DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
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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 these topics being considered for an April 1, 2024 implementation is October 13, 2023. 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 13, 2023 deadline.

CMS will not be presenting the NTAP-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent at the September 12, 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 September 12, 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

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1. Email Address

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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.
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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 Request That Involves Administration of a Therapeutic Agent

**Request is for an April 1, 2024 implementation date and the requestor intends to submit an NTAP application for FY 2025 consideration.*

The slide presentation for this procedure code topic is 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:

September 12-13, 2023	The September 2023 ICD-10 Coordination and Maintenance Committee Meeting will be held virtually by Zoom Webinar.
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 and revisions 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 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/Latest_News
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.**

December 1, 2023	**Deadline for requestors: Those members of the public requesting that topics be discussed at the March 19-20, 2024 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, 2024 implementation date, or an April 1, 2025 implementation date. 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, 2024 implementation date or an April 1, 2025 implementation date.
January 2024	Federal Register notice for the March 19-20, 2024 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
February 2024	Tentative agenda for the Procedure portion of the March 19, 2024 ICD-10 Coordination and Maintenance Committee Meeting posted on CMS webpage at: https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html Tentative agenda for the Diagnosis portion of the March 20, 2024 ICD-10 Coordination and Maintenance Committee Meeting posted on NCHS homepage at: https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm
February 1, 2024	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, 2024	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/Comprehensive-Listing-of-ICD-10-CM-Files.htm https://www.cms.gov/Medicare/Coding/ICD10/

February 1, 2024	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/Comprehensive-Listing-of-ICD-10-CM-Files.htm https://www.cms.gov/Medicare/Coding/ICD10/
March 19-20, 2024	The 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.
March 2024	Recordings and slide presentations of the March 19-20, 2024 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, 2024	Any new or revised ICD-10 codes will be implemented on April 1, 2024.
April 19, 2024	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 19-20, 2024 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2024**.
April 2024	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 2025 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 17, 2024	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 19-20, 2024 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2025.** **Deadline for receipt of public comments on proposed new diagnosis codes and revisions discussed at the March 19-20, 2024**

	ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2025.
May/June 2024	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 7, 2024	**Deadline for requestors: Those members of the public requesting that topics be discussed at the September 10-11, 2024 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, 2025 implementation date or an October 1, 2025 implementation date. 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 April 1, 2025 implementation date or an October 1, 2025 implementation date.
July 2024	Federal Register notice for the September 10-11, 2024 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
August 1, 2024	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, 2024. This rule can be accessed at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/index.html
August 2024	Tentative agenda for the Procedure portion of the September 10, 2024 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 11, 2024 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 10-11, 2024	The September 2024 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 2024	Recordings and slide presentations of the September 10-11, 2024 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, 2024	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 11, 2024	**Deadline for receipt of public comments on proposed new codes discussed at the September 10-11, 2024 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2025.**
November 2024	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, 2025 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/Latest_News
November 13, 2024	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the September 10-11, 2024 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2025.**

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, 2024 and October 1, 2024
- 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 13, 2023 for codes being considered for April 1, 2024 implementation
  - November15, 2023 for codes being considered for 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

Addendum

- May/June 2023 – Final code updates and addendum posted
  - FY 2024 ICD-10-PCS (Procedures)
    https://www.cms.gov/medicare/coding/icd10
  - 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
  - October 13, 2023 for codes being considered for April 1, 2024 implementation
  - November 15, 2023 for codes being considered for October 1, 2024 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 discussed today under consideration for April 1, 2024 or October 1, 2024 implementation

March 19-20, 2024 C&M Code Requests

- December 1, 2023 – Deadline for submitting topics for March 19-20, 2024 C&M meeting
  - Procedure requests to CMS: https://mearis.cms.gov
  - Diagnosis requests to NCHS: nchsicd10cm@cdc.gov

Topic # 01 - Administration of Iodine (^{131}I)-apamistamab (^{131}I-apamistamab)

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of iodine (^{131}I)-apamistamab (^{131}I-apamistamab). The requestor is seeking an April 1, 2024 implementation date.

New Technology Application? Yes. The requestor intends to submit a New Technology Add-on Payment (NTAP) application for FY 2025 consideration.

