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

CENTER FOR MEDICARE

Agenda

ICD-10 Coordination and Maintenance Committee Meeting
Department of Health and Human Services
Centers for Medicare & Medicaid Services
Virtual Meeting
ICD-10-PCS Topics
March 8, 2022

Zoom Webinar and Dial-In Information

- This meeting will be conducted via Zoom Webinar. The URL to join the Zoom Webinar, the password, and the call-in numbers are the same for both days of the meeting. Meeting details for each day are as follows.
- Day 1: March 8, 2022: The meeting will begin promptly at 9:00 AM ET and will end at 5:00 PM ET. Lunch will be held from 12:30 PM to 1:30 PM.
- Day 2: March 9, 2022: The meeting will begin promptly at 9:00 AM ET and will end at 5:00 PM ET. Lunch will be held from 12:30 PM to 1:30 PM.

To minimize feedback to the maximum extent possible, join the meeting using only **ONE** of the options listed below.

Option 1: Remote participants (attendees wishing to both view slides and ask questions during the Q&A portions of the meeting) must join the Zoom Webinar via the web. To join this Zoom Webinar conference from a PC, MAC, iPad, iPhone or Android device as well as, connect to the audio portion of the conference:

Click the following URL:
https://cms.zoomgov.com/j/1617166586?pwd=RUxMNG01Tm1ZTUtKRnc0SVQvK0VUZz09
Passcode: 864061

Option 2: Dial-in access is available for listen-only participants. Listen-only participants are participants who wish to only listen to the meeting and do not wish to comment or ask questions during the Q&A portions of the meeting.

1. From your phone, dial U.S.*: 669-254-5252 or 646-828-7666 or 833-568-8864 (Toll Free)
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*If dialing in from outside of the U.S., visit https://cms.zoomgov.com/u/aohzTG4Jj for a list of Zoom International Dial-in Numbers.

Option 3: To join this Zoom Webinar conference from an H.323/SIP room system:

1. From your room system, dial 161.199.138.10 (US West) or 161.199.136.10 (US East)
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   Passcode: 864061

SIP: 1617166586@sip.zoomgov.com
Passcode: 864061

If you experience technical difficulties during the meeting, please contact Marvelyn Davis for assistance at marvelyn.davis1@cms.hhs.gov or 410-786-2580 Option 7.

Those participating in the Zoom Webinar may ask questions during the Q&A portions of the meeting using the "Raise Your Hand" feature. If time does not permit you to comment or ask a question during the Q&A session, you may submit comments and questions at any time using the "Q&A" feature. All comments and questions submitted using the "Q&A" feature, along with CMS's responses to them, will be posted as soon as possible after the meeting in the "Downloads" section of the CMS web page located at: https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials. Remaining questions may be submitted via the CMS ICD-10 Procedure Code Request mailbox at ICDProcedureCodeRequest@cms.hhs.gov.

Note: Proposals for diagnosis code topics will be led by the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS) and are scheduled to begin following completion of the CMS procedure code proposals on March 8, 2022. Remaining diagnosis code topics will continue to be presented on March 9, 2022. Please visit CDC's website for the Diagnosis agenda located at the following address: http://www.cdc.gov/nchs/icd/icd10cm_maintenance.htm.

Registration for the meeting:
Information on registering can be found at: https://www.eventbrite.com/e/icd-10-coordination-and-maintenance-committee-meeting-tickets-262576061067?aff=ebdsoporgprofile.

***Please note that registration is not required to attend the Zoom Webinar. However, we are providing the ability to register on-line for those required to provide proof of attendance for continuing education purposes.**

Registration for the March 8-9, 2022 ICD-10 Coordination and Maintenance Committee Meeting opened on Tuesday, February 1, 2022, and closed on Tuesday, March 1, 2022.

If you require reasonable accommodation with an interpreter, please contact Mady Hue at 410-786-4510 or marilu.hue@cms.hhs.gov or Andrea Hazeley at 410-786-3543 or andrea.hazeley@cms.hhs.gov at least 72 hours prior to the event.

For questions about the registration process, please contact Mady Hue at marilu.hue@cms.hhs.gov or Andrea Hazeley at andrea.hazeley@cms.hhs.gov.

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

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2. A new subscriber screen will appear. Confirm your primary email address.
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5. Check privacy box confirming your consent to our data privacy. Additional information on our data privacy policy can be found at www.cms.gov/privacy.
6. You should receive a SUCCESS message that states (your email address) has been successfully subscribed to ICD-10 Coordination and Maintenance
7. Click on the Finish button at bottom of screen.
8. You should now be on the Welcome Quick subscribe page. You can subscribe to receive information from a list of topics of your choice from our partner organizations by checking the boxes; unsubscribe by unchecking the boxes.
9. Scroll down to the bottom of the page. Check the data privacy policy box and click on Submit. Additional information on our data privacy policy can be found at www.cms.gov/privacy.
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Topics Being Considered for ICD-10-PCS Procedure Codes

Introductions & Overview 9:00 AM – 9:10 AM	Mady Hue, CMS Co-Chair, ICD-10 Coordination and Maintenance Committee

ICD-10-PCS Topics:

