamab

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of glofitamab.

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

Food and Drug Administration (FDA) Approval? No. Genentech is seeking accelerated approval from the FDA for the treatment of adults with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) after two or more prior therapies. According to the requestor, approval is anticipated in the second or third quarter of 2023.

Background: Diffuse large B-cell lymphoma (DLBCL), the most common form of non-Hodgkin Lymphoma (NHL), involves the malignant proliferation of B lymphocytes or B cells during different stages of development, often resulting in rapidly growing and spreading masses in the lymph nodes.[1,2] Although DLBCL can affect all ages, it is primarily a disease of older people; the median age at diagnosis is 66 years old.[3,4] Based on Surveillance, Epidemiology, and End Results Programs (SEER) 2015-2019 age-adjusted data, the incidence of new cases of DLBCL was 5.6 per 100,000 people per year and the death rate was 1.8 per 100,000 people per year.[5] The incidence of DLBCL cases in the United States is projected to increase by 11% from 2020 to 2025 as a result of the aging population and the underlying higher incidence rate of DLBCL with older age.[6]

The standard of care for first-line (1L) DLBCL treatment is a combination of 5 drugs: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Even though DLBCL is an aggressive cancer, approximately 60% of patients will achieve long-term remission with R-CHOP.[7,8] Of the remaining 40%, approximately 10% to 15% will have primary refractory disease (defined as incomplete response or relapse within 6 months after treatment) and 20% to 25% will relapse, usually within the first 2 years of treatment.[9,10,11] Outcomes are poor for patients for whom 1L R-CHOP treatment fails.

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[1] Types of B-cell Lymphoma. American Cancer Society. 2019:1-3.
[2] Liu Y, Barta SK. Diffuse large B-cell lymphoma: 2019 update on diagnosis, risk stratification, and treatment. Am J Hematol. 2019;94(5):604-16.
[3] Types of B-cell Lymphoma. American Cancer Society. 2019:1-3.
[4] Institute NC. SEER Cancer Stat Facts -Diffuse Large B-Cell Lymphoma. 2022.
[5] Id.
[6] Id.
[7] Crump M, Neelapu SS, Farooq U, Van Den Neste E, Kuruvilla J, Westin JR, et al. Outcomes in refractory diffuse large B–cell lymphoma: results from the international SCHOLAR-1 study. Blood. 2017;130:1800-9.
[8] Kanas G, Ge W, Quek RGW, Keeven K, Nersesyan K, Jon EA. Epidemiology of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) in the United States and Western Europe: population-level projections for 2020-2025. Leuk Lymphoma. 2022;63(1):54-63.
[9] Crump M, Neelapu SS, Farooq U, Van Den Neste E, Kuruvilla J, Westin JR, et al. Outcomes in refractory diffuse large B–cell lymphoma: results from the international SCHOLAR-1 study. Blood. 2017;130:1800-9
[10] Fox CP, Townsend W, Gribben J, Menne T, Kalakonda N, Lynes J. Clinical outcomes in patients with relapsed/refractory large B-cell lymphoma receiving conventional third-line therapy: a multicenter, retrospective, real-world study in the United Kingdom. EHA. 2021;EP539
[11] Morrison VA, Shou Y, Bell JA, Hamilton L, Ogbonnaya A, Raju A. Evaluation of treatment patterns and survival among patients with diffuse large B-cell lymphoma in the USA. Future Oncology. 2019;15:1021-34.

Although numerous treatment options are available, there is currently no standard of care for the treatment of patients with R/R DLBCL. Treatment strategies are largely dependent on specific patient factors, including whether patients are eligible for autologous stem cell transplant (ASCT). ASCT is potentially curative; however, only approximately half of the patients who are R/R after 1L therapy are candidates for this treatment approach owing to advanced age or comorbidities.[12] Of eligible patients, about half do not respond sufficiently to salvage chemotherapy to undergo ASCT.[13] More recently, chimeric antigen receptor (CAR) T-cell therapies have become available for patients with R/R DLBCL. Similar to ASCT, about half of patients who undergo CAR T-cell therapy can achieve long-term remissions.[14,15,16]

Description and Mechanism of Action for Glofitamab
Glofitamab is a novel T-cell engaging bispecific antibody that activates the patient's own immune system to eradicate malignant B cells. Glofitamab is designed to simultaneously bind CD20 on malignant B cells and CD3 on T cells, bringing them into close proximity. Glofitamab binding to CD3 also activates the T cell which induces proliferation and targeted killing of B cells (1).[17] The lysis of B cells mediated by Glofitamab is CD20 specific and does not occur in the absence of the simultaneous binding of the T cell and the target B cell. According to the requestor, the novel structure of Glofitamab (2 CD20 binding domains, 1 CD3 binding domain [2:1 structure]) enables high-avidity, bivalent binding to CD20 that can result in activity against malignant B cells even under low effector-to-target cell ratios (2, 3).[18,19]

In the pivotal NCT03075696 study, glofitamab was well tolerated with a low rate of treatment discontinuation. The most frequent adverse events (AE) was cytokine release syndrome (CRS), with the majority being grade 1 (fever) and occurring on the first dose of glofitamab. AEs of all grades that were reported in ≥15% of patients include: cytokine release syndrome (63.0%), neutropenia (37.7%), anemia (30.5%), thrombocytopenia (24.7%), pyrexia (18.2%), and hypophosphatemia (17.5%).