Food & Drug Administration (FDA) Approval? No. The requestor intends to submit a Biologics License Application (BLA) to the FDA in the second half of 2023 for the use of ^{131}I-apamistamab as a targeted radiation directly to leukemic cells.

Background: Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with the production of normal white blood cells. AML is the most common acute leukemia affecting adults and is frequently diagnosed among people aged 65-74, with the median age diagnosis of 69.[1] Treatment of AML in fit adults usually begins with intensive induction chemotherapy that can be highly toxic and typically entails hospitalization for several weeks. Targeted agents such as hypomethylating agents with or without Bcl-2 inhibitors (venetoclax) and IDH inhibitors are being increasingly used as induction therapy for AML, especially in older and unfit patients, and can be administered as outpatient. Toxicities of induction therapy include cytopenia, infections, bleeding/coagulation abnormalities, tumor lysis syndrome, electrolyte imbalances, impaired nutritional status, and other complications. Treatment-related mortality increases with age.

The goal of induction therapy is to achieve a complete remission (CR; <5 percent blast cells in bone marrow and complete clearance of blasts in blood) as CR is essential for improved outcomes in AML, including a cure. Depending upon age, patient characteristics, and various prognostic features, approximately two-thirds of adults achieve a CR with such regimens, but, unfortunately, relapse rates are high (approximately 50%). For patients who do not achieve a CR following induction therapy, a second, briefer course of re-induction therapy may be given.
Response to therapy is determined by doing a bone marrow aspirate and biopsy 14 days after the completion of re-induction chemotherapy and again upon count recovery (day 28 to 35 from start of induction). Nearly all patients who initially achieve CR will relapse unless consolidation (post-remission) therapy is given. The goal of consolidation therapy, which includes chemotherapy and/or allogeneic hematopoietic stem cell transplantation (alloHCT), is to eliminate residual, undetectable disease and achieve long-term disease control and cure.

Relapsed or refractory (R/R) AML presents as one of the following: 1) primary induction failure after 2 or more cycles of therapy, or 2) first early relapse after a remission duration of fewer than 6 months, or 3) relapse refractory to salvage combination therapy, or 4) second or subsequent relapse.[2] Prognosis for patients with R/R AML is extremely poor. Management is variable and ranges from re-induction with salvage chemotherapy followed by alloHCT to best supportive care. While alloHCT may be curative, most subjects, especially older patients, and those with active

[1] SEER database, accessed May 2023.
[2] Schmid C et al. *Blood.* 2006 ;108(3) :1092-9.

disease, are not considered for transplant due to failure to achieve remission, poor tolerance of conditioning, and substantial transplant-related mortality.[2,3] Outcomes of alloHCT in R/R AML patients using reduced-intensity conditioning regimens are poor due to high post-transplant relapse rates.

Significant challenges must be overcome to enable potentially curative alloHCT in a broader population: the alloHCT candidate 1) must first attain a CR, 2) must tolerate and survive effective conditioning; the recipient 3) must achieve engraftment and post-transplant CR and 4) must surmount alloHCT-related complications including graft failure and serious side effects of sepsis and/or graft versus host disease (GVHD).

Mechanism of Action
^{131}I-apamistamab is an investigational anti-CD45 murine monoclonal antibody (BC8) covalently bound with radioactive isotope iodine (^{131}I). CD45 is expressed on all hematopoietic cells and on most hematopoietic malignancies, including AML. Per the requestor, the use of ^{131}I-apamistamab allows targeted delivery of the radiation dose directly to leukemic cells while sparing healthy organs such as lungs, heart, and GI tract. The requestor states that ^{131}I-apamistamab has been studied in approximately four hundred patients including Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory AML (SIERRA) trial, which was a multicenter, open-label, randomized, controlled, 2 arm, optional 1-way crossover study of ^{131}I-apamistamab versus the investigator's choice of conventional care (CC) in subjects aged 55 or older with active, R/R AML.