1. Implantation of Sphenopalatine Ganglion Stimulator for Ischemic Stroke** Pages 16-18 9:10 AM – 9:25 AM	Andrea Hazeley, CMS Tom Devlin, MD, PhD, FSVIN Director, CHI Memorial Stroke & Neuroscience Center Director, Chattanooga Center for Neurologic Research LLC Professor of Neurology, University of Tennessee Health Science Center
2. Gene Expression Assay** Pages 19-21 9:25 AM – 9:40 AM	Andrea Hazeley, CMS Roy Davis MD, PhD, MHA CMO Immunexpress
3. Posterior Vertebral Tethering* Pages 22-25 9:40 AM – 9:55 AM	Mady Hue, CMS Christopher P. Ames, MD Co-Director, Spinal Surgery and UCSF Spine Center Director, Spine Tumor and Spinal Deformity Surgery Neurosurgeon UCSF
4. Section X Updates Pages 26-33 9:55 AM – 10:10 AM	Mady Hue, CMS
5. Computer-Assisted Transcranial Magnetic Stimulation of the Prefrontal Cortex* Pages 34-37 10:10 AM – 10:25 AM	Andrea Hazeley, CMS Brandon Bentzley, MD, PhD Co-Founder & Chief Science Officer Magnus Medical, Inc.
6. Computer-Aided Analysis for the Detection and Classification of Epileptic Events* Pages 38-40 10:25 AM – 10:40 AM	Andrea Hazeley, CMS Michael R. Sperling, MD Chief, Division of Epilepsy Vice Chair of Research Professor of Neurology Director, Jefferson

	Comprehensive Epilepsy Center Director, Clinical Neurophysiology Laboratory Thomas Jefferson University Kaapo Annala CEO Neuro Event Labs
7. Insertion of Posterior Spinal Motion Preservation Device* Pages 41-42 10:40 AM – 10:55 AM	Mady Hue, CMS Jared D. Ament, MD, MPH Spine Neurosurgery Sierra Neuroscience Institute
8. Insertion of Fenestrated Sacropelvic Fixation System* Pages 43-45 10:55 AM – 11:10 AM	Mady Hue, CMS Isoador H Lieberman, MD, MBA, FRCSC Texas Back Institute
9. Addenda and Key Updates Pages 46-50 11:10 AM – 11:25 AM	Andrea Hazeley, CMS
10. Paired Vagus Nerve Stimulation Therapy Using an External Controller* Pages 51-52 11:25 AM – 11:40 AM	Andrea Hazeley, CMS Gerard E. Francisco, MD The Wulfe Family Chair of Physical Medicine and Rehabilitation Chairman and Professor (With Tenure), Distinguished Teaching Professor, UT Systems Chief Medical Officer and Clinical Scientist, TIRR Memorial Hermann Director, UTHealth NeuroRecovery Research Center at TIRR Memorial Hermann
11. Ex Vivo Autologous Hematopoietic Stem Cell Gene Therapy Pages 53-56 11:40 AM – 11:55 AM	Andrea Hazeley, CMS Kent Christopherson, PHD Senior National Director, US Medical Affairs Orchard Therapeutics

	Milda Kaitz, CPC, CPC-I, CPMA Associate Director; Reimbursement Policy Insights Xcenda
12. Quantitative Flow Ratio for Non-invasive Analysis of Coronary Angiography Pages 57-59 11:55 AM – 12:10 PM	Mady Hue, CMS Hector M. Garcia-Garcia, MD, PhD Professor MedStar Hospital Center
13. Application of Allogeneic Thymus Derived Tissue Pages 60-61 12:10 PM – 12:25 PM	Andrea Hazeley, CMS Christy Steinhart Medical Science Liaison Enzyvant
LUNCH BREAK 12:30 PM to 1:30 PM	
14. Cardiac Perfusion with Intra-arterial Supersaturated Oxygen Pages 62-65 1:30 PM – 1:45 PM	Andrea Hazeley, CMS Gregg W. Stone, MD Director of Academic Affairs Mount Sinai Heart Health System Professor of Medicine – Cardiology Professor of Population Health Sciences and Policy Cardiovascular Institute Icahn School of Medicine at Mount Sinai, New York Kristin J. Schultz, MBA Director, Global Reimbursement and Health Economics ZOLL Circulation
15. Simulation for Assessment of Coronary Obstruction Risk* Pages 66-68 1:45 PM – 2:00 PM	Mady Hue, CMS Lakshmi Prasad Dasi, PhD, FACC, FAIMBE Co-Founder, CTO DASI Simulations
16. Laser Interstitial Thermal Therapy Pages 69-74 2:00 PM – 2:15 PM	Mady Hue, CMS Chengyuan Wu, MD, MSBmE Associate Professor of Neurosurgery and Radiology

Co-Director, Integrated Magnetic Resonance Imaging Center
Fellowship Director, Stereotactic and Functional Neurosurgery
Division of Epilepsy and Neuromodulation Neurosurgery (EN2)
Department of Neurosurgery
Vickie and Jack Farber Institute for Neuroscience
Thomas Jefferson University

Closing Remarks — Mady Hue, CMS
2:15 PM

Additional Therapeutic Agent Topics Also Under Consideration for ICD-10-PCS Codes***

17. Administration of Spesolimab* — Mady Hue, CMS
    Pages 75-76
18. Administration of daratumumab and hyaluronidase-fihj* — Andrea Hazeley, CMS
    Pages 77-78
19. Extracorporeal Antimicrobial Administration During Renal Replacement Therapy* — Andrea Hazeley, CMS
    Pages 79-80
20. Administration of Maribavir* — Andrea Hazeley, CMS
    Pages 81-83
21. Administration of Teclistamab* — Mady Hue, CMS
    Pages 84-85
22. Administration of Mosunetuzumab* — Mady Hue, CMS
    Pages 86-88
23. Administration of afamitresgene autoleucel** — Mady Hue, CMS
    Pages 89-91
24. Administration of tabelecleucel** — Mady Hue, CMS
    Pages 92-95
25. Administration of Treosulfan* — Andrea Hazeley, CMS
    Pages 96-98
26. Administration of inebilizumab-cdon* — Andrea Hazeley, CMS
    Pages 99-100

27. Hyperpolarized Xenon-129 Gas for Imaging of Lung Function* Pages 101-103	Andrea Hazeley, CMS
28. Administration of betibeglogene autotemcel** Pages 104-106	Andrea Hazeley, CMS
29. Administration of Omidubicel** Pages 107-109	Andrea Hazeley, CMS

** 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.*
****NTAP-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent will not be presented at the virtual meeting. The slide presentations for these procedure code topics are available at:* https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.