Glofitamab demonstrated clinically meaningful outcomes in patients with DLBCL with 2 or more lines of prior therapy, including those who were heavily pretreated (59.7% of patients had more than 3 prior lines of therapy) and were highly refractory (90.3% were refractory to a prior therapy). Approximately a third of the patients on the glofitamab pivotal trial had prior CAR T-cell therapy and 90.2% of those patients were refractory to CAR T-cell therapy. Despite the difficult-to-treat characteristics of the patients in the pivotal study, the overall response rate (ORR) was 51.6% with

[12] Sehn LH, Salles G. Diffuse large B-cell lymphoma. N Engl J Med. 2021;384(9):842-58.
[13] Gisselbrecht C, Glass B, Mounier N, Singh Gill D, Linch DC, Trneny M, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010;28(27):4184-90.
[14] Kuhnl A, Kirkwood AA, O'Reilly M, Sanderson R, Tholouli E, Patel A. Outcome of large B-cell lymphoma patients failing CD19 targeted CAR T therapy. Presented at: The 16th International Conference on Malignant Lymphoma; June 18-22, 2021; Virtual 2021.
[15] Vercellino L, Di Blasi R, Kanoun S, Tessoulin B, Rossi C, D'Aveni-Piney M, et al. Predictive factors of early progression after CAR T-cell therapy in relapsed/refractory diffuse large B-cell lymphoma. Blood Adv. 2020;4(22):5607-15.
[16] Chong EA, Ruella M, Schuster SJ. Five-year outcomes for refractory B-cell lymphomas with CAR T-cell therapy. N Engl J Med. 2021;384(7):671-3.
[17] Broske AE, Korfi K, Belousov A, Wilson S, Ooi CH, Bolen CR, et al. Pharmacodynamics and molecular correlates of response to glofitamab in relapsed/refractory non-Hodgkin lymphoma. Blood Adv. 2022;6(3):1025-37.
[18]Bacac M, Colombetti S, Herter S, Sam J, Perro M, Chen S, et al. CD20-TCB with obinutuzumab pretreatment as next-generation treatment of hematologic malignancies. Clin Cancer Res. 2018;24(19):4785-97.
[19]Bacac M, Umaña P, Herter S, Colombetti S, Sam J, Le Clech M, et al. CD20 Tcb (RG6026), a novel "2:1" T cell bispecific antibody for the treatment of B cell malignancies. Blood. 2016;128(22):1836

39.4% of patients achieving a complete response (CR). The median time to first CR was 42 days (95% CI: 42–44).

Inpatient Administration of Glofitamab
The dosing for glofitamab will be determined upon FDA approval. Subject to FDA approval, glofitamab will be administered as an intravenous infusion through a dedicated infusion line according to the dose step-up schedule leading to the recommended dosage of 30 mg (as shown in Table 1), after completion of pre-treatment with obinutuzumab on Cycle 1 Day 1. Each cycle is 21 days. The dose schedule of glofitamab also has a fixed duration (maximum of 12 cycles) in contrast to other therapies that are used until disease progression.

Table 1.
Glofitamab Monotherapy Dose Step-Up Schedule for Patients with Relapsed or Refractory DLBCL

Treatment Cycle, Day		**Dose of Glofitamab**	**Duration of infusion**
Cycle 1 (Pre-treatment and step-up dose)	Day 1	Pre-treatment with obinutuzumab	
	Day 8	2.5 mg	4 hours[a]
	Day 15	10 mg	
Cycle 2	Day 1	30 mg	
Cycle 3 through 12	Day 1	30 mg	2 hours[b]

[a] For patients who experience CRS with their previous dose of glofitamab, the duration of infusion may be extended up to 8 hours.
[b] At the discretion of the treating physician, if the previous infusion was well tolerated. If the patient experienced CRS with a previous dose, the duration of infusion should be maintained at 4 hours.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of glofitamab. Facilities can report the intravenous administration of glofitamab using one of the following ICD-10-PCS codes:

3E03305	Introduction of other antineoplastic into peripheral vein, percutaneous approach
3E04305	Introduction of other antineoplastic into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous administration of glofitamab. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of glofitamab.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD P** Glofitamab Antineoplastic	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 03 - Administration of Posoleucel

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of posoleucel.

New Technology Application? Yes. The requestor intends to submit a New Technology Add-On Payment (NTAP) application for FY 2026 consideration.

Food & Drug Administration (FDA) Approval? No. Posoleucel has been granted a Regenerative Medicine Advanced Therapy (RMAT) designation and is being studied in a pivotal, randomized Phase 3 trial for virus associated hemorrhagic cystitis (vHC). The requestor (AlloVir) plans on submitting a Biologics License Application (BLA) for posoleucel following an analysis of the Phase 3 data.

Background: Conditioning regimens for potentially life-saving transplantations – the two most common types of which are allogeneic hematopoietic stem cell transplants (HSCT) and solid organ transplants (SOT), often require the complete elimination of a patient's own stem cells to prevent rejection of the transplanted cells or organs, leaving patients without a functioning immune system and highly prone to devastating viral infections or diseases, which can cause end-organ damage and mortality.

Infections that can be caused by various types of microorganisms are a major root of mortality and morbidity during this phase of immune deficiency. For 90% of allogeneic HSCT patients, their suppressed immune system allows viruses that were previously in a latent state to reactivate, with more than 60% of HSCT patients experiencing reactivation of more than one potentially fatal virus. Overall, 11% of post HSCT deaths are caused by infections, with one-third of these being viral infections.[1] Currently, there are no approved therapies for most viral infections in the post-transplant setting, with the standard of care treatments having limited efficacy and associated with significant toxicity.

Virus Associated Hemorrhagic Cystitis (vHC) is considered as one of the major difficulties after HSCT[2]. vHC is classified into four grades according to its severity: microscopic hematuria (grade 1), macroscopic hematuria (grade 2), hematuria with clots and need for transfusion (grade 3), and hematuria with clots and impaired renal function (grade 4).[3,4] Current standard of care is supportive, including diuresis and continuous bladder irrigation to mitigate urinary obstruction, antispasmodics and narcotics to alleviate suffering, hyperbaric oxygen, nephrostomies, and/or dialysis for acute renal failure. In some cases, a cystectomy has been required to control life-threatening hemorrhage caused by vHC. The most frequently used antiviral drug for vHC

[1] Kaeuferle T, Krauss R, Blaeschke F, Willier S, Feuchtinger T. Strategies of adoptive T-cell transfer to treat refractory viral infections post allogeneic stem cell transplantation. J Hematol Oncol. 2019;12:13–23.
[2] Mohammadi Najafabadi M, Soleimani M, Ahmadvand M, Soufi Zomorrod M, Mousavi SA. Treatment protocols for BK virus associated hemorrhagic cystitis after hematopoietic stem cell transplantation. Am J Blood Res. 2020 Oct 15;10(5):217-230. PMID: 33224566; PMCID: PMC7675133.
[3] Lunde LE, Dasaraju S, Cao Q, Cohn CS, Reding M, Bejanyan N, Trottier B, Rogosheske J, Brunstein C, Warlick E, Young JA, Weisdorf DJ, Ustun C. Hemorrhagic cystitis after allogeneic hematopoietic cell transplantation: risk factors, graft source and survival. Bone Marrow Transplant. 2015;50:1432–1437.
[4] Cesaro S, Dalianis T, Hanssen Rinaldo C, Koskenvuo M, Pegoraro A, Einsele H, Cordonnier C, Hirsch HH. ECIL guidelines for the prevention, diagnosis and treatment of BK polyomavirus-associated haemorrhagic cystitis in haematopoietic stem cell transplant recipients. J Antimicrob Chemother. 2018;73:12–21.

treatment is cidofovir, however cidofovir is associated with nephrotoxicity.

