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

CENTER FOR MEDICARE

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

Consistent with the requirements of section 1886(d)(5)(K)(iii) of the Social Security Act, applicants submitted requests to create a unique procedure code to describe the administration of a therapeutic agent, such as the option to create a new code in Section X within the ICD-10-PCS procedure code classification. CMS is soliciting public comments regarding any clinical questions or coding options for the 13 listed procedure code topics related to 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 October 1, 2022 implementation is April 8, 2022. Members of the public should send any questions or comments to the CMS mailbox at: ICDProcedureCodeRequest@cms.hhs.gov.

Prior to the meeting, CMS will post a question and answer document on our website at https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials to address clinical or coding questions that members of the public have submitted related to the 13 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 April 8, 2022 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 upcoming virtual meeting on March 8-9, 2022. CMS will present the NTAP-related ICD-10-PCS procedure code requests that do not involve the administration of a therapeutic agent and all non-NTAP-related procedure code requests during the virtual meeting on March 8, 2022.

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

Mady Hue
(410) 786-4510
Marilu.hue@cms.hhs.gov

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

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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 2023.*
***Requestor intends to submit an NTAP application for FY 2024 consideration.*

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

ICD-10 TIMELINE

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

March 8-9, 2022	ICD-10 Coordination and Maintenance Committee Meeting.
March 2022	Recordings and slide presentations of the March 8-9, 2022 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
April 1, 2022	New ICD-10 codes to capture new diseases or technology will be implemented on April 1, 2022.
April 8, 2022	**Deadline for receipt of public comments on proposed new procedure codes and revisions discussed at the March 8-9, 2022 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2022**.
April 2022	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 2023 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/June 2022	Final addendum posted on web pages as follows: **Diagnosis addendum -** https://www.cdc.gov/nchs/icd/icd10cm.htm **Procedure addendum -** https://www.cms.gov/Medicare/Coding/ICD10/index.html
June 10, 2022	**Deadline for requestors: Those members of the public requesting that topics be discussed at the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting, must have their requests submitted to CMS for procedures and NCHS for diagnoses.**

July 2022	Federal Register notice for the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
August 1, 2022	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, 2022. This rule can be accessed at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/index.html
August 2022	Tentative agenda for the Procedure portion of the September 13, 2022 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 14, 2022 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the NCHS webpage at - https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm
August 12, 2022	**On-line registration opens for the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting at:** https://www.eventbrite.com/ Please note that this meeting will be conducted virtually and registration is not required to attend. However, we are providing the ability to register on-line for those required to provide proof of attendance for continuing education purposes. The on-line registration will be available through September 12, 2022.
September 13-14, 2022	The September 2022 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 2022	Recordings and slide presentations of the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm

	Procedure code portion of the recording and related materials– https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
October 1, 2022	New and revised ICD-10-CM and ICD-10-PCS codes go into effect along with MS-DRG changes. Final addendum available on web pages as follows: **Diagnosis addendum –** https://www.cdc.gov/nchs/icd/icd10cm.htm **Procedure addendum –** https://www.cms.gov/Medicare/Coding/ICD10/
October 14, 2022	**Deadline for receipt of public comments on proposed new codes discussed at the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2023.**
November 2022	Any new ICD-10 codes required to capture new technology that will be implemented on the following April 1 will be announced. Information on any new codes to be implemented April 1, 2023 will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd10cm.htm https://www.cms.gov/Medicare/Coding/ICD10/
November 15, 2022	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2023.**

Medicare Electronic Application Request Information System™ (MEARIS™)

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

Effective March 1, 2022, the full release of MEARIS™ became active for ICD-10-PCS code request submissions. ICD-10-PCS code request submissions are due no later than June 10, 2022 to be considered for the September 13-14, 2022 ICD-10 Coordination and Maintenance Committee Meeting.

Moving forward, 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.

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, 2022
- 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 8, 2022 for codes being considered for October 1, 2022 implementation
  - May 9, 2022 for diagnosis codes being considered for October 1, 2023 implementation
- Procedure comments to CMS ICDProcedureCodeRequest@cms.hhs.gov
- Diagnosis comments to NCHS nchsicd10cm@cdc.gov

Proposed and Final Rules

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

Addendum

- May/June 2022 – Final code updates and addendum posted
  - FY 2023 ICD-10-PCS (Procedures) http://www.cms.gov/Medicare/Coding/ICD10/index.html
  - FY 2023 ICD-10-CM (Diagnoses) http://www.cdc.gov/nchs/icd/icd10cm.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 8, 2022 for codes to be implemented on October 1, 2022
  - May 9, 2022 for diagnosis codes to be implemented on October 1, 2023
  - 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 October 1, 2022 implementation

September 13-14, 2022 C&M Code Requests

- June 10, 2022 – Deadline for submitting topics for September 13-14, 2022 C&M meeting
  - Procedure requests to CMS https://mearis.cms.gov.
  - Diagnosis requests to NCHS nchsicd10cm@cdc.gov

Administration of Spesolimab

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? No. The FDA is currently reviewing the Spesolimab Biologics License Application (BLA) and has granted Priority Review. Spesolimab was previously granted both Orphan Drug and Breakthrough Therapy Designation for the treatment of flares in patients with generalized pustular psoriasis (GPP).

Background: Generalized pustular psoriasis **(**GPP) is a heterogenous and potentially life-threatening neutrophilic skin disease, with a considerable burden for patients. GPP is a rare disease, with US prevalence estimated to be less than 1/10,000 and it is characterized by episodes of flares with widespread eruption of sterile, macroscopic pustules that can occur with or without systemic inflammation.[1]

GPP causes significant morbidity and, in some cases, mortality; infectious, metabolic, cardiac, liver, respiratory, and neurological comorbidities have been reported.1 Various factors have been reported to trigger a GPP flare, including pregnancy, severe injury, or viral and bacterial infections. The use and subsequent withdrawal of systemic corticosteroids is a key contributing factor.[2,3]

The immunopathological component of GPP flares has been linked to the IL-36 pathway, with dysregulated signaling stimulating excessive proinflammatory cytokine and chemokine production, leading to neutrophilic and mononuclear inflammatory infiltrates in the epidermis, and the development of sterile, macroscopic pustules.[4]

The clinical, pathological and genetic features associated with GPP establish it as a distinct disease entity from plaque psoriasis.[5,6,7,8] Although there are shared pathways between GPP and plaque psoriasis, the IL-36 pathway is predominantly involved in the pathogenesis of GPP, while the IL-23 axis drives plaque psoriasis.[9,10]

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[1]Strober B, et al. Unmet medical needs in the treatment and management of generalized pustular psoriasis flares: Evidence from a survey of corrona registry dermatologists. Dermatol Ther (Heidelb) 2021.
[2]Zelickson BD, et al. Generalized Pustular Psoriasis. Arch Dermatol 1991;127:1339–1345.
[3] Choon SE, et al. Clinical profile, morbidity, and outcome of adult-onset generalized pustular psoriasis: analysis of 102 cases seen in a tertiary hospital in Johor, Malaysia. Int J Dermatol 2014;53:676–684.
[4] Iznardo H, et al. Exploring the Role of IL-36 Cytokines as a New Target in Psoriatic Disease. Int J Mol Sci. 2021 Apr 21;22(9):4344. doi: 10.3390/ijms22094344.
[5] Furue K, et al. Highlighting Interleukin-36 Signaling in Plaque Psoriasis and Pustular Psoriasis. Acta Derm Venereol 2018;98:5–13.
[6] Johnston A, et al. IL-1 and IL-36 are dominant cytokines in generalized pustular psoriasis. J Allergy Clin Immunol 2017;140:109–120.
[7] Navarini AA, et al. European consensus statement on phenotypes of pustular psoriasis. J Eur Acad Dermatol Venereol 2017;31:1792–1799.
[8] Twelves S, et al. Clinical and genetic differences between pustular psoriasis subtypes. J Allergy Clin Immunol 2019;143:1021–1026.
[9] Gooderham MJ, et al. An update on generalized pustular psoriasis. Expert Rev Clin Immunol 2019;15:907–919.
[10] Liang Y, et al. Psoriasis: a mixed autoimmune and autoinflammatory disease. Curr Opin Immunol 2017;49:1–8.

Description and Mechanism of Action for Spesolimab
Spesolimab is a humanized monoclonal IgG1 antibody (mAb) against human IL36R signaling produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

The product is a sterile, preservative-free, colorless to slightly brownish-yellow, clear to slightly opalescent solution formulated in an acetate buffer suitable for intravenous infusion. Each single-dose 7.5 mL vial contains 450 mg spesolimab.

Binding of spesolimab to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. IL-36R signaling is differentiated from TNF-α, integrin and IL-23 inhibitory pathways by directly and simultaneously blocking both inflammatory and pro- fibrotic pathways. According to the requestor, genetic human studies have established a strong link between IL36R signaling and skin inflammation.

Inpatient Administration of Spesolimab
Spesolimab is administered via an intravenous (IV) injection, as a single 900 mg (2 x 450 mg/7.5 mL vials) intravenous infusion over 90 minutes. If flare symptoms persist, an additional intravenous 900 mg dose may be administered 1 week after the initial dose. Spesolimab must be diluted before use.

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

3E033GC Introduction of other therapeutic substance into peripheral vein, percutaneous approach
3E043GC Introduction of other therapeutic substance into central vein, percutaneous approach

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

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

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 0** Spesolimab Monoclonal Antibody	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of daratumumab and hyaluronidase-fihj

Issue: There are currently no unique ICD-10-PCS codes to describe the administration of daratumumab and hyaluronidase-fihj.

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? Yes. Darzalex Faspro® was granted accelerated approval by the FDA on January 15, 2021 for newly diagnosed light chain amyloidosis. Darzalex Faspro® is also approved for multiple indications for treatment of patients with multiple myeloma (MM), from newly diagnosed MM to relapsed/refractory MM.

Background: Light chain (AL) amyloidosis is a life-threatening blood disorder caused by the increased production of misfolded immunoglobulin light chains by an abnormal proliferation of malignant CD38+ plasma cells. The most frequently affected organs are the heart, kidney, liver, spleen, gastrointestinal tract and nervous system. Patients often have a poor prognosis, due in part to the delay in diagnosis of AL amyloidosis, which frequently presents with symptoms that mimic other, more common conditions, resulting in significant life-threatening cardiac and renal damage by the time of diagnosis. In fact, as many as 30 percent of patients die within the first year after diagnosis owing to cardiac involvement and progression to end stage-renal disease.[1]

Darzalex Faspro® (daratumumab and hyaluronidase-fihj) is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, and is indicated for the treatment of AL amyloidosis in combination with bortezomib, cyclophosphamide and dexamethasone (CyBorD) in newly diagnosed patients. Darzalex Faspro® is the first and only FDA-approved treatment for patients with AL amyloidosis. Darzalex Faspro® is not indicated and is not recommended for the treatment of patients with AL amyloidosis who have New York Heart Association (NYHA) Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.