Continuing Education Credits:
Continuing education credits may be awarded by the American Academy of Professional Coders (AAPC) or the American Health Information Management Association (AHIMA) for participation in CMS ICD-10 Coordination and Maintenance (C&M) Committee Meeting Conference Calls, Meetings and Webcasts.

Continuing Education Information for American Academy of Professional Coders (AAPC)
If you have attended or are planning to attend a CMS ICD-10 Coordination and Maintenance (C&M) Committee Meeting Conference Call, you should be aware that CMS does not provide certificates of attendance for these calls. Instead, the AAPC will accept your e-mailed confirmation and call description as proof of participation. Please retain a copy of your e-mailed confirmation for these calls as the AAPC will request them for any conference call you entered into your CEU Tracker if you are chosen for CEU verification. Members are awarded one (1) CEU per hour of participation.

Continuing Education Information for American Health Information Management Association (AHIMA)
AHIMA credential-holders may claim 1 CEU per 60 minutes of attendance at an educational program. Maintain documentation about the program for verification purposes in the event of an audit. A program does not need to be pre-approved by AHIMA, nor does a CEU certificate need to be provided, in order to claim AHIMA CEU credit. For detailed information about AHIMA's CEU requirements, see the Recertification Guide on AHIMA's web site.

Please note: The statements above are standard language provided to CMS by the AAPC and the AHIMA. If you have any questions concerning either statement, please contact the respective organization, not CMS.

Contact Information

Comments on the procedure code proposals presented at the ICD-10 Coordination and Maintenance Committee meeting should be sent to the following email address: ICDProcedureCodeRequest@cms.hhs.gov

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

Andrea Hazeley
(410) 786-3543
Andrea.hazeley@cms.hhs.gov

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
- Code 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 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 requests for the September 13-14, 2022 C&M meeting
  - Procedure requests to CMS https://mearis.cms.gov
  - Diagnosis requests to NCHS nchsicd10cm@cdc.gov

Topic # 1 - Implantation of Sphenopalatine Ganglion Stimulator for Ischemic Stroke

Issue: There are currently no unique ICD-10-PCS codes to describe the implantation of a sphenopalatine ganglion stimulator for acute ischemic stroke.

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 Ischemic Stroke System (ISS500) is currently under review by the FDA for Premarket Approval (PMA) approval.

Background: The ISS500 is intended to increase cerebral blood flow and reduce disability in adult patients with acute ischemic stroke with confirmed cortical involvement in the anterior circulation who are ineligible or have no access to intravenous tissue-type plasminogen activator (IV-tPA) and endovascular thrombectomy. Treatment with ISS500 is to be initiated between 8 and 24 hours from stroke onset.

Collateral flow augmentation with ISS500 is achieved by electrical stimulation of the sphenopalatine ganglion (SPG), the source of parasympathetic vasodilatory innervation to the collateral network of the anterior cerebral circulation. Preclinical studies have shown that enhancing collateral flow by SPG stimulation (initiated up to 24 hours from onset) reduces cellular ischemic injury, and stabilizes the blood-brain barrier, leading to reduction of the final infarct volume, and improvement of functional outcome. According to the requestor, SPG stimulation treatment has been shown to potentially reduce disability and improve the patient's quality of life.

Technology
ISS500 consists of an implantation subsystem and a treatment subsystem. The role of the implantation subsystem is to assist the implanter in placing the implant (named the Injectable Neuro Stimulator (INS)) next to the SPG through the greater palatine canal. An external radiofrequency-coupled Transmitter supplies energy to the INS. The role of the treatment subsystem is to deliver the stimulation to the patient 4 hours per day, over 5 days, at the correct personalized level of stimulation that is titrated based on patients' comfortable tolerance amounts during treatment.

Procedure Description
1) Placement of the INS is performed in a minimally invasive procedure under local anesthesia, using GuideView, a stereotactic camera equipped guidance system to guide the implanter. INS placement follows these steps:

- A patient reference marker is attached to the patient before the patient undergoes the standard CT imaging procedure. The reference marker (named iPRM) has both optical and CT visible markers. The combination allows the system to match the optical image of the patient to the CT image (a process known as "registration").
- A nose sticker equipped with an optical marker and a CT visible marker is attached to the patient's nose and is used to verify registration accuracy
- The implanter identifies the greater palatine canal on the CT and plans the implantation path.

- The patient is administered local anesthesia
- Guided by the navigation system:
  - implanter punctures the mucosa (1-3 mm) using the puncture tool, and clears a path to the greater palatine canal entrance
  - implanter injects the implant using the Introducer into the canal placing the electrodes next to the SPG
- Following the last treatment session on day 5, the implant is extracted from the patient with forceps at the bedside.