Posoleucel is a polyclonal multi virus-specific T cell (VST) product that recognizes and eradicates actively replicating virus-infected cells. These cells are currently being evaluated for the treatment of viral infections in adults and children after allogeneic HSCT. Posoleucel recognizes and kills virus-infected cells via their native T cell receptor (TCR), which binds to HLA molecules expressed on target cells that present virus-derived peptides. Post allogeneic HSCT, posoleucel provides an immunological bridge between conditioning and reconstitution of the patient's immune systems to treat or prevent viral re-activation until the patient's natural immunity is restored. According to the requestor, restoring immunity during this time of severe immune compromise may substantially reduce or prevent virus-associated morbidity and mortality, and dramatically improve patient outcomes.

Description and Mechanism of Action for Posoleucel
Posoleucel is an investigational, allogeneic, off-the-shelf human leukocyte antigen (HLA)-matched virus-specific T-cell (VST) product reactive to six clinically significant viruses: cytomegalovirus (CMV), Epstein-Barr virus (EBV), BK virus (and the related polyoma JC virus), adenovirus and human herpesvirus-6 (HHV-6). The cells are derived from peripheral blood mononuclear cells (PBMCs) from donors seropositive for all six of these viruses. The cells are expanded and co-cultured with 15-mer peptides overlapping by 11 amino acids spanning antigenic proteins from polyomaviruses BK and JC (VP1 and large T), from adenovirus (hexon and penton), from cytomegalovirus (IE1 and pp65), from Epstein-Barr virus (LMP2, EBNA1, BZLF1), and from human herpesvirus-6 (U90, U11 and U14). The cells have specific anti-virus reactivity for each virus above a pre-specified potency threshold, and predominantly express CD3 (generally greater than 95%) with a mixture of CD4 positive (average 60%) and CD8 positive (average 34%) subsets, including both central (CD45RA-/62L+/CCR7+) and effector (CD45RA-/62L-/CCR7-) memory markers.

Posoleucel is comprised of both CD8+ and CD4+ virus-specific T-cells capable of recognizing actively replicating virus-infected cells, proliferating in response to antigenic stimulation and mediating antiviral effects including the production of cytokines (e.g. interferon (IFN) gamma) and killing of infected cells in patients with infections/diseases associated with the target viruses. The antiviral activities of posoleucel may additionally include the production of other effector cytokines including TNF-alpha and/or GM-CSF and/or effector molecules (e.g. granzyme B and/or perforin). These polyclonal cells recognize viral peptides presented in the context of HLA class I and class II alleles, respectively. The partial HLA match between the allogeneic VST-cell line and infected patient allows the infused T-cells to recognize and selectively kill virus-infected cells.

According to the requestor, safety findings from a completed Phase 2 clinical trial (NCT02108522) in 58 allogeneic hematopoietic stem cell transplant (HCT) recipients with persistent and/or refractory viral infections were consistent with those expected in this patient population, including the known risks of graft-versus-host disease (GVHD). No overt safety signal attributable to posoleucel was detected above and beyond the safety findings expected to be found in patients who have already undergone allogenic HCT and who then present with a severe viral infection caused by 1 or more of the viruses targeted by posoleucel. While all participants in all virus groups experienced treatment-emergent adverse events (TEAEs) during this study, fewer than half of them (43.1%) experienced TEAEs assessed by the Investigator as treatment-related (i.e., possibly, probably, or definitely related to study treatment as judged by the Investigator); TEAEs occurring

in more than 50% of treated participants included: anemia, decreased platelet count, decreased white blood cell count, hypomagnesaemia, decreased neutrophil count, hypokalemia, hyperglycemia, hypoalbuminemia, hypocalcemia, decreased lymphocyte count, and increased aspartate aminotransferase (AST). The most common treatment-related adverse events (greater than 5% of participants) included pyrexia, increased AST, increased bilirubin, decreased neutrophil count, decreased white blood cell count, and maculopapular rash.

Inpatient Administration of Posoleucel
For treatment of viral infections, posoleucel is administered as a course of two intravenous infusions separated by approximately 14 days. An appropriately HLA-matching posoleucel cell line is identified from AlloVir's bank of available drug product lots for an identified patient requiring treatment. Posoleucel is supplied in 6 mL capacity AT-Closed Vials® (Aseptic technologies) at a concentration of 1 X 10^7 virus-specific T-cells (VSTs)/mL in a volume of approximately 2.5 mL/vial. The cryopreserved cells are shipped in the frozen state to the treatment facility. Once the patient is ready for treatment, the cells for a single infusion are thawed, and administered by a health care professional via intravenous infusion by syringe within 30 minutes of thawing. The infusion may be administered through either a central or peripheral intravenous catheter.

The administered dose is based on the patient's body weight: 2 X 10^7 cells (in a volume of 2 mL) per infusion for patients weighing less than 40 kg, and 4 X 10^7 cells (in a volume of 4 mL) per infusion for patients weighing greater than or equal to 40 kg. The total infusion time is approximately 5 minutes. Following infusion of posoleucel, the syringe and intravenous tubing are flushed with normal saline.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of posoleucel. Facilities can report the intravenous administration of posoleucel with one of the following ICD-10-PCS codes:

3E033WK	Introduction of immunostimulator into peripheral vein, percutaneous approach
3E043WK	Introduction of immunostimulator into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous administration of posoleucel. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of posoleucel.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD Q** Posoleucel	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 04 - Administration of Rezafungin

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of rezafungin.