Inpatient Administration of ^{131}I-apamistamab
The therapeutic regimen of ^{131}I-apamistamab takes place in the inpatient setting. The dosimetric infusion will be performed in the outpatient setting, and patients will be admitted as hospital inpatient prior to receiving the therapeutic infusion of ^{131}I-apamistamab. After receiving the therapeutic dose, patients stay in radiation isolation for about 3-7 days following which there are two possible scenarios: 1) the patient remains inpatient and proceeds with fludarabine and low-dose total body irradiation (TBI) followed by alloHCT and engraftment/recovery or 2) the patient is discharged after the therapeutic dose of ^{131}I-apamistamab and receives fludarabine as outpatient to be readmitted for TBI and alloHCT and engraftment/recovery.

The ^{131}I-apamistamab therapeutic dose is administered following a dosimetric dose. The patient is premedicated with antiemetics, antihistamines, hydrocortisone, and acetaminophen prior to initiation of infusion and repeated as needed for any infusion reactions. The therapeutic dose for each subject is individualized, based on the dosimetric findings to deliver 24 Gy radiation to the dose limiting organ (typically liver), or 48 Gy to the bone marrow, whichever is predicted to receive the highest estimated dose of radiation. The therapeutic infusion is to be administered 6 to 14 days after the dosimetric infusion. The day of therapeutic infusion is considered Day -12 relative to the timing of the allogeneic HCT (Day 0).

^{131}I-apamistamab is administered via continuous intravenous infusion over 6-8 hours and is followed by a 1-hour saline flush. Following the administration of the therapeutic infusion of ^{131}I-apamistamab, patients will be scheduled to receive fludarabine on days -4, -3, and -2 prior to the alloHCT, and an immunosuppression regimen will be initiated per the institutional GvHD

[3] Gyurkocza et al. Late Breaking Abstract, Transplantation & Cell Therapy (TCT) 2023.

prophylaxis protocol being used. On Day 0, patients will receive low-dose total body irradiation (TBI), that will be followed by the infusion of the donor hematopoietic stem cells.

^{131}I- apamistamab enabled 100% of patients to undergo alloHCT after receiving the therapeutic dose, compared with 17% of CC treated subjects.[3] Efficacy was measured by the percentage of subjects achieving durable complete remission (dCR) defined as initial CR/complete platelet recovery (CRp) assessed 28-56 days post alloHCT or 28-42 days post initiation of therapy on the CC arm, that lasted ≥180 days. Compared to no subjects achieving dCR in the CC group (0/77, 0%), the dCR rate for the ^{131}I- apamistamab group was 17.1% (13/76) in the Intent to Treat (ITT) Analysis Set and 22.0% (13/59) in the Per Protocol (PP) Analysis Set ($p<0.0001$).[3] The incidence of sepsis was greater than four times lower (6.1% vs. 28.6%); while febrile neutropenia (43.9% vs. 50.0%), mucositis (15.2% vs. 21.4%) and acute GvHD (26.1% vs. 35.7%) were lower in favor of ^{131}I-apamistamab.[3] Per the requestor, ^{131}I-apamistamab infusion can be associated with infusion reactions commonly experienced when patients receive monoclonal antibodies.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of ^{131}I-apamistamab. Facilities can report the intravenous administration of ^{131}I-apamistamab using one of the following 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 ^{131}I-apamistamab. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of ^{131}I-apamistamab.

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 V** Iodine-131 Radiolabeled Apamistamab Antineoplastic	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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

Topic # 02 - Administration of Talquetamab

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of talquetamab. The requester is seeking an April 1, 2024 implementation date.

New Technology Application? Yes. The requestor intends to submit a New Technology Add-On Payment (NTAP) application for FY 2025 consideration.

Food and Drug Administration (FDA) Approval? Yes. The requestor received FDA accelerated approval for TALVEY™ (talquetamab) on August 9, 2023. TALVEY™ (talquetamab) is a bispecific antibody indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody. The indication is approved under accelerated approval based on response rate and durability of response. The requestor received Orphan Drug designation for the treatment of multiple myeloma by the FDA and PRIME designation by the European Commission (2021) and Breakthrough Therapy designation (June 2022).

Background: Multiple myeloma (MM) is a rare blood cancer that affects plasma cells. MM occurs when healthy cells turn into abnormal cells that multiply and produce abnormal antibodies called M proteins. The abnormalities can affect bones, kidneys, and the body's ability to make healthy white and red blood cells and platelets. Multiple myeloma remains incurable, and most patients eventually relapse, even with the advent of new treatments.[1] Novel, innovative therapies are needed to improve long-term survival and outcomes.