2) Treatment delivery includes the following stages (done daily over 5 days):
- Setting up the Energy Delivery and Control (EDC) system, which is used to power and control the INS. The EDC consists of a Driver, a Transmitter, and a Controller unit.
- Positioning the Transmitter for optimal energy transfer
- Adaptation – identification of the personalized stimulation level for the patient
- Delivering treatment – delivering the personalized stimulation to the SPG for 4 hours
- Completing treatment – removal of Transmitter and single use sticker from the patient

Current Coding: There are no unique ICD-10-PCS codes to describe the implantation of a sphenopalatine ganglion stimulator for ischemic stroke. Facilities can report the procedure using the body part value Y Peripheral Nerve in table 01H, Insertion of Peripheral Nervous System, with approach value 3 Percutaneous and device value M Neurostimulator Lead.

Section	**0** Medical and Surgical
Body System	**1** Peripheral Nervous System
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device*	*Qualifier*
Y Peripheral Nerve	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**1** Radioactive Element **2** Monitoring Device **M** Neurostimulator Lead **Y** Other Device	**Z** No Qualifier

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the implantation of a sphenopalatine ganglion stimulator. Continue coding as listed in current coding.

Option 2. In table 01H, Insertion of Peripheral Nervous System, add existing body part value K Head and Neck Sympathetic Nerve, applied to the approach value 3 Percutaneous and the device value M Neurostimulator Lead to identify the implantation of a sphenopalatine ganglion stimulator.

Section	**0** Medical and Surgical
Body System	**1** Peripheral Nervous System
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device*	*Qualifier*
ADD K Head and Neck Sympathetic Nerve **Y** Peripheral Nerve	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**1** Radioactive Element **2** Monitoring Device **M** Neurostimulator Lead **Y** Other Device	**Z** No Qualifier

Option 3. Create new codes in section X table X0H Insertion of Nervous System, to identify the implantation of a sphenopalatine ganglion stimulator.

Section	**X** New Technology
Body System	**ADD 0** Nervous System
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
ADD K Sphenopalatine Ganglion	**3** Percutaneous	**ADD Q** Neurostimulator Lead	**8** New Technology Group 8

CMS Recommendation: Option 3, as described above.

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

Topic # 2 - Gene Expression Assay

Issue: There are currently no unique ICD-10-PCS codes to describe a gene expression assay of a blood specimen.

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? Yes. SeptiCyte® RAPID received FDA 510(k) clearance on November 29, 2021 as a class II medical device as an aid to differentiate sepsis from infection negative systemic inflammation.

Background: Sepsis is a difficult to diagnose, clinical syndrome defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection[1]. There are approximately 2 million U.S. sepsis hospitalizations annually, and sepsis is the most common cause of hospital deaths.[2]

Early and appropriate identification and management of sepsis patients remains the main factor in predicting sepsis outcomes. However, there are numerous issues that prevent the attainment of this goal. These include:

- Differentiating between infection versus non-infection causes of the patient's acute illness.
- Sepsis screening tools have wide variability in accuracy in identifying true sepsis patients, with most having poor predictive values.
- Establishing that there is a dysregulated host response present.
- Specimen cultures are slow to generate results, and are often without beneficial findings impacting effective therapy or contributing to inappropriate therapy.
- The lack of a coordinated program focusing on sepsis screening, interventions, metrics and coding.

The most recent Surviving Sepsis Campaign guidelines for the management of sepsis include recommendations for initiation of antimicrobials within 1 or 3 hours or for antimicrobial deferment with ongoing re-evaluation for alternative diagnoses[3].

SeptiCyte® RAPID is an objective measurement which quantifies the expression of prevalent genes involved in the host response to systemic infection. SeptiCyte® RAPID's 1-hour result time coupled with it being culture-independent aids providers in determining the likelihood of sepsis and aligns with the Surviving Sepsis Campaign antimicrobial recommendations of deferment or initiation within 1 or 3 hours.
There have been three clinical validation studies on the diagnostic performance of the SeptiCyte® technology. SeptiCyte® statistically significantly differentiated patients with sepsis versus infection negative systemic inflammation ($P<0.05$) with an overall area under the receiver

[1] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) JAMA 2016;315(8):801-810.
[2] Frank CE, Buchman TG, Simpson SQ, et al. Sepsis among Medicare beneficiaries: 4. Precoronavirus disease 2019 Update January 2012-February 2020. Critical Care Medicine 2021;49(12):2058-2069.

operating curve (AUROC) of 0.84.[3] When compared to standard care, SeptiCyte® contributed to a decrease in false positive sepsis cases by 4.5%, an increase in true negative cases by 9.4% and impacted indeterminant cases by 9.4.[4]

Technology
SeptiCyte® RAPID is a gene expression assay using a reverse transcription polymerase chain reaction to measure the relative expression levels of host response genes isolated from whole blood collected in PAXgene® Blood RNA Tubes. SeptiCyte® RAPID generates a score (SeptiScore®), in approximately 1 hour. An increasing SeptiScore® correlates with an increasing likelihood of infection-positive systemic inflammation.

Procedure Description
SeptiCyte® RAPID consists of collection of blood in a PAXgene® blood RNA tube followed by pipetting 900µl directly from PAXgene blood tube to the lysis chamber of the test cartridge. The test cartridge is used with the Idylla™ platform, which is a fully automated RT-PCR based molecular testing system.

Inside the cartridge, a combination of chemical reagents, lytic enzymes, heat, and High Intensity Focused Ultrasound (HIFU) induces lysis of the cells within the cartridge. The nucleic acids are liberated for subsequent reverse transcription quantitative real-time PCR (RT-qPCR) amplification. All necessary reagents for RT-qPCR are present in a stable formulation and are used to amplify specific biomarkers indicative for probability of sepsis. Detection and relative quantification of these specific targets is achieved through 5'-exonucleolytic release of fluorophores from labeled nucleic acid probes bound to amplification targets. The fluorescence is detected by the Idylla™ Instrument in real time.