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

Food & Drug Administration (FDA) Approval? No. In the United States, rezafungin was designated by the FDA as a Qualified Infectious Disease Product (QIDP) in 2017. In September 2022, the FDA granted priority review to Melinta Therapeutics for its New Drug Application (NDA) for rezafungin for the treatment of candidemia and invasive candidiasis in patients 18 years of age or older. According to the requestor, the FDA assigned a Prescription Drug User Fee Act (PDUFA) target action date of March 22, 2023.

Background: Candidemia and invasive candidiasis are rare, serious, and life-threatening infections. According to the Centers for Disease Control and Prevention (CDC), the average rate of new infections is approximately 9 per 100,000 people, and there are approximately 25,000 cases per year.[1] These infections occur in patients who are already sick with other diseases and are associated with high morbidity and mortality. Patients who are at risk of invasive fungal infections include the critically ill, immunosuppressed, post-surgical, and those with central venous catheters. Invasive infection with Candida in this already vulnerable patient population often results in severe illness and death.

In a recent analysis of a large United States (US) patient database, Candida infections accounted for 40% of all invasive fungal infections.[2] Patients with these invasive infections can suffer from a range of comorbidities on top of their underlying condition, including fever and septic shock. Candidemia and invasive candidiasis are associated with a long length of hospital stay, with an estimated additional 3 to 13 days of hospitalization after diagnosis. Additionally, the mortality rate in patients with these infections is greater than 40%.[3,4,5,6,7,8,9,10,11]

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[1] Centers for Disease Prevention and Control (CDC). Fungal Diseases: Statistics. August 24, 2021. https://www.cdc.gov/fungal/diseases/candidiasis/invasive/statistics.html.
[2] Menzin J, Meyers JL, Friedman M et al. Mortality, length of hospitalization, and costs associated with invasive fungal infections in high risk patients. Am J Health Syst Pharm. 2009; 66: 1711–1717.
[3] Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, et al. Nococomial bloodstream infections in US hospitals: Analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis. 2004; 39: 309–317.
[4] Falagas ME, Apostolou KE, Pappas VD. Attributable mortality of candidemia: a systematic review of matched cohort and case-control studies. Eur J Clin Microbiol Infect Dis. 2006; 25(7): 419–425.
[5] Pfaller MA, Diekema DJ. Epidemiology of Invasive Candidiasis: a Persistent Public Health Problem. Clin Microbiol Rev. 2007; 20(1): 133–163.
[6] Labelle AJ, Micek ST, Roubinian N, Kollef MH. Treatment-related risk factors for hospital mortality in Candida bloodstream infections. Crit Care Med. 2008; 36(11): 2967–2972.
[7] Pfaller MA, Diekema DJ. Epidemiology of invasive mycoses in North America. Crit Rev Microbiol. 2010; 36: 1–53.
[8] Slavin MA, Sorrell TC, Marriott D, Thursky KA, Nguyen Q, Ellis DH, et al.; Australian Candidemia Study, Australasian Society for Infectious Diseases. Candidaemia in adult cancer patients: risks for fluconazole-resistant isolates and death. J Antimicrob Chemother. 2010; 65(5): 1042–1051.
[9] Andes DR, Safdar N, Baddley JW, et al. Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: a patient-level quantitative review of randomized trials. Clin Infect Dis. 2012; 54: 1110–1122.
[10] Mikulska M, Del Bono V, Ratto S, Viscoli C. Occurrence, presentation and treatment of candidemia. Expert Rev Clin Immunol. 2012; 8(8): 755–765.
[11] Mylonakis E, Clancy CJ, Ostrosky-Zeichner L, Garey KW, Alangaden GJ, et al. T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial. Clin Infect Dis. 2015; 60(6): 892–899.

Echinocandins are recommended as first-line antifungal agents by practice guidelines for the treatment of candidemia and invasive candidiasis due to their well-established efficacy and safety profile and strong fungicidal activity. Currently approved echinocardins include caspofungin, micafungin, and anidulafungin, however, no new antifungal agents have been approved for treatment of candidemia and invasive candidiasis since anidulafungin in 2007.

Mechanism of Action
Rezafungin is an echinocandin, a class of antifungal drugs that inhibits the synthesis of 1,3-beta-D-glucan, an essential component of fungal cell walls. It is a sterile, lyophilized product that contains rezafungin acetate, a semisynthetic lipopeptide synthesized from a fermentation product of Aspergillus nidulans. Rezafungin acetate is a hygroscopic, white to off-white powder, freely soluble in water, soluble in methanol, and sparingly soluble in ethanol.

Inpatient Administration of Rezafungin
Rezafungin is administered once a week, via intravenous infusion of a loading dose over approximately one hour on day 1, followed by a maintenance dose on day 8. An infusion may be slowed, or paused and restarted at a lower rate, if infusion-related reactions occur.

For the 400 mg dose, aseptically reconstitute 2 vials with 9.5 mL of sterile water for injection, to provide a concentration of 20 mg/mL in each vial. For the 200 mg dose, aseptically reconstitute 1 vial with 9.5 mL of sterile water for injection, to provide a concentration of 20 mg/mL.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of rezafungin. Facilities can report the intravenous administration of rezafungin using one of the following codes:

3E03329	Introduction of other anti-infective into peripheral vein, percutaneous approach
3E04329	Introduction of other anti-infective into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous administration of rezafungin. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of rezafungin.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD R** Rezafungin	**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 # 05 - Administration of SER-109

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of SER-109.

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

Food & Drug Administration (FDA) Approval? No. In 2015, the FDA granted SER-109 Orphan Drug Designation and Breakthrough Designation for the treatment of *Clostridioides difficile* (*C. diff*) infection (CDI). According to the requestor, the FDA accepted the Biologics License Application (BLA) for SER-109 on October 26, 2022, and provided a Prescription Drug User Fee Act (PDUFA) action date of April 26, 2023.