Mechanism of Action
Daratumumab is a human IgG- kappa monoclonal antibody that targets CD38, an enzymatic protein that is uniformly expressed on the surface of human plasma cells, specialized white blood cells which normally produce antibodies to fight infection. Daratumumab binds to the CD38 protein on the surface of the malignant plasma cells which are responsible for abnormal amyloid protein production in AL amyloidosis. By doing this, daratumumab directly kills the malignant CD38+ plasma cells from the direct anti-tumor effect[2,3] and/or directs the immune system to destroy them from immunomodulation and immune mediated activity.[4] The other therapies currently used to treat amyloidosis have different mechanisms of action.

[1] Merlini et al. Systemic immunoglobin light chain amyloidosis. Nat Rev Dis Primers. 2018; 4:38-19.
[2] de Weers et al.Daratumumab, a Novel Therapeutic Human CD38 Monoclonal Antibody, Induces Killing of Multiple Myeloma and Other Hematogical Tumors. J Immunol 2011;186:1840-1848.
[3] Overdijk et al. Antibody-mediated phagocytosis contributes to the anti-tumor activity of the therapeutic antibody daratumumab in lymphoma and multiple myeloma. MAbs.2015;7:311-321.
[4] Krejcik J, Casneuf T, Nijhof IS, et al. Daratumumab depletes CD38+ immune regulatory cells, promotes T-cell expansion, and skews T-cell repertoire in multiplemyeloma. Blood 2016; 128: 384-94.

In Darzalex Faspro®, daratumumab is co-formulated with recombinant human hyaluronidase (rHuP20), which critically allows daratumumab to be administered in a volume of 15 mL by a 3-5 minute injection under the skin, compared to the 500-1000 mL volume and 3-7 hour administration time required for IV daratumumab. Given the cardiac and renal dysfunction which afflicts many AL amyloidosis patients and makes them poor candidates for large volume IV administration, rHuP20 is a critical component of Darzalex Faspro®.

Inpatient Administration of Darzalex Faspro®
The recommended dosage for Darzalex Faspro® for newly diagnosed light chain amyloidosis is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously over approximately 3-5 minutes in combination with bortezomib, cyclophosphamide and dexamethasone. The injection site should be approximately 3 inches to the right or left of the navel. The dosage schedule is below.

Weeks	**Schedule**
Weeks 1-8	Weekly (total of 8 doses)
Weeks 9-24[a]	Every two weeks (total of 8 doses)
Weeks 25 onwards until disease progression or a maximum of 2 years[b]	Every four weeks

[a] First dose of the every-2-week dosing schedule is given at Week 9
[b] First dose of the every-4-week dosing schedule is given at Week 25

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

3E013GC Introduction of other therapeutic substance into subcutaneous tissue, percutaneous approach

Coding Options

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

Option 2. Create new codes in section X, New Technology, to identify the subcutaneous injection of daratumumab and hyaluronidase-fihj.

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 1** Daratumumab and Hyaluronidase-fihj	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Extracorporeal Antimicrobial Administration during Renal Replacement Therapy

Issue: There are currently no unique ICD-10-PCS codes to describe the instillation of taurolidine and heparin in a central venous catheter (CVC) during renal replacement therapy.

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? No. In the United States, DefenCath™ was designated by the FDA as a Qualified Infectious Disease Product (QIDP) in 2015 and has been granted FDA Fast Track status. CorMedix received a complete response letter from the FDA for the New Drug Application (NDA) for DefenCath™ in the first quarter of 2021 and is currently preparing responses to the manufacturing deficiencies and plans to resubmit the NDA.

Background: In the United States, approximately 80 percent of patients initiate hemodialysis (HD) with a tunneled, cuffed dual-lumen catheter, and approximately 20 percent of all prevalent hemodialysis patients use such catheters.[1] Tunneled catheters are associated with a number of complications and, in particular, catheter-related bloodstream infection (CRBSI). Despite improvements and initiatives to control infection, hemodialysis catheter biofilm can develop within 24 hours and can lead to life-threatening infections, costing the U.S. healthcare system billions of dollars annually.

Typically, patients receive three HD sessions per week. Beneficiaries likely to receive dialysis during an inpatient stay, and therefore potentially at risk for CRBSI, include those with a diagnosis of end stage renal disease (ESRD), chronic kidney disease (CKD), acute kidney injury (AKI), or acute tubular necrosis (ATN). The incidence of CRBSIs is approximately one to two episodes per catheter-year and gram-positive organisms are responsible for most CRBSIs.[2]

DefenCath™, an investigational drug product, is under development for use as a catheter lock solution (CLS) with the aim of reducing the risk of CRBSIs from in-dwelling catheters in patients receiving chronic hemodialysis through a central venous catheter (CVC). Upon approval, DefenCath™ is expected to be the first and only FDA-approved antimicrobial CLS in the United States.

Technology
DefenCath™ is a proprietary formulation of taurolidine 1.35%, and heparin 1000 units/mL. Taurolidine, the antimicrobial compound in DefenCath™, is a derivative of the amino acid taurine, with in vitro studies indicating broad antimicrobial activity against gram-positive and gram-negative bacteria, including antibiotic resistant strains, as well as mycobacteria and clinically relevant fungi including Aspergillus. CorMedix has completed a Phase 3 clinical trial, known as LOCK-IT-100, which demonstrated a significant and clinically relevant 71% decrease in catheter-related bloodstream infection (CRBSI) in patients receiving hemodialysis for the treatment of kidney failure when compared with heparin alone, which is the current standard of care for a catheter lock solution.

[1] Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis 2006; 48 Suppl 1:S2.
[2] Allon M. Dialysis catheter-related bacteremia: treatment and prophylaxis. Am J Kidney Dis 2004; 44:779.

Procedure
DefenCath™ will be available in a single dose vial. The dosing amount is calibrated to the volume of the catheter lumen. It is instilled to the fill volume printed on the catheter hubs of the arterial and venous lumens as a lock solution at the conclusion of each dialysis session. Each single vial dose has enough volume to fill both lumens of the dialysis catheter. DefenCath™ is aspirated, not flushed, before beginning the next dialysis session. DefenCath™ is not to be injected into the patient and there is no intended systemic administration.

Current Coding: The instillation of taurolidine and heparin in a central venous catheter (CVC) during renal replacement therapy is not reported separately for inpatient hospital coding. Facilities report the hemodialysis procedure using the appropriate code from the table below.

Section	**5** Extracorporeal or Systemic Assistance and Performance		
Body System	**A** Physiological Systems		
Operation	**1** Performance: Completely taking over a physiological function by extracorporeal means		
Body System	*Duration*	*Function*	*Qualifier*
D Urinary	**7** Intermittent, Less than 6 Hours Per Day **8** Prolonged Intermittent, 6-18 hours Per Day **9** Continuous, Greater than 18 hours Per Day	**0** Filtration	**Z** No Qualifier

Coding Options

Option 1. Do not create new ICD-10-PCS codes to describe the instillation of taurolidine and heparin in a CVC during renal replacement therapy. Continue coding as listed in current coding.

Option 2. Create a new code in section X, New Technology, to identify the instillation of taurolidine and heparin in a CVC during renal replacement therapy. A separate code would continue to be reported for the hemodialysis.

Section	**X** New Technology		
Body System	**Y** Extracorporeal		
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*
Y Extracorporeal	**X** External	**ADD 2** Taurolidine Anti-infective and Heparin Anticoagulant	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of Maribavir

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? Yes. Maribavir received Priority Review for post-transplant recipients with cytomegalovirus (CMV) infection in those resistant/refractory to prior anti-CMV treatment and Breakthrough Therapy Designation as a treatment for CMV infection and disease in transplant patients resistant or refractory to prior therapy. Maribavir also has an Orphan Drug Designation for treatment of clinically significant CMV viremia and disease in at-risk patients. Maribavir received FDA approval on November 23, 2021.

Background: CMV is a beta herpesvirus that commonly infects humans; serologic evidence of prior infection can be found in 40%-100% of various adult populations.[1] CMV typically resides latent and asymptomatic in the body but may reactivate during periods of immunosuppression. Serious disease may occur in individuals with compromised immune systems, which includes patients who receive immunosuppressants associated with various types of transplants including Hematopoietic Cell Transplant (HCT) or Solid Organ Transplant (SOT).[2,3] Out of the estimated 200,000 adult transplants per year globally, CMV is one of the most common viral infections experienced by transplant recipients, with an estimated incidence rate between 16-56% in SOT recipients and 30-70% in HCT recipients.[3,4,5,6,7,8]

In transplant recipients, reactivation of CMV can lead to serious consequences including loss of the transplanted organ and, in extreme cases, can be fatal.[9,10] Existing therapies to treat post-transplant CMV infections may demonstrate serious side effects that require dose adjustments or may fail to adequately suppress viral replication.[11,12,13]

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[1] Krech U. Complement-fixing antibodies against cytomegalovirus in different parts of the world. Bull WHO. 1973;49:103-106.
[2] de la Hoz R. Diagnosis and treatment approaches to CMV infections in adult patients. J Clin Virol. 2002;25:S1-S12.
[3] Azevedo L, Pierrotti L, Abdala E, et al. Cytomegalovirus infection in transplant recipients. Clinics. 2015;70(7):515-523. doi:10.6061/clinics/2015(07)09.
[4] World Health Organization. International Report on Organ Donation and Transplantation Activities- Executive Summary 2018; 2020. Accessed December 2, 2020. http://www.transplant-observatory.org/wp-content/uploads/2020/10/glorep2018-2.pdf.
[5] World Health Organization. Haematopoietic Stem Cell Transplantation HSCtx. Accessed December 2, 2020. https://www.who.int/transplantation/hsctx/en/.
[6] Razonable RR, Eid AJ. A Viral infections in transplant recipients. Minerva Med. 2009;100(6):23.
[7] Styczynski J. Who Is the Patient at Risk of CMV Recurrence: A Review of the Current Scientific Evidence with a Focus on Hematopoietic Cell Transplantation. Infect Ther. 2018;7:1-16.
[8] Cho S-Y, Lee D-G, Kim H-J. Cytomegalovirus Infections after Hematopoietic Stem Cell Transplantation: Current Status and Future Immunotherapy. Int J Mol Sci. 2019;20(2666):1-17.
[9] Fishman JA. Infection in Organ Transplantation. Am J Transplant. 2017;17:856-879.
[10] Kenyon M, Babic A, eds. The European Blood and Marrow Transplantation Textbook for Nurses. Springer International Publishing; 2018. doi:10.1007/978-3-319-50026-3.
[11] Martín-Gandul C, Pérez-Romero P, González-Roncero FM, et al. Clinical impact of neutropenia related with the preemptive therapy of CMV infection in solid organ transplant recipients. *J Infect.* 2014;69(5):500-506. doi:10.1016/j.jinf.2014.07.001.
[12] Chemaly RF, Chou S, Einsele H, et al. Definitions of Resistant and Refractory Cytomegalovirus Infection and Disease in Transplant Recipients for Use in Clinical Trials. *Clin Infect Dis.* 2019;68(8):1420-1426. doi:10.1093/cid/ciy696.
[13] Beyer K. Outpatient Foscarnet Administration Incorporating Home Infusions Is Feasible Greatly Enhancing the Care of Hematopoietic Stem Cell Transplant Recipients. *Biol Blood Marrow Transpl.* 2017;23:S18-S391.