SeptiCyte® RAPID discriminates between patients with sepsis and non-infectious systemic inflammation due to other acute illnesses within a 1-hour timeframe. The SeptiScore®, coupled with the full clinical picture of the patient, can aid providers to determine a course of action to optimize sepsis management and minimize risk of unnecessary treatment within the time constraints of sepsis therapy.

Current Coding: The performance of gene expression assay of a blood specimen is not reported separately for inpatient hospital coding.

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify SeptiCyte® RAPID molecular analysis of a blood specimen. Continue coding as listed in current coding.

Option 2. Create new codes in section X table XXE, Measurement of Physiological Systems, to identify SeptiCyte® RAPID molecular analysis of a blood specimen.

[3] Miller RR, Lopansri BK, Burke JP, et al. Validation of a host response assay, SeptiCyte Lab, for discriminating sepsis from systemic inflammatory response syndrome in ICU. American Journal of Respiratory and Critical Care Medicine 2018;198(7); 903-913.
[4] McHugh LC. Modeling improved patient management and hospital savings with SeptiCyte LAB in the diagnosis of sepsis at ICU admission. Infectious Disease Society of America, Symposium IDWeek 2018;A2022.

Section	**X** New Technology
Body System	**X** Physiological Systems
Operation	**E** Measurement: Determining the level of a physiological or physical function at a point in time

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
5 Circulatory	**X** External	**ADD 3** Infection, Whole Blood Reverse Transcription and Quantitative Real-time Polymerase Chain Reaction	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 3 - Posterior Vertebral Tethering

Issue: There are currently no unique ICD-10-PCS codes to describe posterior vertebral body tethering to augment the ligamentous complex of the posterior spine to mitigate the risk of post-operative proximal junctional kyphosis and proximal junctional failure.

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 LigaPASS 2.0™ PJK Prevention System was granted Breakthrough Device Designation (Q211613) on September 2, 2021. The indications for use are spinal trauma surgery, use in sublaminar or facet wiring techniques; spinal reconstructive surgery, incorporated into the construct for the purpose of correction of spinal deformities such as idiopathic and neuromuscular scoliosis in patients 8 years of age and older, adult scoliosis and kyphosis; spinal degenerative surgery as an adjunct to spinal fusions; intended for use at the non-fused level(s) adjacent to a posterior spinal instrumentation construct when ligament augmentation is considered appropriate to mitigate the risk of post-operative proximal junctional kyphosis (PJK) and proximal junctional failure (PJF). The LigaPASS system may also be used in conjunction with other medical implants made of titanium or cobalt-chrome alloy whenever wiring may help secure the attachment of other implants. 510(k) clearance is pending.

Background: Proximal junctional kyphosis (PJK) is a well-recognized complication in patients undergoing posterior instrumented fusion for spinal deformity. It is characterized by abnormal kyphosis immediately above the uppermost instrumented vertebrae (UIV), which itself is determined using the sagittal Cobb angle between the inferior endplate of the UIV and superior endplate of the second vertebral body above the UIV (UIV +2). The clinical definition of PJK varies but is generally recognized as an increase in kyphosis of more than 10°-20° compared to the preoperative baseline. PJK can present as a spectrum that ranges from asymptomatic radiographic findings to the most severe form of proximal junctional failure (PJF), which includes radiographic evidence of PJK coupled with clinical sequela such as pain, neurological deficit, and impaired quality of life requiring reoperation.[1] Post-operative rates of PJK vary by the tested definition, but most range from 17% to 39%. One report on 1005 adult spinal deformity (ADS) patients showed that PJK onset tended to occur early after the operation, with 69% of cases observed in the first 6 weeks and 78% within the first 12 months.[2]

Proximal junctional failure (PJF) is recognized as one of the most frequent reasons for reoperation after adult spinal deformity surgery. It is considered the most severe form of progression. PJF has been associated with a higher need for revision surgery, a greater risk of neurologic injury, increased deformity, and pain. The condition is also referred to as "topping off syndrome," "proximal junctional fracture," and "proximal junctional acute collapse," all of which highlight the associated structural failure and mechanical instability that marks the progression of PJK to PJF.[3]

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[1] Scheer, Justin K., et al. "Results of the 2014 SRS survey on PJK/PJF: a report on variation of select SRS member practice patterns, treatment indications, and opinions on classification development." Spine 40.11 (2015): 829-840

[2] Segreto, Frank A., et al. "Incidence of acute, progressive, and delayed proximal junctional kyphosis over an 8-year period in adult spinal deformity patients." Operative Neurosurgery 18.1 (2020): 75-82.

[3] Hyun, Seung-Jae, et al. "Proximal junctional kyphosis and proximal junctional failure following adult spinal deformity surgery." Korean Journal of Spine 14.4 (2017): 126.

Technology
The LigaPASS 2.0™ PJK Prevention System consists of a braided polyethylene terephthalate (PET) band and titanium alloy medial open connector with 2 set screws. According to the requestor, the LigaPASS 2.0™ PJK Prevention System bands allow the surgeon to create a posterior vertebra anchorage without the use of a pedicle screw or hook. Instead of a pedicle screw or hook, the LigaPASS 2.0™ PJK Prevention System bands are laced through the spinous processes of the vertebra to provide additional support to the junction between the fused segments and adjacent non-instrumented levels and then connected to a LigaPASS 2.0™ PJK Prevention System connector to make the rod-bone connection. The LigaPASS 2.0™ PJK Prevention System bands are comprised of a PET braid and pure titanium (T40) malleable leads at the ends of the bands. The requestor stated the malleable tips help the surgeon to lace the band around the vertebra and can be bent by the surgeon to make passing the band under and through the vertebral body easier.