Background: *C. diff* is the leading cause of hospital-acquired infections (HAIs) in the United States, and is connected with over 20,000 deaths.[1,2] *C. diff* colonizes the human intestinal tract after the normal gut flora has been disrupted and is the causative organism of antibiotic-associated colitis including pseudomembranous colitis. The primary risk factor for CDI is exposure to broad-spectrum antibiotics, which leads to compositional and functional changes in the gastrointestinal microbiome and renders patients susceptible to increased germination of *C. diff* spores.[3] Antibiotic-induced loss of Firmicutes bacteria enables *C. diff* spore germination and launches a cycle of recurrence; most CDI recurrences occur within the days and weeks after completion of an antibiotic regimen, as the disrupted microbiome facilitates increased *C. diff*.[4]

While antibiotics are necessary to treat CDI, antibiotics alone are often insufficient to achieve a sustained clinical response. Antibiotics kill the toxin-producing *C. diff* bacteria, but also kill beneficial flora, including Firmicutes bacteria. Furthermore, antibiotics do not kill dormant *C. diff* spores. After treatment discontinuation, these spores germinate into toxin-producing vegetative bacteria, which thrive in an environment depleted of Firmicutes bacteria, thereby causing recurrent infections. According to the requestor, a two-pronged approach of first using antibiotics to kill vegetative *C. diff* bacteria, followed by SER-109 to repair the microbiome, is key to managing CDI and preventing recurrence.[5,6,7]

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[1] Guh AY, Mu Y, Winston LG, et al. Trends in U.S. burden of Clostridioides difficile infection and outcomes. N Engl J Med 2020; 382: 1320– 1330.
[2] Ressler A, Wang J, Rao K. Defining the black box: a narrative review of factors associated with adverse outcomes from severe Clostridioides difficile infection. Ther Adv Gastroenterol 2021, Vol. 14: 1–16.
[3] Theriot CM, Bowman AA, Young VB. Antibiotic-induced alterations of the gut microbiota alter secondary bile acid production and allow for Clostridium difficile spore germination and outgrowth in the large intestine. mSphere 2016;1(1):e00045-15.
[4] Abujamel T, Cadnum JL, Jury LA, et al. Defining the vulnerable period for re-establishment of Clostridium difficile colonization after treatment of C. difficile infection with oral vancomycin or metronidazole. PLoS One 2013;8(10):e76269- e76269.
[5] McGovern B, Ford C, Henn M, SER-109, an Investigational Microbiome Drug to Reduce Recurrence After Clostirioides difficile infection: Lessons Learned from a Phase 2 trial. Clin Infect Dis 2021 Jun 15; 72(12): 2132-2140.
[6] Feuerstadt P, Louie T, Lashner M. SER-109, an oral microbiome therapy for recurrent Clostridioides difficile Infection. N Engl J Med 2022; 386:200-9.
[7] Khanna S, Pardi DS, Kelly CR, et al., A Novel Microbiome Therapeutic Increases Gut Microbial Diversity and Prevents Recurrent Clostridium difficile Infection, The Journal of Infectious Diseases, Volume 214, Issue 2, 15 July 2016, Pages 173–181, https://doi.org/10.1093/infdis/jiv766

Description and Mechanism of Action for SER-109
SER-109, an investigational microbiome therapeutic, is a consortium of purified Firmicutes bacteria spores administered to prevent recurrent *C. diff* infection. SER-109 prevents recurrent CDI by repairing the microbiome by replenishing Firmicutes bacteria. While the specific mechanism of action of SER-109 is still under investigation, findings from the ECOSPOR III clinical trial indicate that SER-109 results in more rapid and durable engraftment of the Firmicutes bacteria relative to placebo, producing bile-acid profiles that are known to inhibit *C. diff* spore germination and bacterial replication, and thus reduce rates of recurrent infection.[8] Types of adverse events (AEs) were primarily gastrointestinal and mild to moderate in nature.[9] AEs remained consistent across clinical trials for SER-109, even when dosage amount increased from Phase II to Phase III.

Inpatient Administration of SER-109
SER-109 is administered to patients with recurring CDI who first completed a standard of care course of prescribed antibiotics. The proposed dose is four capsules taken orally once daily on an empty stomach before the first meal of the day for three consecutive days. Each capsule contains a minimum of 1x10^6 spore colony-forming units. One day before the first dose of SER-109, patients should be administered 10 oz of magnesium-citrate or, based on medical judgment, 250 mL polyethylene glycol electrolyte solution, to reduce residual antibiotics in the gastrointestinal tract. The recommended dosage and administration are subject to final FDA approval.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of SER-109. Facilities can report the oral administration of SER-109 using the following code:

3E0DXGC Introduction of other therapeutic substance into mouth and pharynx, external approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the oral administration of SER-109. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the oral administration of SER-109.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
D Mouth and Pharynx	**X** External	**ADD N** SER-109	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

[8] Feuerstadt P, Louie T, Lashner M. SER-109, an oral microbiome therapy for recurrent Clostridioides difficile Infection. N Engl J Med 2022; 386:200-9.
[9] Lee Y, Lim W, Bloom C, Bezlotoxumab (Zinplava) for Clostridium Difficile Infection: The First Monoclonal Antibody Approved to Prevent the Recurrence of a Bacterial Infection. Drug Forecast 2017;42:735-738.

Topic # 06 - Administration of Sulbactam-Durlobactam

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of sulbactam-durlobactam (SUL-DUR).

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

Food & Drug Administration (FDA) Approval? SUL-DUR was granted Fast Track and Qualified Infectious Disease Product (QIDP) Designation on July 21, 2017, for the treatment of hospital-acquired and ventilator-associated bacterial pneumonia and bloodstream infections due to *Acinetobacter*. On September 30, 2022, Entasis Therapeutics submitted a New Drug Application (NDA) for SUL-DUR to the FDA with a proposed indication of the treatment of adults with infections due to *Acinetobacter baumannii-calcoaceticus* complex (ABC) organisms, including multi-drug resistant and carbapenem-resistant strains. According to the requestor, SUL-DUR was accepted for priority review on November 29, 2022 and the target Prescription Drug User Fee Act (PDUFA) date is May 29, 2023.

Background: *Acinetobacter baumannii (A. baumannii)* is a Gram-negative bacterial pathogen that has emerged globally as a major cause of hospital-acquired infections. While pneumonia and bacteremia are the most common infections caused by ABC, these organisms can also cause urinary tract infections, skin and soft tissue infections, wound infections, osteomyelitis, and meningitis.