LIVTENCITY™ (maribavir) is a cytomegalovirus (CMV) pUL97 kinase inhibitor indicated for the treatment of adults and pediatric patients (12 years of age and older and weighing at least 35 kg) with post-transplant CMV infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet.[14]

Mechanism of Action
LIVTENCITY™ (maribavir) is a novel, orally bioavailable benzimidazole riboside antiviral with a mechanism of action that is differentiated from current CMV antivirals. Unlike currently utilized agents that all inhibit CMV DNA polymerase, maribavir attaches to the pUL97 encoded serine/threonine kinase at the adenosine triphosphate (ATP) binding site, abolishing phosphotransferase required for a variety of essential viral processes such as DNA replication, encapsidation, and nuclear egress.[15,16,17]

Inpatient Administration of Maribavir
The recommended dosage in adults and pediatric patients (12 years of age and older and weighing at least 35 kg) is 400 mg (two 200 mg tablets) taken orally twice daily with or without food. If maribavir is co-administered with carbamazepine, the dosage of maribavir should be increased to 800 mg twice daily. If maribavir is co-administered with phenytoin or phenobarbital, the dosage of maribavir should be increased to 1,200 mg twice daily.[14]

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

3E0DX29	Introduction of other anti-infective into mouth and pharynx, external approach
3E0G729	Introduction of other anti-infective into upper G.I., via natural or artificial opening
3E0H729	Introduction of other anti-infective into lower G.I., via natural or artificial opening

Coding Options

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

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

[14] LIVTENCITY™ (maribavir) Prescribing Information, https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215596lbl.pdf
[15] Biron KK, Harvey RJ, Chamberlain SC, et al. Potent and selective inhibition of human cytomegalovirus replication by 1263W94, a benzimidazole L-riboside with a unique mode of action. Antimicrob Agents Chemother. 2002;46(8):2365-2372. doi:10.1128/AAC.46.8.2365-2372.2002.
[16] Wolf DG, Courcelle CT, Prichard MN, Mocarski ES. Distinct and separate roles for herpesvirus-conserved UL97 kinase in cytomegalovirus DNA synthesis and encapsidation. Proc Natl Acad Sci U S A. 2001;98(4):1895-1900. doi:10.1073/pnas.98.4.1895.
[17] Shannon-Lowe CD, Emery VC. The effects of maribavir on the autophosphorylation of ganciclovir resistant mutants of the cytomegalovirus UL97 protein. Herpesviridae. 2010;1(1):4. Published 2010 Dec 7. doi:10.1186/2042-4280-1-4.

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 3** Maribavir Anti-infective	**8** New Technology Group 8
G Upper GI **H** Lower GI	**7** Via Natural or Artificial Opening	**ADD 3** Maribavir Anti-infective	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of Teclistamab

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-On Payment (NTAP) application for FY 2023 consideration.

Food and Drug Administration (FDA) Approval: On June 1, 2021, teclistamab was granted aBreakthrough Therapy designation for treatment in adults with measurable multiple myeloma that is relapsed or refractory to established multiple myeloma therapies. In December 2021, the requestor submitted a Biologics License Application (BLA) to the FDA seeking approval of teclistamab.

Background: Significant improvements have been made in the treatment of multiple myeloma, particularly at first diagnosis and during early relapse. However, despite improved outcomes, myeloma remains incurable as most patients' disease eventually becomes refractory to multiple therapies, leading to disease relapse and fewer treatment options. Novel, innovative therapies are needed to improve long-term survival and outcomes for relapsed and refractory multiple myeloma (R/R MM, particularly for patients with multiple prior treatments. Bispecific antibodies (bsAbs) represent a new class of drug that engage the patient's immune system to fight cancer by redirecting the patient's own T cells toward cells expressing a tumor-specific antigen.

Description and Mechanism of Action for Teclistamab
Teclistamab is a full-sized immunoglobulin G (IgG) antibody with two distinct antigen binding regions: one that binds CD3 on T cells and another that binds B Cell Maturation Antigen (BCMA) on myeloma cells. This dual binding brings T cells into proximity with target myeloma cells and triggers T cell activation, leading to a cascade of 'effector' events whereby T cells are induced to produce chemicals that then destroy the myeloma cells.

According to the requestor, the structure of teclistamab is advantageous versus approved bispecific platforms since it is designed to mimic naturally-occurring IgG antibodies. This affords longer stability and negates the need for continuous infusion, allowing for not only intermittent dosing but also the potential for delivery via a more convenient subcutaneous route. Teclistamab was specifically designed using the Duobody platform to generate a full-sized IgG4 antibody with dual specificity for CD3 and BCMA via single-arm exchange of the antigen binding fragments (Fab portions) of CD3 and BCMA- specific antibodies. The Duobody platform also allows for engineering of the various domains to optimize performance and limit toxicity. For example, the requestor stated the specificity of CD3 binding can be altered to mitigate toxicity related to avid binding to T cells. In addition, the 'stalk' portion, or Fc domain, of the Duobody has been inactivated to eliminate engagement of other mechanisms of action (e.g. antibody-dependent cellular cytotoxicity via natural killer (NK) cells), which helps to control the magnitude of the anti-tumor immune response and limit it primarily to T cell redirection.

Inpatient Administration of Teclistamab
Teclistamab is administered subcutaneously. Patients receiving teclistamab receive two priming doses: 60 μg/kg for the first priming dose, and 300μg/kg for the second priming dose. For the third dose onward, patients receive 1500 μg/kg doses once weekly until disease progression or unacceptable toxicity.

Current Coding: There is no unique ICD-10-PCS code to describe the administration of teclistamab. Facilities can report the administration of teclistamab with the following ICD-10- PCS code:

3E01305 Introduction of other antineoplastic into subcutaneous tissue, percutaneousapproach

Coding Options

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

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

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 4** Teclistamab Antineoplastic	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of Mosunetuzumab

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food and Drug Administration (FDA) Approval? Mosunetuzumab was granted Breakthrough Therapy Designation (BTD) by the FDA on July 14, 2020. FDA approval is anticipated by June 30, 2022, for the proposed indication of treatment for adults with relapsed or refractory follicular lymphoma (R/R FL) who have received at least 2 prior systemic therapies.

Background: Non-Hodgkin's Lymphoma (NHL) is one of the leading causes of cancer death in the United States.[1] Follicular lymphoma (FL) is the second-most common sub-type of NHL diagnosed in the U.S. and Western Europe, and accounts for approximately 20% to 30% of all NHL cases.[2] The rate of new cases of follicular lymphoma was 2.7 per 100,000 men and women per year based on 2014–2018 cases, age-adjusted,[3,4] affecting approximately 16,000[5] individuals in the United States.

FL is a slow-growing, incurable lymphoma arising from the transformation of B cells into malignant cells, characterized by a prolonged course during which patients can experience multiple relapses between disease-free periods.[6] The primary disease pathology involves abnormal, uncontrolled growth and proliferation of malignant B cells, grouped in clusters (or follicles).[7,8] FL can lead to enlargement of specific lymph node regions; involvement of other lymphatic tissues, such as the spleen or bone marrow; and metastasis to other bodily tissues and organs.[9]

Individuals with FL can experience multiple relapses, and for those who progress from front-line therapies, the disease-free intervals become shorter with increased refractoriness with each

[1] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2015. CA Cancer J. Clin. 2015;65(1):5-29. doi:10.3322/caac.21254.
[2] Ambinder AJ, Shenoy PJ, Malik N, et al. Exploring risk factors for follicular lymphoma. Adv. Hematol. 2012;2012:1-13. doi:10.1155/2012/626035.
[3] National Cancer Institute. Cancer Stat Facts: NHL – Follicular Lymphoma. *SEER*. Accessed on October 28, 2021 from https://seer.cancer.gov/statfacts/html/follicular.html.
[4] Dreyling M, Ghielmini M, Rule S, et al. ESMO Guidelines Committee. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol. 2016;27(suppl 5):v83-v90. doi:10.1093/annonc/mdw400.
[5] Jaglowski SM, Linden E, Termuhlen AM, Flynn JM. Lymphoma in adolescents and young adults. Semin. Oncol. 2009;36(5):381-418. doi:10.1053/j.seminoncol.2009.07.009.
[6] Carbone A, Roulland S, Gloghini A, et al. Follicular lymphoma. Nat. Rev. Dis. Primers. 2019:5(1)P83. doi:10.1038/s41572-019-0132-x.
[7] Nann D, Ramis-Zaldivar JE, Müller I, et al. Follicular lymphoma t(14;18)-negative is genetically a heterogeneous disease. Blood Adv. 2020;4(22):5652-5665. doi:10.1182/bloodadvances.2020002944
[8] Carbone A, Roulland S, Gloghini A, et al. Follicular lymphoma. Nat. Rev. Dis. Primers. 2019:5(1)P83. doi:10.1038/s41572-019-0132-x.
[9] Carbone A, Roulland S, Gloghini A, et al. Follicular lymphoma. Nat. Rev. Dis. Primers. 2019:5(1)P83. doi:10.1038/s41572-019-0132-x.

subsequent progression/relapse.[10,11] Reviews of pertinent literature, including an analysis from the National LymphoCare Study, have indicated a higher risk of death in patients with early progression of disease.[12,13] The GALLIUM study showed mortality risk was higher the earlier patients progressed within the first 24 months of first line (1L) chemoimmunotherapy.[14]

According to the requestor, patients with FL who have received at least two prior systemic therapies are associated with particularly poor prognosis. For instance, adult FL patients treated over multiple years at one center showed median progression free survival (PFS) for first line (IL) of treatment was 4.8 years, decreasing to 1.6 for 2L and 1 for 3L. Median event free survival (EFS) was 3.8, 1.1, and 0.8 year, respectively, for 1L, 2L, and 3L treatment. For subsequent lines of treatment, both median PFS and EFS were <1 year.[15] Among these patients, there exists further high-risk subgroups such as patients who are refractory to prior therapy, which further limits treatment options.

Description and Mechanism of Action for Mosunetuzumab
Mosunetuzumab is a full-length, fully humanized immunoglobulin G1 (IgG1) bispecific (BsAb) antibody targeting both CD3 (on the surface of T cells) and CD20 (on the surface of B cells).[16,17] As a T-cell recruiting BsAb targeting CD20-expressing B cells, mosunetuzumab is a conditional agonist; target B-cell termination is observed only upon simultaneous binding to CD20 on B cells and CD3 on T cells.[18] The requestor stated that mosunetuzumab is anticipated to be the first-in-class CD20/CD3 BsAb therapy in non-Hodgkin's lymphoma (NHL), with anticipated approval for the treatment of third-line or greater (3L+) FL.

Inpatient Administration of Mosunetuzumab
Mosunetuzumab monotherapy is administered IV in 21-day cycles with step-up dosing (C1 Day [D]1: 1mg; C1D8: 2mg; C1D15 and C2D1: 60mg; C3D1+ 30mg). The treatment duration involves 8 cycles for patients with complete response (CR) and up to 17 cycles for those who achieved partial response or stable disease unless disease progression or unacceptable toxicity occurred.