The requestor stated that the LigaPASS 2.0™ PJK Prevention System connectors allow surgeons to attach a rod to a vertebral body without the use of the pedicle. Instead of a pedicle screw, the LigaPASS 2.0™ PJK Prevention System connector uses a facet band to make the rod-bone connection. The connectors are comprised of a connector body, a rod set screw, a locking set screw for the band, and a polyester band. The body of these connectors is manufactured from titanium alloy (Ti-6Al-4V). The part is compatible with any rods made of titanium or cobalt chromium alloys between diameters 5.5 mm and 6.0 mm.

Procedure
According to the requestor, LigaPASS 2.0™ is used as an adjunct with spinal fusion procedures, including both initial fusion and revision. Initial fusions are performed via standard techniques. For revision procedures, the prior fusion may be assessed by CT scan or by surgical inspection and new bone graft may be placed at the prior fusion site as needed. Notably, existing instrumentation is commonly removed. Fusion is then extended to additional segments beyond the prior fusion with placement of new instrumentation, including rods and screws, across the entire construct, sometimes together with additional pelvic fixation.

The procedure begins with drilling holes in the spinous process at several levels, starting at the level adjacent to the fusion and extending to levels that are being fused. Therefore, the LigaPASS 2.0™ begins at the spinous process beyond where the fusion and instrumentation stop. A band is threaded through the hole drilled in the uppermost spinous process and laced side-to-side through the holes in the other spinous processes. Another band is then threaded side-to-side through the same spinous processes in the opposite direction. At each level, the bands are run under the interspinous ligaments and supraspinous ligaments which connect the spinous processes.

The bands are then run through connectors which are placed on the fusion rods. The surgeon finishes by adjusting the tension on the LigaPASS 2.0™ as needed, then locking the bands within the connectors.

The requestor stated that LigaPASS 2.0™ provides additional support to prevent development of PJK at the junction between the fused segments and the adjacent non-instrumented levels. Portions of the posterior ligamentous complex, which includes the interspinous ligaments and the supraspinous ligaments, can be removed or compromised during spine fusion or weakened by

atrophy or degeneration. Placement of LigaPASS 2.0™ serves to augment and reinforce the function of the posterior ligamentous complex.

Use of LigaPASS 2.0™ is generally documented in fusion procedure reports with the terms ligament augmentation, ligament repair, and ligamentoplasty of the posterior ligamentous complex. It may also be documented as a spinal tether.

The requestor stated that the LigaPASS 2.0™ differs significantly from other spinal tethers. For example, another type of tether device currently available is implanted unilaterally in the anterior column of the spine using screws placed in the vertebral bodies of an adolescent patient who has not reached skeletal maturity. This tether device treats scoliosis without fusion by slowly exerting tension to reposition the vertebrae while the child grows. In contrast, LigaPASS 2.0™ is placed bilaterally in the posterior column of the spine by threading through the spinal processes. It is used with fusion and prevents PJK by augmenting and reinforcing key spinal ligaments.

Current Coding: There are no unique ICD-10-PCS codes to describe posterior vertebral tethering. Code the procedure using the body part values C, Upper Spine Bursa and Ligament and D, Lower Spine Bursa and Ligament in code table 0MU, Supplement of Bursae and Ligaments and the device value J Synthetic Substitute. Fusion procedures performed would be coded separately.

Section	**0** Medical and Surgical
Body System	**M** Bursae and Ligaments
Operation	**U** Supplement: Putting in or on biological or synthetic material that physically reinforces and/or augments the function of a portion of a body part

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
0 Head and Neck Bursa and Ligament **1** Shoulder Bursa and Ligament, Right **2** Shoulder Bursa and Ligament, Left **3** Elbow Bursa and Ligament, Right **4** Elbow Bursa and Ligament, Left **5** Wrist Bursa and Ligament, Right **6** Wrist Bursa and Ligament, Left **7** Hand Bursa and Ligament, Right **8** Hand Bursa and Ligament, Left **9** Upper Extremity Bursa and Ligament, Right **B** Upper Extremity Bursa and Ligament, Left **C** Upper Spine Bursa and Ligament **D** Lower Spine Bursa and Ligament **F** Sternum Bursa and Ligament	**0** Open **4** Percutaneous Endoscopic	**7** Autologous Tissue Substitute **J** Synthetic Substitute **K** Nonautologous Tissue Substitute	**Z** No Qualifier

G Rib(s) Bursa and Ligament **H** Abdomen Bursa and Ligament, Right **J** Abdomen Bursa and Ligament, Left **K** Perineum Bursa and Ligament **L** Hip Bursa and Ligament, Right **M** Hip Bursa and Ligament, Left **N** Knee Bursa and Ligament, Right **P** Knee Bursa and Ligament, Left **Q** Ankle Bursa and Ligament, Right **R** Ankle Bursa and Ligament, Left **S** Foot Bursa and Ligament, Right **T** Foot Bursa and Ligament, Left **V** Lower Extremity Bursa and Ligament, Right **W** Lower Extremity Bursa and Ligament, Left			

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the use of a vertebral body tethering system for treatment of current postoperative kyphosis or for prevention of postoperative kyphosis. Continue coding as listed in current coding.

Option 2. Create a new section X table XKU, New Technology, Supplement of Muscles, Tendons, Bursae and Ligaments, with body part values C, Upper Spine Bursa and Ligament and D, Lower Spine Bursa and Ligament and device value 6 Posterior Vertebral Tether. Fusion procedures performed would be coded separately.