According to the requestor, treatment of infections due to ABC is a serious unmet need. Infections caused by *A. baumannii* are associated with high morbidity and mortality and have become increasingly difficult to treat due to the emergence of multi-drug resistant (MDR) and carbapenem-resistant *Acinetobacter baumannii* strains (CRAB). Globally, *A. baumannii* was among the five leading pathogens contributing to the most deaths attributable to antimicrobial resistance in 2019. In 2019, an estimated 326,000 deaths globally were associated with carbapenem-resistant *A. baumannii*. The rise in carbapenem-resistant *A. baumannii* is of particular concern, leaving no clear "standard of care" antibiotic regimen for these infections. Carbapenem-resistant *Acinetobacter* is classified by the United States Centers for Disease Control and Prevention as an "urgent threat" pathogen and is ranked as "priority 1, critical" on the World Health Organization (WHO) global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics[1].

Description and Mechanism of Action for Sulbactam-Durlobactam
SUL-DUR is a pathogen-targeted β-lactam/β-lactamase inhibitor combination of sulbactam and durlobactam being developed for the treatment of infections caused by ABC, including carbapenem-resistant and multidrug-resistant isolates. Sulbactam is a penicillin derivative and classified as a beta-lactamase inhibitor but also has intrinsic antibacterial activity against *Acinetobacter baumannii* and other members of the ABC. Sulbactam is bactericidal due to its inhibition of penicillin-binding proteins PBP1 and PBP3, which are essential enzymes required for

[1] Antibiotic Resistance Threats in the United States, 2019/ https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

bacterial cell wall synthesis. Sulbactam is susceptible to degradation by many beta-lactamases expressed in ABC.

Durlobactam is a covalent, reversible, diazabicyclooctane beta-lactamase inhibitor with a broad spectrum of activity against Ambler Classes A, C and D beta-lactamases, including those that degrade sulbactam. Durlobactam effectively restores sulbactam activity against ABC organisms due to its potent inhibition of serine β-lactamases.

The clinical development program for SUL-DUR consists of six Phase 1 studies, one Phase 2 study, and one Phase 3 study. SUL-DUR has shown a favorable clinical profile with demonstration of linear pharmacokinetics (PK), minimal drug interactions, and good penetration into the lung. According to the requestor, SUL-DUR has been generally well-tolerated, with no drug-related serious adverse events or deaths in Phase 1 studies. In the Phase 3 study, SUL-DUR met the primary efficacy and safety objectives of the study, achieving noninferiority versus colistin in 28-day all-cause mortality and a statistically significant reduction in the incidence of nephrotoxicity. Adverse events in the safety population were comparable between treatment groups. The most common adverse reaction reported in more than one patient (>2% of patients) treated with SUL-DUR was diarrhea, which was reported in 4/91 (4.4%) of patients.

Inpatient Administration of Sulbactam-Durlobactam
Upon FDA approval, the recommended dose of SUL-DUR will be 1 g sulbactam and 1 g durlobactam every six hours by intravenous (IV) infusion over three hours in adults with a creatinine clearance (CLcr) of 45 to 129 mL/min. SUL-DUR is supplied in 3-vials that contain sterile powders that must be reconstituted with sterile water and further diluted in a 100 mL infusion bag of 0.9% Sodium Chloride for Injection using aseptic technique prior to intravenous infusion. The prepared solution should be brought to ambient room temperature (over 15-30 min) prior to infusion to the patient. Adjustments to the dosing regimen for SUL-DUR are recommended for patients with CLcr <45 mL/min. A higher dose of SUL-DUR (1.5 g sulbactam/1.5 g durlobactam every six hours) is recommended for patients with CLcr ≥130 mL/min.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of sulbactam-durlobactam. Facilities can report the intravenous administration of sulbactam-durlobactam with one of the following ICD-10-PCS codes:

3E03329	Introduction of other anti-infective into peripheral vein, percutaneous approach
3E04329	Introduction of other anti-infective into central vein, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous administration of sulbactam-durlobactam. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of sulbactam-durlobactam.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD K** Sulbactam-Durlobactam	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 07 - Administration of Quizartinib

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of quizartinib.

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

Food & Drug Administration (FDA) Approval? No. Quizartinib has been designated by the FDA as an orphan drug for the treatment of acute myeloid leukemia (AML). On October 20, 2022, the FDA granted quizartinib priority review status. According to the requestor, the FDA assigned a Prescription Drug User Fee Act (PDUFA) target action date of April 24, 2023.

Background: AML is a rapidly growing type of blood cancer in which immature bone marrow cells are overproduced and accumulate in bone marrow and other tissues. Quizartinib is a novel kinase inhibitor with a proposed indication in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation monotherapy following consolidation, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive as detected by an FDA-approved test.

Quizartinib is an orally administered, highly selective and potent second-generation type II FMS-like tyrosine kinase 3 inhibitor. It is the only small-molecule FLT3 inhibitor to be expressly developed and optimized to target and treat FLT3-ITD AML, present in approximately 27% of AML patients.[1] ITD is the primary driver mutation associated with aggressive disease, resulting in increased relapse rate and reduced overall survival.[2]

Mechanism of Action
Quizartinib is a small molecule inhibitor of the receptor tyrosine kinase FLT3. Quizartinib and its major metabolite AC886 competitively bind to the adenosine triphosphate (ATP) binding pocket of FLT3 with high affinity (Kd = 1.3 nM and 0.54 nM, respectively). Quizartinib and AC886 inhibit FLT3 kinase activity, preventing autophosphorylation of the receptor, thereby inhibiting further downstream FLT3 receptor signaling and blocking FLT3-ITD-dependent cell proliferation.

Inpatient Administration of Quizartinib
The proposed dosing for quizartinib is 35.4 mg orally by mouth in combination with standard chemotherapy once daily for two weeks in each cycle of induction. For patients who achieved complete remission (CR) or complete remission with incomplete hematologic recovery (CRi), quizartinib should be administered at 35.4 mg once daily for two weeks in each cycle of consolidation chemotherapy followed by quizartinib continuation monotherapy initiated at 26.5 mg once daily. After two weeks, the continuation dose should be increased to 53 mg once daily if the QT interval corrected by Fridericia's formula (QTcF) is less than or equal to 450 ms. Continuation therapy may be continued for up to 36 cycles.