[10] Rivas-Delgado A, Magnano L, Moreno-Velazquez M, et al. Response duration and survival shorten after each relapse in patients with follicular lymphoma treated in the rituximab era. Br. J. Haematol. 2019;184(5):753-759. doi:10.1111/bjh.15708.
[11] Link BK, Day BM, Zhou X, et al. Second-line and subsequent therapy and outcomes for follicular lymphoma in the United States: data from the observational National LymphoCare Study. Br. J. Haematol. 2019;184(4):660-663. doi:10.1111/bjh.15149.
[12] Casulo C, Byrtek M, Dawson KL, et al. Early relapse of follicular lymphoma after rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone defines patients at high risk for death: an analysis from the National LymphoCare Study. J. Clin. Oncol. 2015;33(23):2516-2522. doi:10.1200/JCO.2014.59.7534.
[13] Casulo C, Le-Rademacher J, Dixon J, et al. Validation of POD24 as a robust early clinical endpoint of poor survival in follicular lymphoma: results from the Follicular Lymphoma Analysis of Surrogacy Hypothesis (FLASH) Investigation using individual data from 5,453 patients on 13 clinical trials. Blood. 2017;130(Suppl_1):412. doi:10.1182/blood.V130.Suppl_1.412.412.
[14] Seymour JF, Marcus R, Davis A, et al. Association of early disease progression and very poor survival in the GALLIUM study in follicular lymphoma: benefit of obinutuzumab in reducing the rate of early progression. Haematologica. 2019;104:1202-1208. doi:10.3324/haematol.2018.209015.
[15] Alperovich A, Batlevi C, Smith K, et al. Benchmark of progression free survival for multiple lines of therapy in follicular lymphoma treated in the rituximab era. Blood. 2016;128:2955. doi:10.1182/blood.V128.22.2955.2955.
[16] Atwell S, Ridgway JBB, Wells JA, Carter P. Stable heterodimers from remodeling the domain interface of a homodimer using a phage display library. i. 1997;270:26-35. doi:10.1006/jmbi.1997.1116.
[17] Spiess C, Merchant M, Huang A, Zheng Z, Yang N-Y, Peng J, et al. Bispecific antibodies with natural architecture produced by co-culture of bacteria expressing two distinct half-antibodies. Nat. Biotechnol. 2013;31:753-759. doi:10.1038/nbt.2621.
[18] Sun LL, Ellerman D, Mathieu M, et al. Anti-CD20/CD3 T-cell dependent bispecific antibody for the treatment of B-cell malignancies [abstract]. Sci. Transl. Med. 2015;7(287):287ra70. doi:10.1126/scitranslmed.aaa4802.

Current Coding: Facilities can report the intravenous administration of mosunetuzumab with 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 intravenous administration of mosunetuzumab. Continue coding as listed in current coding.

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

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 5** Mosunetuzumab Antineoplastic	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of afamitresgene autoleucel (afami-cel)

Issue: There are no unique ICD-10-PCS codes to describe the administration of afamitresgene autoleucel (afami-cel).

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

Food and Drug Administration (FDA) Approval? Afami-cel has received Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA, as well as Orphan Drug Designation for the treatment of synovial sarcoma (SyS). The requestor plans to submit a Biologics License Application (BLA) for afami-cel in second-line+ SyS and myxoid round cell liposarcoma (MRCLS) in patients aged 16-75 years, inclusive.

Background: SyS and MRCLS are two types of soft tissue sarcoma which have a high propensity for metastatic progression after definitive primary tumor multimodality treatment involving surgical resection +/- neo(adjuvant) local and systemic therapies. The median age of onset of metastatic disease is typically during adult years before age 40 for SyS and middle age in MRCLS, with median overall survival (OS) of 24.7 months and 29.9 months, respectively, from onset of first-line metastatic therapy.[1]

Typically, first-line metastatic treatment of both SyS and MRCLS involves alkylating agent chemotherapy (e.g., ifosfamide) containing regimens. Post first-line treatment, despite there being second-line+ metastatic standard-of-care therapies available (e.g., pazopanib for SyS or trabectedin for MRCLS), the prognostic benefit from these agents is very limited, with progression-free survival (PFS) and overall survival (OS) progressively shortening per treatment line.[1,2] Therefore, there is an unmet medical need to find effective therapies for post first-line metastatic SyS and MRCLS that lead to durable and sustained efficacy.

Description and Mechanism of Action for Afamitresgene Autoleucel (afami-cel)
Similar to CAR T-cell therapy in hematological malignancies, afamitresgene autoleucel (afami-cel) is an autologous adoptive cell transfer (ACT) therapy.[3,4] All autologous ACT therapies share the common process of collecting a patient's T-cells (leukapheresis) followed by activating, expanding, and engineering the T-cells *ex vivo.* The transduced T-cells, which are specific to each patient, are then supplied for patient re-infusion.

The first step in the manufacture of afami-cel is T-cell collection through leukapheresis. Subsequently, T-cells are isolated from the apheresis material *ex vivo* and a genetic sequence

[1] Pollack SM, Somaiah N, Araujo DM, et al. Clinical outcomes of patients with advanced synovial sarcoma or myxoid/round cell liposarcoma treated at major cancer centers in the United States. Cancer Med. 2020;9:4593–4602. https://doi.org/10.1002/cam4.3039
[2] Savina, M., Le Cesne, A., Blay, JY. et al. Patterns of care and outcomes of patients with METAstatic soft tissue SARComa in a real-life setting: the METASARC observational study. BMC Med 15, 78 (2017). https://doi.org/10.1186/s12916-017-0831-7
[3] Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly adp-a2m4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 Connective Tissue Oncology Society (CTOS) Virtual Annual Meeting.
[4] Joseph P Sanderson, Darragh J Crowley, Guy E Wiedermann, Laura L Quinn, Katherine L Crossland, Helen M Tunbridge, Terri V Cornforth, Christopher S Barnes, Tina Ahmed, Karen Howe, Manoj Saini, Rachel J Abbott, Victoria E Anderson, Barbara Tavano, Miguel Maroto & Andrew B Gerry (2020) Preclinical evaluation of an affinity-enhanced MAGE-A4-specific T-cell receptor for adoptive T-cell therapy, OncoImmunology, 9:1, DOI: 10.1080/2162402X.2019.1682381

is transduced by a lentivirus vector into the patient's T-cells. This transduction encodes the T-cells for an affinity optimized T-cell receptor (TCR) that specifically recognizes the cancer testis antigen known as melanoma-associated antigen (MAGE)-A4. MAGE-A4 is expressed across a range of solid tumors at varying frequencies, but its expression is prevalent and high in SyS and MRCLS.[3] Afami-cel can only be administered to patients who have a specific inborn immune signature known as HLA-A*02.[3,4]

Overall, the requestor stated that afami-cel is a unique personalized cancer treatment which redirects the patient's own immune cells to target and destroy solid tumors. At a population level, however, its overall utility will be limited to a subgroup of SyS and MRCLS patients who express both MAGE-A4 and HLA-A*02 biomarkers.

The requestor asserts that the unique therapeutic proposition which afami-cel will bring to the treatment of metastatic SyS and MRCLS is that, once administered as a single intravenous infusion, the transduced T-cells persist within the systemic circulation of the patient, potentially leading to durable anti-cancer activity. Evidence of durable activity has been reported in a subset of patients treated with afami-cel in the ongoing registration-directed phase 2 SPEARHEAD-1 trial in advanced SyS and MRCLS (NCT04044768).[3] This type of therapeutic modality and mechanism of action is distinct from current standard-of-care agents in sarcoma, which are traditionally administered over multiple cycles of treatment with the potential attendant risks of cumulative patient toxicities developing.

According to the requestor, afami-cel belongs to a class of T-cell products they have developed known as specific peptide enhanced affinity receptor (SPEAR) T-cells, which are targeted against cancer antigens such as MAGE-A4. Antigen-specific activation of afami-cel, via TCR-peptide-HLA-A*02 complex, results in T-cell cytokine secretion and direct killing of MAGE-A4 expressing cancer cells through the release of potent endogenous cytocidal chemicals (interferon-gamma and granzyme B) released by the T-cells.[4]

Inpatient Administration of Afamitresgene Autoleucel (afami-cel)
Post manufacture of afami-cel, and similar to the paradigm of CAR T-cell treatment in hematological malignancies, re-infusion of the transduced SPEAR T-cell product into SyS and MRCLS patients can only happen after the patient's immune system has been pre-conditioned with two specific chemotherapy agents, fludarabine and cyclophosphamide, administered in combination on an outpatient basis over four consecutive days. Three days after completion of this pre-conditioning chemotherapy regimen, the patient is admitted into the hospital as an inpatient to receive between 1 to 10 billion transduced T-cells (afami-cel dose range) as a single intravenous infusion administered through a central or peripheral vein. At this time, inpatient administration is considered mandatory for post infusion safety monitoring especially for potential immunological adverse events, such as cytokine release syndrome (CRS), which occurred in 66% of the advanced SyS and MRCLS patients treated with afami-cel in the registration-directed phase 2 SPEARHEAD-1 trial (NCT04044768).[3]

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of afami-cel. Facilities can report the intravenous administration of afami-cel with 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 intravenous administration of afamitresgene autoleucel. Continue coding as listed in current coding.

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

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 6** Afamitresgene Autoleucel Immunotherapy	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of Tabelecleucel (tab-cel®)

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

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

Food and Drug Administration (FDA) Approval? No. On February 27, 2015, the FDA granted Breakthrough Therapy Designation to Allogeneic Epstein-Barr Virus (EBV) Specific Cytotoxic T Lymphocytes (i.e., tabelecleucel) for the treatment of rituximab-refractory Epstein-Barr virus associated lymphoproliferative disorders (EBV-LPD). The biologics license application (BLA) for tabelecleucel is expected to be submitted to the FDA in 2022 with a request for priority review. If FDA approved, tabelecleucel would be the first and only FDA-approved therapy to treat patients with Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD).

Background: EBV+ PTLD is a rare, acute, and potentially deadly lymphoma that is a direct consequence of suppression of T-cell activity by immunosuppressive agents following transplant. It can impact patients that have undergone a solid organ transplant (SOT) or an allogeneic hematopoietic cell transplant (HCT). The source of disease is Epstein-Barr virus (EBV), which is one of the most common human viruses and infects 90% of people before adulthood. Once infected, individuals harbor lifelong dormant EBV infections that the immune system can usually control but cannot clear. A consequence of EBV infection may include B-cell immortalization. In immunosuppressed transplant patients, EBV infection remains unchecked, resulting in EBV-infected B cells that may proliferate uncontrollably and lead to EBV+ PTLD. There are currently no FDA-approved treatments for EBV+ PTLD and treatment approaches include reduction of immunosuppression (RIS), anti-CD20 therapy, and chemotherapy. EBV+ PTLD after failure of initial treatment can be an aggressive, often deadly disease in which survival can be low, with some patients dying within a few months.

It is estimated that a few hundred patients are impacted in the US annually by EBV+ PTLD. The median time to EBV+ PTLD from HCT is about 2-4 months, with the majority of cases occurring within the first year after transplant. In the solid organ transplant (SOT) setting, the median time to EBV+ PTLD is 1-2 years (but can develop from within a few months to more than 20 years after the transplant); the risk of developing EBV+ PTLD is a lifetime risk due to immunosuppression.