Section	**X** New Technology
Body System	**K** Muscles, Tendons, Bursae and Ligaments
Operation	**ADD U** Supplement: Putting in or on biological or synthetic material that physically reinforces and/or augments the function of a portion of a body part

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
ADD C Upper Spine Bursa and Ligament **ADD D** Lower Spine Bursa and Ligament	**0** Open	**ADD 6** Posterior Vertebral Tether	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 4 - Section X Update
March 2022 ICD-10 Coordination and Maintenance Committee Meeting

Background:
At the September 11-12, 2018 ICD-10 C&M Committee Meeting we announced our plans to begin analyzing the frequency of the New Technology Group 1 codes within Section X as it has been 3 years since the implementation of these codes. We stated that we would consider the following during our review.

- Was the procedure code related to a new technology add-on payment application (NTAP)?
- If yes, was the technology approved for the NTAP?
- What is the frequency (total number of cases) of this procedure code as reported in the data for FYs 2016, 2017 and 2018?
- Based on review of the data and the clinical aspects of each procedure code, we will propose one of the options below
    1. Leave the code in Section X (e.g. procedure codes related to the administration of a specific medication)
    2. Reassign the code to the Med/Surg or other section of ICD-10-PCS and delete from Section X (e.g. NTAP has expired, data analysis and clinical review justifies incorporating this technology/procedure into the main Med/Surg section)
    3. Delete the Section X code (e.g. the procedure is not reported as anticipated in the data, therefore the absence of a unique code for this technology/procedure in the classification has minimal impact)

For the March 2019 ICD-10 C&M meeting we provided the findings from our initial analysis with regard to the frequency in which the New Technology Group 1 codes had been reported in the data.

At the September 2019 meeting we did not propose any changes to the New Technology Group 1 codes and stated we would continue to monitor the data.

For the March 2020 ICD-10 C&M meeting we shared the results of our analysis for the New Technology Group 2 codes within Section X as it has been 3 years since the implementation of those codes. We provided the frequency (total number of cases) of the New Technology Group 2 procedure codes as reported in the data for FYs 2017, 2018, and 2019. We also updated the data for the New Technology Group 1 codes to include the frequency of the codes for FY 2019.

We revised the format in which we display the findings from our analyses. We created an Excel spreadsheet with 2 specific tabs labeled accordingly as Group 1 Codes and Group 2 Codes. On each tab is the list of ICD-10-PCS codes, code description, frequency by fiscal year and if the technology was approved for the NTAP.

At the September 2020 ICD-10 C&M meeting we reviewied the updated analysis results in more detail and encouraged participants to consider the options listed above while reviewing the data for discussion. Commenters suggested adding another option for consideration.

At the March 2021 ICD-10 C&M meeting we proposed changes based on the public comments received and discussed a new approach to consider for future proposals.

At the September 2021 ICD-10 C&M meeting we reviewed the finalized changes based on the public comments received and shared our analysis results for the Group 3 Codes from FY 2018, 2019 and 2020.

For this March 2022 ICD-10 C&M meeting we are displaying the updated data for Group 2 and Group 3 codes with the CMS recommendation.

Fourth Option Issue
We received overall support for the addition of the fourth option for the Section X codes which was described as creating a unique code in another section of ICD-10-PCS and deleting the existing section X code. As a result, based on review of the data and the clinical aspects of each section X procedure code, we will continue to propose one of the four options listed below

1. Leave the code in Section X (e.g. procedure codes related to the administration of a specific medication)
2. Reassign the code to the Med/Surg or other section of ICD-10-PCS and delete from Section X (e.g. NTAP has expired, data analysis and clinical review justifies incorporating this technology/procedure into the main Med/Surg section)
3. Delete the Section X code (e.g. the procedure is not reported as anticipated in the data, therefore the absence of a unique code for this technology/procedure in the classification has minimal impact)
4. Create a new code in Med/Surg or other section of ICD-10-PCS and delete the code from Section X. (e.g. NTAP has expired, data analysis and clinical review justifies uniquely identifying the technology in the Med/Surg section)

We also received support for

- establishing guiding principles in connection with the fourth option
- adding another column to the far right to identify the CMS recommendation
- reminding requestors that Section X codes are temporary and may be subject to one of the four listed options at a future meeting
- CMS continuing to present recommendations for the Section X codes and allowing the public to comment versus having the public submit specific requests

Section X_March 2022 Update
Group 2

ICD-10-PCS Code	Description	FY 2017		FY 2018		FY 2019		FY 2020		FY 2021		Total Freq	CMS Recommendation	Technology Brand Name
		Freq.	NTAP	Freq.	NTAP	Freq.	NTAP	Freq.	NTAP	Freq.	NTAP			
X2A5312	Cerebral embolic filtration, dual filter in innominate artery and left common carotid artery, percutaneous approach, new technology group 2	142	NO	1,957	NO	4,598	YES	5,817	YES	5,737	NO	18,251	Option 1. Leave the code in Section X.	Sentinel® Cerebral Protection System
X2RF032	Replacement of aortic valve using zooplastic tissue, rapid deployment technique, open approach, new technology group 2	541	NO	1,400	YES	1,066	NO	576	NO	434	NO	4,017	Option 4. Create new codes in Table 02R with new qualifier "rapid deployment technique" to identify the replacement of aortic valve with zooplastic tissue using the rapid deployment technique	Elite™ Valve System (INTUITY) and LivaNova Perceval Valve (Perceval)
X2RF332	Replacement of aortic valve using zooplastic tissue, rapid deployment technique, percutaneous approach, new technology group 2	892	NO	1,022	NO	1,562	NO	1,054	NO	937	NO	5,467		Elite™ Valve System (INTUITY)
X2RF432	Replacement of aortic valve using zooplastic tissue, rapid deployment technique, percutaneous endoscopic approach, new technology group 2	2	NO	5	NO	10	NO	7	NO	4	NO	28		
XHRPXL2	Replacement of skin using porcine liver derived skin substitute, external approach, new technology group 2	158	NO	200	NO	201	NO	165	NO	81	NO	805	Option 3. Existing codes in Table 0HR can be reported. Proposing to add a substance key entry for MIRODERM Biologic Wound Matrix	MIRODERM Biologic Wound Matrix
XNS0032	Reposition of lumbar vertebra using magnetically controlled growth rod(s), open approach, new technology group 2	0	YES	21	NO	31	NO	23	NO	27	NO	102	Option 3. Existing codes in Tables 0PS, 0QS, 0PW and 0QW respectively, using the vertebra body part values and the device value Internal Fixation Device can be reported.	MAGEC® Spinal Bracing Distraction system
XNS0332	Reposition of lumbar vertebra using magnetically controlled growth rod(s), percutaneous approach, new technology group 2	0	YES	1	NO	0	NO	1	NO	3	NO	5		
XNS3032	Reposition of cervical vertebra using magnetically controlled growth rod(s),	0	YES	12	NO	16	NO	12	NO	6	NO	46		