[1] Levis, M. *Future Oncol*. 2014, 10(9):1571-1579.
[2] See: NCCN AML Guidelines (February 2022). Grimwade D, et al. *Blood* 2016, 127(1): 29-41. Schneider F, et al. *Ann Hematol* 2012, 1(9): 18. Kottaridis PD, et al. *Blood* 2001, 98(6): 1752-1759.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of quizartinib. Facilities can report the oral administration of quizartinib using the following code:

3E0DX05 Introduction of other antineoplastic into mouth and pharynx, external approach

Coding Options

Option 1. Do not create a new ICD-10-PCS code for the oral administration of quizartinib. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the oral administration of quizartinib.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
D Mouth and Pharynx	**X** External	**ADD J** Quizartinib Antineoplastic	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 08 - Administration of Elranatamab

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of elranatamab.

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

Food & Drug Administration (FDA) Approval? No.

Background: Multiple myeloma (MM) is an incurable malignancy that affects a type of white blood cell called plasma cells. In 2020, it is estimated that more than 32,000 people were diagnosed and nearly 13,000 died from multiple myeloma in the US. Multiple myeloma is associated with substantial morbidity and mortality and approximately 25% of patients have a median survival of two years or less. Treatment of relapsed and refractory multiple myeloma (RRMM) constitutes a specific unmet medical need. Patients with relapsed and refractory disease are defined as those who, having achieved a minimal response or better, experience disease progression while on therapy, or experience disease progression within 60 days of completion of their last therapy. Patients generally experience multiple lines of therapy before eventually succumbing to their disease.

According to the requestor, elranatamab offers a new mechanism of action for the treatment of RRMM. If FDA-approved, elranatamab will potentially be used for the treatment of adult patients with RRMM who have received at least four prior lines, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Description and Mechanism of Action for Elranatamab
Elranatamab is a heterodimeric humanized full-length bispecific antibody directed to B cell maturation antigen (BCMA) and CD3. According to the requestor, bispecific antibodies offer an emerging immunotherapeutic approach that allows the direct targeting of cytotoxic T cells to tumor cells. For elranatamab, the two targets are BCMA (which has high specific expression on normal plasma cells and on myeloma cells) and CD3 (which is expressed on T-cells). Elranatamab is proposed to act through direct bridging of the BCMA cell-surface antigen and the extracellular CD3 subunit expressed on T cells. Elranatamab binds to the CD3 on the T-cells and binds to the BCMA on the myeloma cells thereby bringing the cells in close proximity. The engagement of the CD3 on the T-cell activates the T-cell, leading to the T-cells releasing cytokines that result in the killing of the close-proximity MM cell.

Immuno-oncology therapies that harness T-cell activation are associated with cytokine release syndrome (CRS) and immune cell-associated neurotoxicity syndrome (ICANS). There were 123 patients in the safety population (meaning safety is assessed for all of these patients) of the MagnetisMM3 (MM3) clinical study cohort A (no prior exposure to BCMA therapies). The first four patients in the MM3 study received a single 44 mg step-up dose while the remaining 119 patients received the 12mg/32mg step-up regimen. For the analysis of CRS and ICANS, the first four patients who received a different step-up regimen (44 mg) were excluded from the analyses. For analysis of all other side effects, all 123 patients were analyzed. The most common side effect in the MM3 study was CRS that occurred in 67 (56.3%) of the 119 participants.

All of these events were mild (Grade 1, 42.0%) to moderate (Grade 2, 14.3%) in nature (no grade 3 or higher events were reported), and most CRS events occurred after the first (44.5%) or second (20.2%) step-up dose. Immune effector cell-associated neurotoxicity syndrome occurred in 4 (3.4%) of 119 participants and all of these events were mild (Grade 1, 0.8%) to moderate (Grade 2, 2.5%) in nature. The most common hematologic side effects seen in 20% or more of participants were anemia in 48.0%, neutropenia in 48.0%, thrombocytopenia in 30.1%, and lymphopenia in 26.0%. These were also the most common severe (Grade 3) or life threatening (Grade 4) side effects. The most common non-hematologic side effects seen in 20% or more of participants were diarrhea in 39.0%, decreased appetite in 32.5%, fatigue in 34.1%, injection site reaction in 26.0%, nausea in 26.0%, COVID-19 related in 25.2%, hypokalemia in 23.6%, pyrexia in 23.6%, cough in 22.0% and headache in 22.0%. Most of these side effects were mild to moderate in severity. Infections of any grade were reported in 66.7% of patients. A total of 35.0% of patients had Grade 3/4 infections.

Inpatient Administration of Elranatamab
Elranatamab is provided as a solution in a histidine buffer at pH 5.8, in 40 mg/mL single-dose vials for subcutaneous injection. Elranatamab therapy begins with a priming regimen for the first two subcutaneous injections with 12 mg given on day 1 and 32 mg on day 4 of the first cycle (1 cycle = 4 weeks). Premedication with dexamethasone, diphenhydramine, and acetaminophen is required prior to the two priming doses and the first full dose. Dosing thereafter is 76 mg once weekly by subcutaneous injection. Dosing frequency is reassessed after 6 months, and dose frequency may be reduced to every two weeks (Q2W) in patients with a response persisting for $\geq$ 2 months.

Current Coding: There are no unique ICD-10-PCS codes to describe the subcutaneous injection of elranatamab. Facilities can report the subcutaneous injection of elranatamab with the following ICD-10-PCS code:

3E01305	Introduction of other antineoplastic into subcutaneous tissue, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the subcutaneous injection of elranatamab. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the subcutaneous injection of elranatamab.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
1 Subcutaneous Tissue	**3** Percutaneous	**ADD L** Elranatamab Antineoplastic	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 09 - Administration of Epcoritamab

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of epcoritamab, a novel CD3xCD20 bispecific monoclonal antibody.

New Technology Application? Yes, the requestor has submitted a New Technology Add-on Payment (NTAP) application for FY2024 consideration.

Food & Drug Administration (FDA) Approval? No. The requestor, Genmab US, Inc. (Genmab) and AbbVie, Inc. (AbbVie), submitted a Biologics License Application (BLA) to the FDA who granted priority review for epcoritamab for the treatment of adult patients with relapsed or refractory (R/R) Large B-Cell Lymphoma (LBCL), after two or more lines of systemic therapy. According to the requestor, the FDA assigned a Prescription Drug User Fee Act (PDUFA) target action date of May 21, 2023.