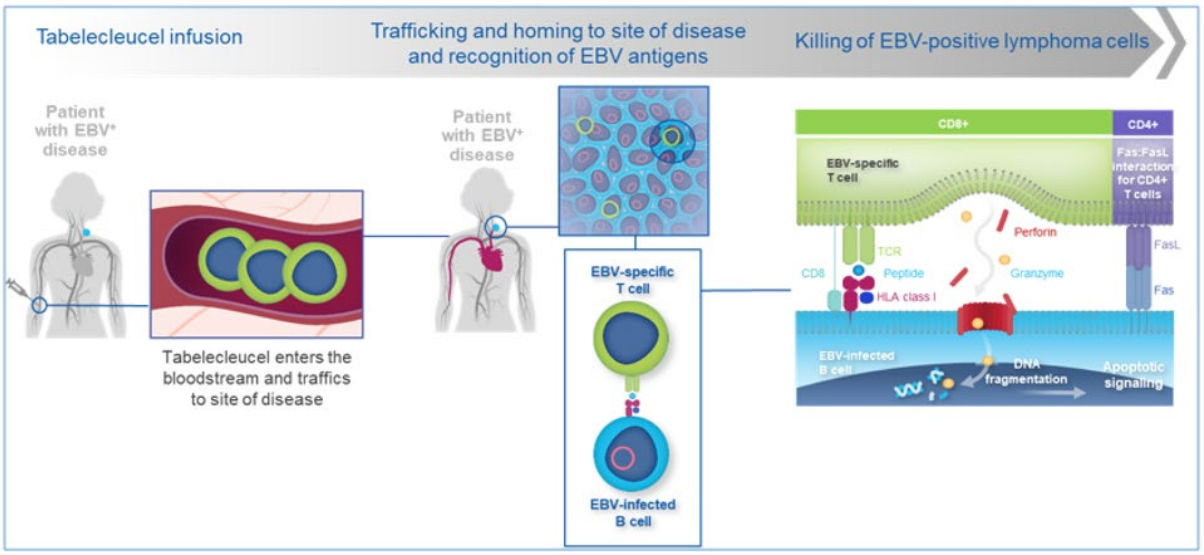
Description and Mechanism of Action for Tabelecleucel
Tabelecleucel is an allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy which targets and eliminates EBV-positive cells in a human leukocyte antigen (HLA)-restricted manner. It can be used for patients following a solid organ or allogeneic hematopoietic cell transplantation (HCT).

Tabelecleucel is produced from T cells harvested from eligible human donors. The tabelecleucel manufacturing process uses human and animal-derived materials. Tabelecleucel is tested for specificity of lysis of EBV+ targets, T-cell HLA restriction of specific lysis, and verification of low alloreactivity.

The cells are characterized and cryopreserved at a nominal concentration of 5 x 10^7 cells/mL in DMSO, HSA, and buffered saline for future use as a readily available therapy, based on patient need. The treatment is supplied as single-use vials; a specific lot is selected for each patient from an existing inventory based on appropriate HLA restriction. Tabelecleucel inventory is intended to cover approximately 95% of patients.

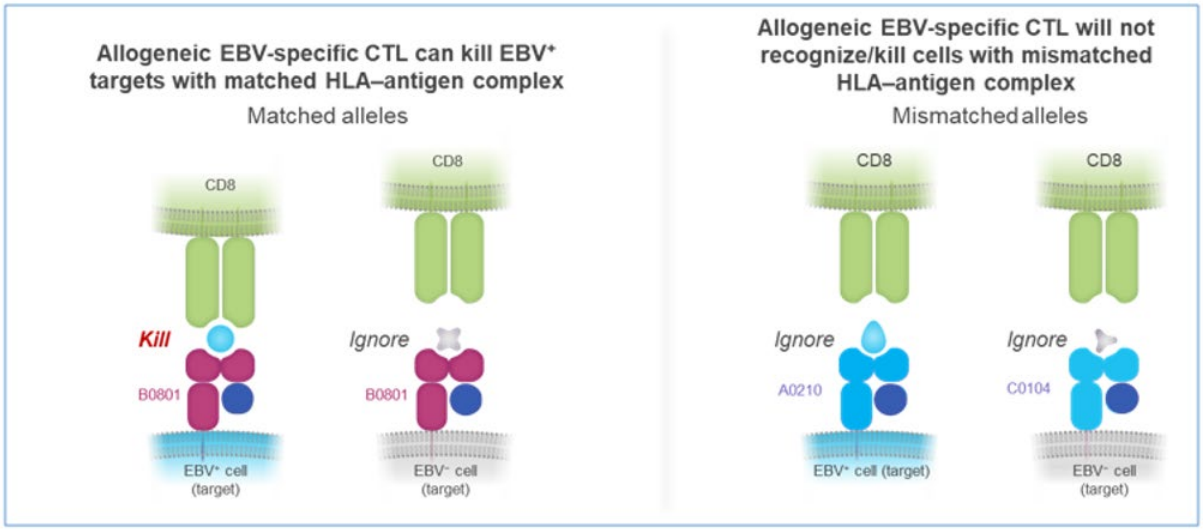
According to the requestor, the T-cell receptor of each clonal population within tabelecleucel recognizes an EBV peptide in complex with a specific HLA molecule on the surface of target cells (the restricting HLA allele) and allows tabelecleucel to exert cytotoxic activity against the EBV-infected cell. Mouse models demonstrate that tabelecleucel administered intravenously preferentially localizes to and infiltrates EBV+ B lymphoblastoid cell line (BLCL) tumors. In studies of tumor bearing mice, tabelecleucel induced tumor regression and improved survival.

Figure 1. Tabelecleucel mechanism of action



Tabelecleucel traffics to the site of disease, where it binds to EBV+ cells in an HLA-restricted manner, resulting in T-cell activation, expansion, and tumor cell lysis. The treatment does not interfere with existing immune function, thereby maintaining the integrity of the non-EBV infected B-cells. Tabelecleucel targets and eliminates EBV-expressing cells when its T-cell receptor (TCR) recognizes a specific HLA–antigen complex, an interaction known as HLA restriction; it identifies and accumulates in the EBV+ tumors that express the same HLA restricted allele, and it is activated only through exposure to the EBV antigen in an HLA-restricted manner. The requestor reported that after stimulation with EBV-infected cells, tabelecleucel exhibits a robust activation signature and induces polyfunctionality by secreting effector and chemoattractive cytokines.

Figure 2. Tabelecleucel targets the site of disease without harming normal cells



Inpatient Administration of Tabelecleucel
For patients receiving chronic corticosteroid therapy, the dose of these drugs should be reduced as much as is clinically safe and appropriate; recommended no greater than 1 mg/kg per day of prednisone or equivalent. Tabelecleucel has not been evaluated in patients receiving corticosteroid doses greater than 1 mg/kg per day of prednisone or equivalent.

In clinical studies, patients received cyclosporine, tacrolimus, sirolimus, and other immunosuppressive therapies, used at the lowest dose considered clinically safe and appropriate.

A single dose of tabelecleucel contains 2×10^6 viable T cells per kg of body weight. Tabelecleucel is administered as an intravenous (IV) injection over 5 to 10 minutes. During each 35-day cycle, patients receive tabelecleucel on days 1, 8, and 15, followed by observation, during which a response is assessed at approximately day 28. The number of cycles to be administered is determined by the patient's response to treatment. Maximum response is defined as a complete response (CR) for 2 consecutive cycles or a partial response (PR) for 3 consecutive cycles. If maximum response is not obtained, patients may be switched to a tabelecleucel lot with a different HLA restriction.

Current Coding: There are no unique ICD-10-PCS codes to describe the administration of tabelecleucel. Facilities can report the intravenous administration of tabelecleucel with 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 intravenous administration of tabelecleucel. Continue coding as listed in current coding.

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

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 7** Tabelecleucel Immunotherapy	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of Treosulfan

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? No. Treosulfan received orphan-drug designation from the U.S. Food and Drug Administration (FDA) on April 8, 2015. Treosulfan is currently under review by the FDA under a New Drug Application (NDA) with a proposed indication for: (1) use in combination with fludarabine as a preparative regimen for allogenic hematopoietic stem cell transplantation (alloHSCT) in adult and pediatric patients older than one year with acute myeloid leukemia (AML); and (2) use in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients older than one year with myelodysplastic syndrome (MDS).

Background: MDS and AML exist along a continuous spectrum of disease starting with early-stage MDS, which may progress to AML, characterized by an overproduction of immature blood cells, resulting in a lack of healthy, mature blood cells in patients. MDS and AML are disease states that significantly impact the Medicare population with the median age of diagnosis being 71 for MDS and 68 for AML.[1]

MDS comprises a group of hematologic malignancies characterized by clonal hematopoiesis, one or more cytopenias (i.e., anemia, neutropenia, and/or thrombocytopenia), and abnormal cellular maturation. MDS shares clinical and pathologic features with AML, but MDS has a lower percentage of blasts in peripheral blood and bone marrow (by definition, <20 percent). MDS is categorized using the World Health Organization (WHO) classification system based on the number of cytopenic and dysplastic lineages, percentage of blasts and ring sideroblasts, and cytogenetic findings. Patients with MDS are at risk for symptomatic anemia, infection, bleeding, and transformation to AML, the incidence of which varies widely across MDS subtypes.

AML refers to a large and diverse category of clinically aggressive hematologic neoplasms that are characterized by accumulation of myeloid blasts in bone marrow, blood, or other tissues and distinguished by arrested myeloid maturation. In AML, malignant transformation of myeloid-committed progenitor cells impairs maturation of cells that were otherwise destined to give rise to granulocytic, monocytic, erythroid, and/or megakaryocytic elements. Clinically, AML is manifested by symptoms and signs associated with cytopenias (e.g., anemia, infections, and/or bleeding bruising), which may be accompanied by constitutional symptoms, metabolic abnormalities, and various complications.

Around 5-10% of patients with solid tumors who are treated with chemotherapy, radiation or autologous stem cell transplantation develop treatment-related MDS or AML. A majority of MDS and AML cases, however, are de novo and not a function of prior treatment with chemotherapy or radiation, and a majority of de novo cases involve Medicare-aged patients. Both AML and MDS are malignant cancers that can be associated with high relapse rates and

[1] ASCO (American Society of Clinical Oncology) https://www.cancer.net/

low overall survival rates. Chemotherapy or other drug therapies are the first line of treatment. Allogenic hematopoietic stem cell transplantation may be used after chemotherapy as a second phase of treatment and may provide an opportunity for a cure.

Conditioning/preparative treatments prior to alloHSCT have traditionally included Myeloablative Conditioning (MAC), which may include high-dose total body irradiation (TBI) and high-dose chemotherapy-based regimens; and Reduced Intensity Conditioning (RIC), in which cytotoxic components of the regimen are reduced or replaced with less toxic but immunosuppressive agents. However, MAC regimens can be associated high treatment-related toxicity and transplantation-related mortality (TRM), while RIC regimens usually pose a higher risk of relapse.

Treosulfan is a new chemical entity and a novel prodrug of a bifunctional alkylating agent that is used as a preparative regimen for alloHSCT. According to the requestor, Treosulfan was developed in an effort to address the need for improved alloHSCT conditioning regimens that can reduce treatment-related toxicity and the risk of TRM without increasing the incidence of relapse. Treosulfan also potentially addresses the need for conditioning regimens that are appropriate for children with malignant disorders that are indicated for alloHSCT.