Immunotherapies, which include chimeric antigen receptor T-cell (CAR-T) therapy as well as some antibody-based therapies, engage the patient's immune system to fight cancer. These therapies (bispecifics) essentially use the patient's own immune system to fight cancer by binding to the patient's T-cells, and to multiple myeloma cells expressing a specific surface antigen.

Bispecific antibodies (bsAbs) are a new class of drug, which can facilitate T-cell engagement without the need for patient cell collection and external manipulation. G protein-coupled receptor class C group 5 member D (GPRC5D) is an orphan, seven transmembrane G-protein coupled receptor that is normally expressed in plasma cells. GPRC5D mRNA is overexpressed in the bone marrow of patients with multiple myeloma with low expression in normal tissues. Additionally, GPRC5D protein is overexpressed on multiple myeloma cells from bone marrow samples with a distribution that mimics BCMA.[2] According to the requestor, taken together, data suggests that GPRC5D is a potential target for anti-myeloma therapy.

[1] Rajkumar, SV. Multiple myeloma: Every year a new standard? *Hematological Oncology*. 2019; 37(S1): 62– 65. https://doi.org/10.1002/hon.2586

[2] Smith, Eric L et al. GPRC5D is a target for the immunotherapy of multiple myeloma with rationally designed CAR T cells. *Science translational medicine* 2019; 11(485): eaau7746. doi:10.1126/scitranslmed.aau7746

Mechanism of Action
TALVEY™ (talquetamab) is a full-sized bispecific antibody that binds to CD3-expressing T-cells to myeloma cells that express GPRC5D, resulting in activation of the T-cell receptor pathway and lysis of GPRC5D-expressing MM cells. This is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T-cells. These activated T-cells also lead to the production of cytokines, chemical signals that activate other T-cells to create a microenvironment that leads to further immune activation, augmenting the anti-tumor response.[1] Talquetamab was developed by controlled fragment antigen binding arm exchange from two parental antibodies using the DuoBody platform which generates a full-sized antibody. Per the requestor, this structure is advantageous as it is designed to mimic naturally occurring IgG antibodies resulting in longer stability. Additionally, talquetamab can be administered subcutaneously (SC) and does not require bolus or continuous intravenous (IV) infusion.

Inpatient Administration of Talquetamab
Talquetamab is a drug administered via subcutaneous injection. Patients will follow either a weekly or biweekly (every two weeks) treatment schedule. Under both the weekly and biweekly dosing schedule, patients should be admitted to the hospital for the priming doses. It is expected that the subsequent treatment doses will be administered in an ambulatory care setting. Patients on the weekly dosing schedule will receive three priming doses during the first five days of treatment: 10 μg/kg for the first priming dose, 60 μg/kg for the second priming dose, and 40 μg/kg for the third priming dose and once per week for the treatment dose thereafter. Patients receiving treatment on a biweekly dosing schedule will receive four priming doses during the first seven days of treatment: 10 μg/kg for the first priming dose, 60 μg/kg for the second priming dose, 40 μg/kg for the third priming dose, and 80 μg/kg for the fourth priming dose and once every two weeks for the treatment dose thereafter.

Most of the high-grade adverse events (AE) were cytopenias, which were limited to the first few cycles of administration. The most common AEs were cytokine release syndrome (CRS), skin related events and dysgeusia.[3] Low rates of grade 3/4 nonhematologic AEs were observed and low rates of discontinuation due to AEs were observed with once weekly (QW) (4.9%) and once every 2 weeks (Q2W) (6.2%) dosing schedules. Cytokine Release Syndrome (CRS) occurred in 79% and 72% of patients respectively, but 2% and 1% of patients developed grade 3 CRS.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of talquetamab. Facilities can report the subcutaneous administration of talquetamab using the following 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 administration of talquetamab. Continue coding as listed in current coding.

[3] Chari A, et al. Presented at 64th American Society of Hematology (ASH) Annual Meeting; December 10-13, 2022; New Orleans, LA.

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

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 2** Talquetamab Antineoplastic	**9** New Technology Group 9

CMS Recommendation: Option 2, as described above.

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