Background: Lymphomas represent a disease characterized by the transformation of cells lymphoid tissue, lymphocytes, and histiocytes. Lymphomas can be morphologically divided into Hodgkin's and non-Hodgkin's Lymphomas (NHL). NHLs, which account for 90% of all lymphomas, are a heterogeneous group of lymphoproliferative diseases arising from transformed B-lymphocyte progenitor cells (85-90%) or, more rarely, transformed T-lymphocyte progenitor cells (10-15%).[1,2,3] With an estimated 509,000 new cases globally, NHL is the most common form of hematologic malignancy.[4] Clinically, B-cell lymphomas can be characterized indolent (slow growing) and aggressive (fast growing). An aggressive subtype, LBCL, characterized by B-cells greater than 17μm in diameter, is a constellation of B-cell lymphomas consisting of Diffuse Large B-cell Lymphoma (DLBCL), Primary Mediastinal B-cell Lymphoma (PMBCL), High Grade B-cell Lymphoma (HGBCL), and Grade 3B Follicular Lymphoma (G3b FL).[5,6] DLBCL is the most common making up ~90% of all LBCLs (and 30% of all NHLs more generally). PMBCL, HGBCL and G3b FL make up less than 5% of all LBCLs.[7,8]

As R/R LBCL patients progress through lines of treatment, prognosis decreases.[9] While treatment of R/R LBCL has improved in recent years due to increased therapeutic options, patients who have

[1] Parihar, A., Singh, R., Shaik, S., Negi, B., Rajguru, J., Patil, P., & Sharma, U. (2020). Non-Hodgkin's lymphoma: A review. Journal of Family Medicine and Primary Care, 9(4), 1834. https://doi.org/10.4103/jfmpc.jfmpc_1037_19

[2] Singh, R., Shaik, S., Negi, B. S., Rajguru, J. P., Patil, P. B., Parihar, A. S., & Sharma, U. (2020). Non-Hodgkin's lymphoma: A review. Journal of family medicine and primary care, 9(4), 1834–1840.

[3] Gouveia, G. R., Siqueira, S. A., & Pereira, J. (2012). Pathophysiology and molecular aspects of diffuse large B-cell lymphoma. Revista brasileira de hematologia e hemoterapia, 34(6), 447–451.

[4] NHL Subtypes | Leukemia and Lymphoma Society. (n.d.). Retrieved September 13, 2022, from https://www.lls.org/lymphoma/non-hodgkin-lymphoma/nhl-subtypes

[5] Swerdlow, S. H., & Cook, J. R. (2020). As the world turns, evolving lymphoma classifications-past, present and future. Human pathology, 95, 55–77.

[6] Ganapathi, K. A., Brown, L. E., Prakash, S., & Bhargava, P. (2021). New developments in non-Hodgkin lymphoid malignancies. Pathology, 53(3), 349–366.

[7] Ganapathi, K. A., Brown, L. E., Prakash, S., & Bhargava, P. (2021). New developments in non-Hodgkin lymphoid malignancies. Pathology, 53(3), 349–366.

[8] Thandra, K. C., Barsouk, A., Saginala, K., Padala, S. A., Barsouk, A., & Rawla, P. (2021). Epidemiology of Non-Hodgkin's Lymphoma. Medical sciences (Basel, Switzerland), 9(1), 5.

[9] Crump, M., Neelapu, S. S., Farooq, U., Van Den Neste, E., Kuruvilla, J., Westin, J., Link, B. K., Hay, A., Cerhan, J. R., Zhu, L., Boussetta, S., Feng, L., Maurer, M. J., Navale, L., Wiezorek, J., Go, W. Y., & Gisselbrecht, C. (2017). Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. Blood, 130(16), 1800–1808.

failed at least two prior therapies still have very poor prognosis.[10,11,12] According to the requestor, for these third line patients there is a high unmet need for a treatment option that is well tolerated, provides a deep and durable response, and is widely available for all patient subtypes.

Mechanism of Action
Epcoritamab is a full-length IgG1 bispecific antibody derived from a humanized mouse anti-human CD3 mAb and a human anti-CD20 mAb. CD3 is a protein complex and T-cell co-receptor involved in activating both CD8+ T-cells (cytotoxic T-cells) and CD4+ T-cells (T helper cells). CD20 is a B-cell specific marker, which is expressed on mature B-cells, including malignant B-cells of LBCL and not expressed on hematopoietic stem cells and lymphoid progenitor cells. By simultaneously binding CD3 expressing T-cells and CD20 expressing B-cells, epcoritamab induces activation and cytotoxic activity of the T-cells against the malignant B-cells in a process that is strictly dependent on epcoritamab binding to both targets.

Inpatient Administration of Epcoritamab
Epcoritamab is administered by subcutaneous injection over the course of 28-day cycles.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of epcoritamab. Facilities can report the subcutaneous injection of epcoritamab using the following code:

3E0130M Introduction of antineoplastic, monoclonal antibody, into subcutaneous tissue, percutaneous approach

Coding Options

Option 1. Do not create a new ICD-10-PCS code for the subcutaneous injection of epcoritamab. Continue coding as listed in current coding.

Option 2. Create a new code in section X, New Technology, to identify the subcutaneous injection of epcoritamab.

Section	**X** New Technology
Body System	**W** Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
1 Subcutaneous Tissue	**3** Percutaneous	**ADD S** Epcoritamab Monoclonal Antibody	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

[10] Susanibar-Adaniya, S., & Barta, S. K. (2021). 2021 Update on Diffuse large B cell lymphoma: A review of current data and potential applications on risk stratification and management. American Journal of Hematology, 96(5), 617–629.
[11] Snider, J. T., McMorrow, D., Song, X., Diakun, D., Wade, S. W., & Cheng, P. (2022). Burden of Illness and Treatment Patterns in Second-line Large B-cell Lymphoma. Clinical therapeutics, 44(4), 521–538.
[12] Jalbert, J. J., Wu, N., Chen, C. I., Ambati, S., Ge, W., & Arnason, J. E. (2022). Real-World Treatment Patterns After CD19-Directed CAR T Cell Therapy Among Patients with Diffuse Large B Cell Lymphoma. Advances in Therapy, 39(6), 2630–2640.