According to the requestor, a Treosulfan-based regimen can be critical to the success of alloHSCT. The treatment helps prepare a patient's body for alloHSCT by: (1) eradicating existing bone marrow tissue to provide space for engraftment of transplanted donor stem cells; (2) preventing rejection of the incoming donor stem cells by host immune cells; and (3) helping to eradicate existing disease. A Treosulfan-based regimen can also facilitate the newly transplanted donor cells in mounting an effective immune response against disease as a result of the alloHSCT process.

A Phase 3 clinical trial was conducted comparing a Treosulfan+fludarabine preparative regimen for alloHSCT to a busulfan+fludarabine RIC preparative regimen for alloHSCT in patients with AML or MDS who were indicated for alloHSCT but considered at an increased risk for standard MAC regimens (based on age (≥50 years), an HSCT-specific comorbidity index of more than 2, or both. According to the requestor, the trial demonstrated an advantage for the Treosulfan-based regimen as compared to the busulfan-based RIC regimen in terms of 24-month event free survival (EFS), 24-month overall survival (OS) (p value 0.0082), and 24-month TRM (p value 0.020). [2]

Mechanism of Action
The activity of Treosulfan is due to the spontaneous, pH-dependent conversion into a mono-epoxide intermediate and L-diepoxybutan. The epoxides form alkylate and cross-link nucleophilic centers of deoxyribonucleic acid (DNA) and other biological molecules, are involved in various physiological functions, and are considered responsible for the stem cell depleting, immune-suppressive and antineoplastic effects.

Inpatient Administration of Treosulfan
Treosulfan is administered via intravenous infusion and must be reconstituted prior to such infusion. Each vial of Treosulfan (containing either 1 g or 5 g Treosulfan) is reconstituted with

[2] *See* Dietrich Wilhelm Beelen, et al., *Treosulfan or Busulfan plus Fludarabine as Conditioning Treatment Before Allogeneic Haemopoietic Stem Cell Transplantation for Older patients with Acute Myeloid Leukemia or Myelodysplastic Syndrome (MC-Flud.T.14/L): A Randomised, Non-Inferiority, Phase 3 Trial,* THE LANCET HAEMATOLOGY, Oct. 9, 2019, available at https://doi.org/10.1016/S2352-3026(19)30157-7.

0.45% Sodium Chloride Injection, United States Pharmacopeial Convention (USP), 0.9% Sodium Chloride Injection, USP, 5% Dextrose Injection, USP, or Sterile Water for Injection, USP in its original glass container. According to the product's anticipated labeling, a 1 g vial should be reconstituted with 20 mL of solution, while a 5 g vial should be reconstituted with 100 mL of solution.

Although FDA approval remains pending, the recommended dosage of Treosulfan is anticipated to be 10 grams per square meter (10 g / m^2) of body surface area (BSA) per day of treatment, given as a two-hour intravenous infusion, and with treatment provided on three consecutive days (day -4, -3, -2) in conjunction with fludarabine before hematopoietic stem cell infusion (which occurs on day 0).

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

3E033GC	Introduction of other therapeutic substance into peripheral vein, percutaneous approach
3E043GC	Introduction of other therapeutic substance into central vein, percutaneous approach

Coding Options

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

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

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 8** Treosulfan	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Administration of inebilizumab-cdon

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

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? Yes. FDA approval was obtained on June 11, 2020, for the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) positive.

Background: NMOSD is a rare, severe autoimmune disease of the central nervous system that causes damage to the optic nerve, spinal cord and brain/brainstem. Approximately 80 percent of all patients with NMOSD test positive for anti-AQP4 antibodies.[1] Relapses are unpredictable and can lead to permanent disability. NMOSD affects approximately 10,000-15,000 people in the U.S with well recognized ethnic, geographic and gender disparities[2,3].

NMOSD is characterized by recurrent attacks of optic neuritis (inflammation of the optic nerve) and/or transverse myelitis (inflammation of the spinal cord). Regions of the brain may also be affected. Attacks can be severe and result in life-altering disability (such as blindness and paralysis). Recurring attacks can have cumulative effects resulting in significant morbidity and mortality. The goal of therapy is to reduce the risk of relapse and disability progression.

Mechanism of Action
According to the requestor, UPLIZNA® (inebilizumab-cdon) is the first and only FDA-approved anti-CD19 B-cell depleter for the treatment of NMOSD in adults who are anti-aquaporin-4 (AQP4) antibody positive[4] and targets a wide spectrum of B-cells that play a role in NMOSD.[5,6] UPLIZNA® binds specifically to CD19, targeting an extended range of the B-cell lineage that contributes to the multi-mechanistic disease activity of NMOSD, including plasmablasts and some plasma cells.[7]

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[1] Wingerchuck, D. (2009, November 15). Neuromyelitis optica: Effect of gender. Journal of the Neurological Sciences. Retrieved October 6, 2021, from https://pubmed.ncbi.nlm.nih.gov/19740485/.
[2] Ibid.
[3] Flanagan, E.P. et al. (2016, April 4). Epidemiology of aquaporin-4 autoimmunity and Neuromyelitis Optica Spectrum. Wiley Online Library. Retrieved October 6, 2021, from https://onlinelibrary.wiley.com/doi/10.1002/ana.24617.
[4] Marignier, R. et al. (2021, March 26). Disability outcomes in the N-momentum trial of inebilizumab in Neuromyelitis Optica Spectrum disorder. Neurology(R) neuroimmunology & neuroinflammation. Retrieved October 6, 2021, from https://pubmed.ncbi.nlm.nih.gov/33771837/.
[5] Schiopu, E. et al. (2016, June 7). Safety and tolerability of an anti-CD19 monoclonal antibody, Medi-551, in subjects with systemic sclerosis: A phase I, randomized, placebo-controlled, escalating single-dose study. Arthritis Research & Therapy. Retrieved October 6, 2021, from https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-016-1021-2.
[6] Herbst, R. et al. (2010, October 1). B-cell depletion in vitro and in vivo with an afucosylated anti-cd19 antibody. Journal of Pharmacology and Experimental Therapeutics. Retrieved October 6, 2021, from https://jpet.aspetjournals.org/content/335/1/213.long.
[7] Marignier, R. et al. (2021, March 26). Disability outcomes in the N-momentum trial of inebilizumab in Neuromyelitis Optica Spectrum disorder. Neurology(R) neuroimmunology & neuroinflammation. Retrieved October 6, 2021, from https://pubmed.ncbi.nlm.nih.gov/33771837/.

Aquaporin-4 autoantibodies (AQP4-IgG) are highly specific to NMOSD; AQP4 is expressed on astrocytes throughout the central nervous system. In NMOSD, AQP4 autoantibodies bind to AQP4, resulting in astrocyte cell death and inflammation. A sub-population of B-lineage cells, CD19+ plasmablasts/plasma cells produce AQP4 autoantibodies. Certain CD19+ B-cells are increased in the blood of AQP4-IgG seropositive individuals with NMOSD, with the highest levels observed during an attack. By depleting a wide range of B-cells that express CD19 (including plasmablasts and some plasma cells), UPLIZNA® may reduce the risk of NMOSD attacks in AQP4-IgG+ patients. UPLIZNA® was studied in the largest-ever clinical trial conducted in patients with NMOSD (N-MOmentum). The trial found that patients taking UPLIZNA® experienced fewer relapses and fewer hospitalizations than placebo. Compared with placebo, patients treated with UPLIZNA® had a reduced risk of 3-month confirmed disability progression (CDP).[4]

Inpatient Administration of inebilizumab-cdon
UPLIZNA® is initially administered as a 300 mg IV infusion followed 2 weeks later by a second 300 mg intravenous infusion. UPLIZNA® must be diluted prior to administration in an intravenous bag containing 250 mL of 0.9% sodium chloride injection. The IV infusion lasts approximately 90 minutes. For patients who are hospitalized due to an NMOSD attack or relapse, the first dose may be given in the inpatient setting.

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

3E033GC	Introduction of other therapeutic substance into peripheral vein, percutaneous approach
3E043GC	Introduction of other therapeutic substance into central vein, percutaneous approach

Coding Options

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

Option 2. Create new codes in section X, New Technology, to identify intravenous administration of inebilizumab-cdon.

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 9** Inebilizumab-cdon	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Hyperpolarized Xenon-129 Gas for Imaging of Lung Function

Issue: There are currently no unique ICD-10-PCS codes to describe use of hyperpolarized Xenon-129 gas during Magnetic Resonance Imaging (MRI) to enable visualization and quantification of lung function.

New Technology Application? Yes. The requestor has submitted a New Technology Add-on Payment (NTAP) application for FY 2023 consideration.

Food & Drug Administration (FDA) Approval? No. XENOVIEW™ and the HPX Hyperpolarization system devices, the final dose equivalent bag, and protocol are all currently under FDA Center for Drug Evaluation and Research (CDER) review as a drug/device combination.

Background: The rise of an aging population with pulmonary disease, coupled with a growing population of patients living with long-haul COVID-19, create a disease matrix with a critical need to employ an efficient, and accurate imaging method to better assess the pulmonary function in the lung with a favorable safety profile. Some of these patients may have comorbidities and risk factors whereby nephrotoxicity and ionizing radiation should be avoided.

According to the requestor, XENOVIEW™ lung MRI was specifically designed to address many of the unmet needs in the diagnosis and ongoing assessment of lung diseases. XENOVIEW™ lung MRI requires the new drug XENOVIEW™ to be activated through a complex hyperpolarization process to create the Hyperpolarized (HP) Xenon 129 (Xe-129) for lung MRI. When hyperpolarized Xenon 129 gas is inhaled, a Xenon-equipped MRI scanner is used to image the hyperpolarized Xe-129 distribution throughout the lungs. In order to equip existing MRI scanners to image Xenon (Xe) nuclei instead of hydrogen nuclei as in tradition MRI, a broadband, multichannel amplifier module needs to be added to the scanner and a Xe-specific transmit/receive coil must be used. XENOVIEW™ lung MRI provides an ionizing-radiation-free method to image pulmonary structure and function. With the inhalation of an inert noble gas over a 10-second duration, the radiologist can visualize multiple 3-D slices and quantify abnormalities in ventilation, barrier uptake, and red blood cell transfer.

XENOVIEW™ lung MRI reports reveal information about lung function and anatomy beyond spirometry, gamma scintigraphy, chest CT, or SPECT CT without nephrotoxicity[1] and without imparting any ionizing radiation. By imaging lung function in the anatomical context of the patient's own thoracic cavity, XENOVIEW™ lung MRI provides a unique way to assess physiologic function in the distal pulmonary spaces where disease might originate. Patient populations to potentially benefit from XENOVIEW™ lung MRI include those with chronic obstructive pulmonary disease, asthma, cystic fibrosis, bronchiolitis obliterans, interstitial lung disease, patients recommended for surgical lung resection or lung transplant.

[1] https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-new-warnings-using-gadolinium-based-contrast-agents-patients-kidney.

Technology
HP Xe-129's unique properties when used for lung MRI allows the production of high-resolution, 3-dimensional (3-D) MR images. HP Xe-129 is able to characterize regional distribution of gas of the lungs and enable a novel image of pulmonary function. These images enable physicians to visualize the spatial distribution of the patient's pulmonary function and lung ventilation clearly, accurately, and quantitatively. This characterization is possible due to the Xenon signal that resonates at different frequencies in each of the three compartments of alveolar gas-exchange: the airspaces (ventilation), barrier tissue of the lung parenchyma (membrane), and the pulmonary vasculature (transfer to red blood cells).

Procedure
The XENOVIEW™, a colorless and odorless gas blend for inhalation that consists of 89% Helium, 10% Nitrogen, and 1% Xenon, is provided in a size 302 aluminum gas cylinder gas stored at room temperature 20–25°C (68–77°F). The draft recommended dose is 75 mL dose equivalent (DE) of hyperpolarized Xe-129 gas (250mL–750 mL total Xenon) mixed with Nitrogen, (99.999% purity) as an inert buffer to ensure that the total volume of gas contained in the XENOVIEW™ DE Bag is 1 liter (L).

This monoatomic, inert, stable, noble gas requires multi-step manipulation in a room near the MRI suite to produce the final drug HP Xe-129 dose delivery bag. A dose of XENOVIEW™ gas is withdrawn from the multi-dose cylinder and transferred into the Hyperpolarizer. Once hyperpolarization is complete, the resulting HP Xe-129 gas blend is tested for level of polarization in the dose delivery bag using the HPX Polarization Measurement Station within 5 minutes prior to patient administration. The operator of the polarizer must ensure that the produced dose achieves ≥50 mL DE in order to produce a high-quality MR image. HP Xe-129 can be stored in the XENOVIEW™ DE bag on the HPX Polarization Measurement Station at room temperature for up to 60 minutes.

The patient is prepped in the usual manner for MRI with the additional step of providing instruction for inhalation of the HP Xe-129. First, the patient is coached on the appropriate 10–15 second breath hold to inhale XENOVIEW™. An anatomical proton scan is first acquired to delineate the thoracic cavity. Then, upon inhalation, HP Xe-129 is introduced into the lungs. Under MRI, a unique signal is created and picked up in each compartment of the lungs, through the larger air spaces, and through the 23 branches of the lungs, enabling a signal from the ventilated alveoli. The signal is also captured during the gas exchange diffusion across the alveolar membrane and ultimately to the red blood cells. Image interpretation requires that the radiologist learn the algorithms to analyze the XENOVIEW™ lung MRI image. After imaging, the hyperpolarized Xe-129 is exhaled from the body during normal respiration.

The protocol — including handling, calculation of the intended DE bag and polarizer flow rate, synchronized operation of the hyperpolarizer optical cell oven and laser, cryogenic isolation of the Xe from the Xe-129 blend, titration of the nitrogen excipient volume, final collection of HP Xe-129 dose, quality assurance, and labeling of the measured DE suitable for patient administration from the initial non-hyperpolarized preparation blend — takes about 1 hour per dose in addition to the supervised shutdown of the device at the end of the day (estimated 15 minutes).

Current Coding: The use of hyperpolarized Xenon 129 during MRI imaging is not reported separately for inpatient hospital coding. Facilities report the MRI of lung function using the appropriate code from the table below.

Section	**B** Imaging
Body System	**B** Respiratory System
Type	**3** Magnetic Resonance Imaging (MRI): Computer reformatted digital display of multiplanar images developed from the capture of radiofrequency signals emitted by nuclei in a body site excited within a magnetic field

Body Part	*Contrast*	*Qualifier*	*Qualifier*
G Lung Apices	**Y** Other Contrast	**0** Unenhanced and Enhanced **Z** None	**Z** None
G Lung Apices	**Z** None	**Z** None	**Z** None

Coding Options

Option 1. Do not create new ICD-10-PCS codes for an MRI of lung function using hyperpolarized Xenon 129. Continue coding as listed in current coding.

Option 2. Create new qualifier value 3 Hyperpolarized Xenon 129 (Xe-129), applied to table BB3 of section B, Imaging of Respiratory System, to identify an MRI of lung function using hyperpolarized Xenon 129.

Section	**B** Imaging
Body System	**B** Respiratory System
Type	**3** Magnetic Resonance Imaging (MRI): Computer reformatted digital display of multiplanar images developed from the capture of radiofrequency signals emitted by nuclei in a body site excited within a magnetic field

Body Part	*Contrast*	*Qualifier*	*Qualifier*
ADD 4 Lungs, Bilateral	**Z** None	**ADD 3** Hyperpolarized Xenon 129 (Xe-129)	**Z** None
G Lung Apices	**Y** Other Contrast	**0** Unenhanced and Enhanced **Z** None	**Z** None
G Lung Apices	**Z** None	**Z** None	**Z** None

CMS Recommendation: Option 2, as described above.

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

Administration of betibeglogene autotemcel

Issue: There are no unique ICD-10-PCS codes to describe the administration of betibeglogene autotemcel (beti-cel), an autologous hematopoietic stem cell transplant-based *ex vivo* gene therapy.

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

Food & Drug Administration (FDA) Approval? No. The FDA granted beti-cel Orphan Drug status and Breakthrough Therapy designation for the treatment of transfusion-dependent β-thalassemia (TDT). The FDA has accepted the Biologics License Application (BLA) for betibeglogene autotemcel (beti-cel) for priority review.

Background: β-thalassemia, a genetic disease resulting from mutations in the β-globin gene, is characterized by reduced or absent production of the functional β-globin protein necessary to form adult hemoglobin (HbA). In the absence of sufficient β-globin, excess unpaired α-globin impairs development and survival of red blood cells (RBCs), leading to chronic anemia, lack of HbA production, and other serious complications.[1,2,3] HbA is the predominant type of hemoglobin (Hb) for normal RBC production beyond infancy.[3] Depending on severity and clinical management, β-thalassemia is classified as either transfusion-dependent β-thalassemia (TDT), wherein lifelong, regular packed RBC transfusions are required for patient survival, or non-transfusion-dependent β-thalassemia (NTDT), wherein patients may require occasional transfusions or frequent transfusions for a defined period of time.[4,5] Patients with TDT require lifelong supportive care with regular packed RBC transfusions—typically given every 3 to 4 weeks—to mitigate anemia, suppress ineffective erythropoiesis, and enable survival.[5]

Description of betibeglogene autotemcel (beti-cel)
Beti-cel is a one-time gene addition therapy for patients with transfusion-dependent β-thalassemia (TDT) that directly addresses the underlying genetic cause of the disease.[6] Beti-cel has been evaluated globally in 63 pediatric, adolescent, and adult patients with TDT.[7] The treatment regimen for patients with TDT, comprising mobilization/apheresis, myeloablative conditioning, and beti-cel infusion, had a safety profile consistent with the known effects of mobilization with granulocyte-

[1] Thein SL. The molecular basis of β-thalassemia. Cold Spring Harb Perspect Med. 2013;3(5):a011700. doi: 10.1101/cshperspect.a011700.
[2] Amjad F, Fatima T, Fayyaz T, Aslam Khan M, Imran Qadeer M. Novel genetic therapeutic approaches for modulating the severity of β-thalassemia (review). Biomed Rep. 2020;13(5):48. doi: 10.3892/br.2020.1355
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[4] Cappellini MD, et al, eds. *Guidelines for Management of Transfusion-dependent Thalassaemia (TDT).* Nicosia, Cyprus: Thalassaemia International Federation; 2021.
[5] Taher A, Vichinsky E, Musallam K, Cappellini MD, Viprakasit V. Guidelines for the Management of Non-Transfusion Dependent Thalassemia (NTDT). Nicosia, Cyprus: Thalassaemia International Federation; 2013.
[6] Zynteglo [summary of product characteristics]. June 2020. Available at: https://www.ema.europa.eu/en/documents/product-information/zynteglo-epar-product-information_en.pdf. Accessed: January 12, 2021.
[7] Yannaki E, Locatelli F, Kwiatkowski JL, et al. Betibeglogene autotemcel gene therapy for the treatment of transfusion dependent β-thalassemia: updated long term efficacy and safety results [abstract S257]. Presented at: European Hematology Association Virtual Congress; June 9 -17, 2021.

colony stimulating factor (G-CSF) and plerixafor and myeloablation with single-agent busulfan.[8,9] Beti-cel gene therapy uses autologous hematopoietic stem cells (HSCs), and therefore, no donor is required.[10] Immunologic complications such as graft rejection and graft versus host disease (GVHD) are not expected, and no long-term immunosuppression is needed.[11] Beti-cel is potentially curative through achievement of transfusion independence and near normal Hb. In phase 3 studies, the majority of patients (32/36 [89%]) achieved transfusion independence, defined as weighted average Hb ≥ 9 g/dL without packed RBC transfusions for ≥ 12 months.[12] All patients in the long-term follow-up study, LTF-303, who achieved transfusion independence had maintained transfusion independence at last follow-up.[13]

Mechanism of Action

One-time treatment with beti-cel *ex vivo* gene therapy adds functional copies of a modified HBB gene, $\beta^{A\text{-}T87Q}$, into patients' HSCs through transduction of autologous CD34+ cells with BB305 lentiviral vector (LVV), thereby addressing the underlying genetic cause of TDT. $\beta^{A\text{-}T87Q}$-globin expression is designed to correct the α/β-globin imbalance in erythroid cells. After myeloablative conditioning and beti-cel infusion, transduced autologous CD34+ HSCs engraft in the bone marrow and differentiate to produce RBCs containing biologically active $\beta^{A\text{-}T87Q}$-globin (a modified β-globin protein) that will combine with α-globin to produce functional gene therapy–derived adult Hb, HbA^{T87Q}.[6] Following successful engraftment and achievement of transfusion independence, the effects of beti-cel are expected to be lifelong,[6] with stably transduced HSCs serving as a long-term reservoir for future RBC production.

Inpatient Administration of betibeglogene autotemcel (beti-cel)

The treatment regimen for patients with TDT comprises mobilization/apheresis to collect the patient's own stem cells, manufacturing of the drug product utilizing those cells as the starting material (during which the patient remains out of the hospital), myeloablative conditioning, and intravenous infusion of beti-cel into a vein. The myeloablative conditioning and beti-cel infusion are expected to occur in the inpatient setting. In some cases, the mobilization and apheresis procedures may take place in the inpatient setting. Similar to an autologous or allogeneic stem cell transplant, following beti-cel infusion, the patient is expected to remain hospitalized for a period of time to allow for reconstitution of the immune system. In phase 3 clinical trials, the median

[8] Locatelli F, Kwiatkowski JL, Walters MC, et al. Betibeglogene autotemcel in patients with transfusion-dependent β-thalassemia: Updated results from HGB-207 (Northstar-2) and HGB-212 (Northstar-3) [abstract S266]. Presented at: European Hematology Association Virtual Congress; June 9 -17, 2021.

[9] Yannaki E, Locatelli F, Kwiatkowski JL, et al. Betibeglogene autotemcel gene therapy for the treatment of transfusion dependent β-thalassemia: updated long term efficacy and safety results [abstract S257]. Presented at: European Hematology Association Virtual Congress; June 9 -17, 2021.

[10] Thompson AA, Walters MC, Kwiatkowski J, Rasko JEJ, Ribeil JA, Hongeng S, et al. Gene therapy in patients with transfusion-dependent β-thalassemia. N Engl J Med. 2018;378(16):1479-1493. doi: 10.1056/ NEJMoa1705342.

[11] Champlin R. Selection of Autologous or Allogeneic Transplantation. In: Kufe DW, Pollock RE, Weichselbaum RR, et al, eds. Holland-Frei Cancer Medicine, 6th ed. Hamilton, ON: BC Decker; 2003. Available from: https://www.ncbi.nlm.nih.gov/books/NBK12844/.

[12] Locatelli F, Kwiatkowski JL, Walters MC, et al. Betibeglogene autotemcel in patients with transfusion-dependent β-thalassemia: Updated results from HGB-207 (Northstar-2) and HGB-212 (Northstar-3) [abstract S266]. Presented at: European Hematology Association Virtual Congress; June 9 -17, 2021.

[13] Thompson A, Locatelli F, Yannaki E, et al. Restoring iron homeostasis in patients who achieved transfusion independence after treatment with betibeglogene autotemcel gene therapy: Results from up to 7 years of follow up. [abstract 573]. Presented at : American Society of Hematology Annual Meeting & Exposition; Dec 9-14, 2021

duration of hospitalization from admission for conditioning to post-infusion discharge was 45 and 42.5 days in HGB-207 and HGB-212, respectively.[14]

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

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

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the intravenous administration of betibeglogene autotemcel (beti-cel). Continue using codes as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify the intravenous administration of betibeglogene autotemcel (beti-cel).

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

CMS Recommendation: Option 2.

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

[14] Locatelli F, Kwiatkowski JL, Walters MC, et al. Betibeglogene autotemcel in patients with transfusion-dependent β-thalassemia: Updated results from HGB-207 (Northstar-2) and HGB-212 (Northstar-3) [abstract S266]. Presented at: European Hematology Association Virtual Congress; June 9 -17, 2021.

Administration of Omidubicel

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

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

Food & Drug Administration (FDA) Approval? No. The Biologics License Application (BLA) for omidubicel is expected to be submitted to the FDA during the first half of 2022 with a request for priority review. Earlier regulatory designations for omidubicel were 1) Orphan Drug designation for enhancement of cell engraftment and immune reconstitution in patients receiving HSCT and 2) Breakthrough Therapy designation for improvement of neutrophil engraftment in patients receiving umbilical cord blood transplantation for hematological malignancies.

Background: Omidubicel is under investigation as a donor source for patients with serious, life-threatening hematologic malignancies such as lymphoma and leukemia, in need of a potentially curative allogeneic hematopoietic stem cell transplant (HSCT). The therapy is based on manipulation of hematopoietic progenitor cells with proprietary nicotinamide (NAM)-based technology in combination with cytokines and preserves the multipotency of progenitor cells for long-term repopulation, while increasing cell quantity for transplantation. If approved, omidubicel will provide a donor source that greatly increases the reliability of and accessibility to allogeneic HSCT.

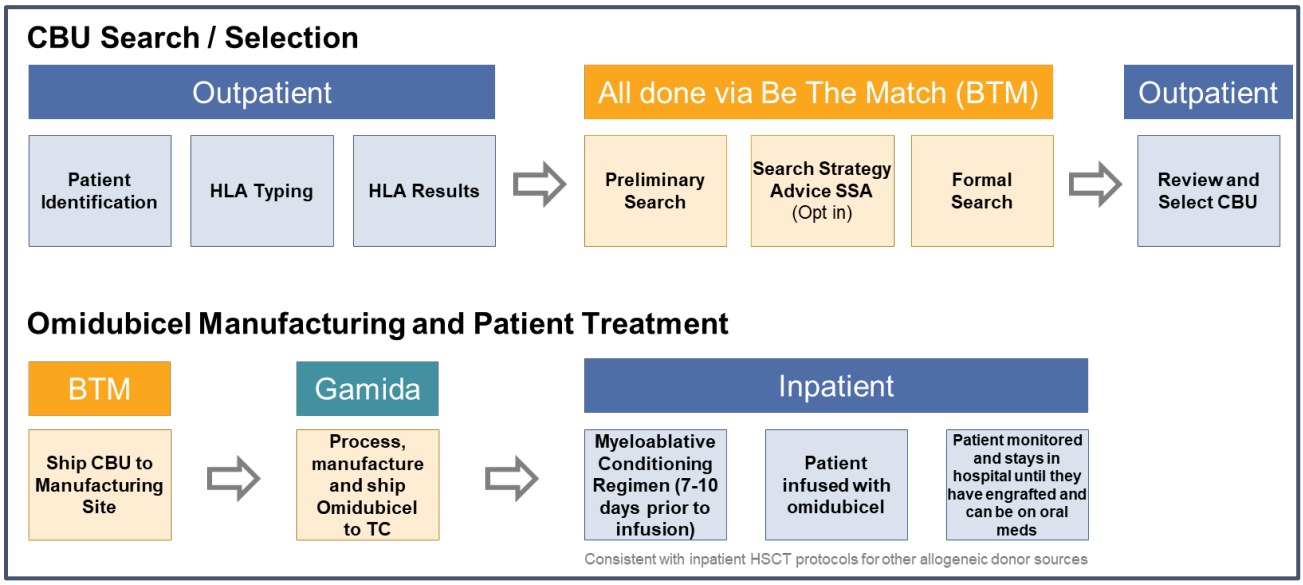
According to the requestor, the safety and efficacy of omidubicel advanced cell therapy donor source was demonstrated in an international, multi-center, randomized Phase 3 registration study (NCT02730299) designed to evaluate safety and efficacy of omidubicel (intent to treat [ITT] n=62) compared with standard, unmanipulated cord blood unit donor source (ITT n=63). The requestor states that the results of the pivotal Phase 3 clinical study provide evidence that omidubicel advanced cell therapy provides substantial clinical improvement for patients with high-risk hematologic malignancies with the need for an allogeneic HSCT and receive omidubicel.[1]

Mechanism of Action
Omidubicel is a patient-specific advanced cell therapy donor source derived from the CD133+ fraction of a single umbilical cord blood unit, utilizing proprietary NAM technology that inhibits differentiation and enhances the functionality of cultured hematopoietic stem and progenitor cells. Omidubicel contains stem cells capable of repopulating the bone marrow, effecting hematopoiesis and complete immune recovery after conditioning therapy. The addition of NAM allows for regulated cell proliferation while preserving cell function and stemness which leads to enhanced *in vivo* homing and *in vivo* engraftment.

The following figure details the journey from cord blood unit (CBU) identification and selection, the processing and manufacturing of omidubicel, and the shipment to transplant centers for patient administration. The time for processing, manufacturing and shipment of omidubicel to the

[1] Horwitz ME, et al. Omidubicel versus standard myeloablative umbilical cord blood transplantation: results of a Phase III randomized study. Blood. June 22, 2021. https://doi.org/10.1182/blood.2021011719.

transplant treatment center is ~30 days. During the omidubicel Phase 3 study, patients were admitted to the hospital where the myeloablative conditioning regimen was administered 7 to 10 days prior to administration of omidubicel.



Abbreviations: Cord Blood Unit (CBU); Human Leukocyte Antigen (HLA)

Inpatient Administration of Omidubicel

Omidubicel, an advanced cell therapy donor source for allogeneic HSCT, is available as cell suspensions for intravenous infusion. Central venous access is recommended. Infusion is to be given by gravity without infusion pump support.

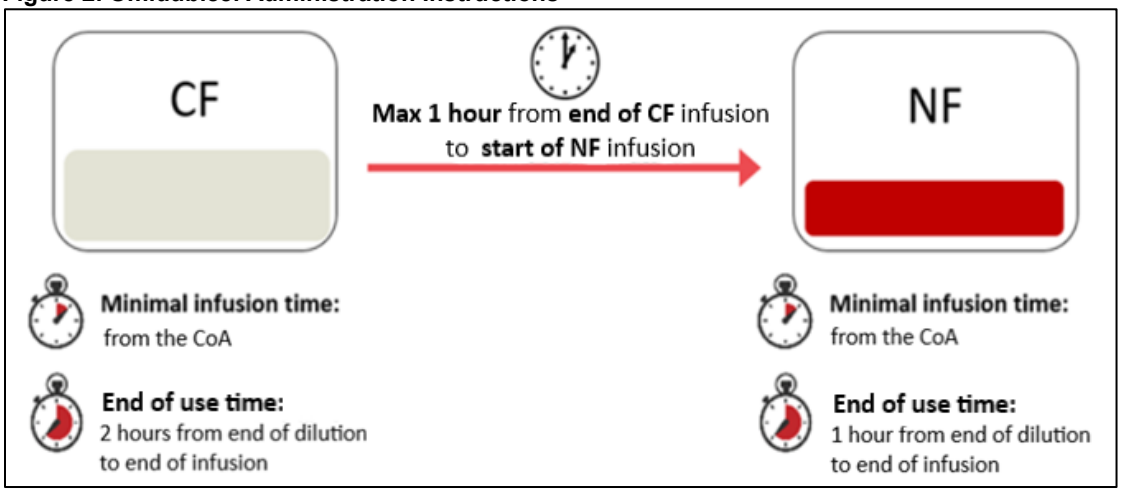
- A single dose of omidubicel contains 2 separate infusions that are prepared from 2 cryopreserved cell suspension bags that are thawed and diluted prior to infusion with their dedicated infusion solutions. The actual number of total viable cells and % of CD34+ cells in the product is reported on the Certificate of Analysis (CoA) that can be accessed via the Gamida Cell Assist portal.
    1) Omidubicel cultured fraction (CF): a suspension of allogeneic, expanded, hematopoietic CD34+ progenitor cells. Contains a minimum of 8.0×10^8 total viable cells with a minimum of 7.0% (5.6×10^7) CD34+ progenitor cells suspended in approximately 10% DMSO at the time of cryopreservation.
    2) Omidubicel non-cultured fraction (NF): a suspension of allogeneic non-expanded, hematopoietic mature myeloid and lymphoid cells from the same cord blood unit. Contains a minimum of 4.0×10^8 total viable cells with a minimum of 2.4×10^7 CD3+ cells suspended in approximately 10% dimethyl sulfoxide DMSO at the time of cryopreservation.

  Both fractions must be kept frozen in the vapor phase of liquid nitrogen (LN) until the patient is ready for infusion. The fractions must be thawed and then infused in a consecutive manner: CF followed by the NF.

- On the day of transplantation, at the clinical site, the CF and the NF are thawed, diluted with the Infusion Solution and infused. The final volume of the CF after thawing and

dilution is approximately 100 mL and of the NF is approximately 50 mL. Figure 2 summarizes the administration instructions for omidubicel.

Figure 2. Omidubicel Administration Instructions



Abbreviations: Cultured Fraction (CF); Certificate of Analysis (CoA); Non-cultured Fraction (NF)

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

30233X3	Transfusion of allogeneic unrelated cord blood stem cells into peripheral vein, percutaneous approach
30243X3	Transfusion of allogeneic unrelated cord blood stem cells into central vein, percutaneous approach

Coding Options

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

Option 2. Create new codes in section X, New Technology, to identify intravenous transfusion of omidubicel.

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

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**ADD C** Omidubicel	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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