	open approach, new technology group 2													
XNS3332	Reposition of cervical vertebra using magnetically controlled growth rod(s), percutaneous approach, new technology group 2	0	YES	0	NO	0	NO	1	NO	0	NO	1		
XNS4032	Reposition of thoracic vertebra using magnetically controlled growth rod(s), open approach, new technology group 2	0	YES	11	NO	23	NO	13	NO	18	NO	65		
XNS4332	Reposition of thoracic vertebra using magnetically controlled growth rod(s), percutaneous approach, new technology group 2	0	YES	0	NO	0	NO	1	NO	1	NO	2		
XRG0092	Fusion of occipital-cervical joint using nanotextured surface interbody fusion device, open approach, new technology group 2	1	NO	1	NO	0	NO	1	NO	0	NO	3	Option 3. Existing Index entries under "Fusion, body part, nanotextured" are also being proposed for deletion. Existing codes in Tables 0RG and 0SG can be reported that indicate an anterior interbody fusion was performed.	Titan™ Spinal Systems, Titan Endoskeleton ™
XRG1092	Fusion of cervical vertebral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	43	NO	34	NO	21	NO	29	NO	33	NO	160		
XRG2092	Fusion of 2 or more cervical vertebral joints using nanotextured surface interbody fusion device, open approach, new technology group 2	137	NO	77	NO	61	NO	91	NO	80	NO	446		
XRG4092	Fusion of cervicothoracic vertebral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	6	NO	3	NO	3	NO	7	NO	4	NO	23		
XRG6092	Fusion of thoracic vertebral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	2	NO	3	NO	2	NO	2	NO	5	NO	14		
XRG7092	Fusion of 2 to 7 thoracic vertebral joints using nanotextured surface interbody fusion device, open approach, new technology group 2	3	NO	4	NO	1	NO	3	NO	2	NO	13		
XRG8092	Fusion of 8 or more thoracic vertebral joints using nanotextured surface	0	NO	0	NO	0	NO	1	NO	0	NO	1		

	interbody fusion device, open approach, new technology group 2													
XRGA092	Fusion of thoracolumbar vertebral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	6	NO	4	NO	2	NO	0	NO	2	NO	14		
XRGB092	Fusion of lumbar vertebral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	75	NO	127	NO	146	NO	186	NO	173	NO	707		
XRGC092	Fusion of 2 or more lumbar vertebral joints using nanotextured surface interbody fusion device, open approach, new technology group 2	52	NO	68	NO	59	NO	79	NO	82	NO	340		
XRGD092	Fusion of lumbosacral joint using nanotextured surface interbody fusion device, open approach, new technology group 2	55	NO	70	NO	104	NO	148	NO	135	NO	512		
XW03372	Introduction of inactivated coagulation factor xa into peripheral vein, percutaneous approach, new technology group 2	8	NO	4	NO	337	YES	662	YES	885	YES	1,896	Option 1. Leave the code in Section X.	AndexXa™ (Andexanet alfa)
XW04372	Introduction of inactivated coagulation factor xa into central vein, percutaneous approach, new technology group 2	2	NO	0	NO	35	YES	57	YES	63	YES	157		
XW03392	Introduction of defibrotide sodium anticoagulant into peripheral vein, percutaneous approach, new technology group 2	8	YES	3	YES	6	YES	2	NO	7	NO	26	Option 3. Existing codes 3E0[34]3GC can be reported. Proposing to add substance key entries for Defitelio/defibrotide sodium anticoagulant.	Defitelio®
XW04392	Introduction of defibrotide sodium anticoagulant into central vein, percutaneous approach, new technology group 2	1	YES	1	YES	6	YES	1	NO	1	NO	10		
XW0DX82	Introduction of uridine triacetate into mouth and pharynx, external approach, new technology group 2	5	YES	4	YES	1	NO	1	NO	3	NO	14	Option 1. Leave the code in Section X.	Vistogard™

Section X_March 2022 Update
Group 3

ICD-10-PCS Code	Description	FY 2018		FY 2019		FY 2020		FY 2021		Total Freq	CMS Recommendation	Technology Brand Name
		Freq.	NTAP	Freq.	NTAP	Freq.	NTAP	Freq.	NTAP			
XK02303	Introduction of concentrated bone marrow aspirate into muscle, percutaneous approach, new technology group 3	17	NO	39	NO	15	NO	18	NO	89	Option 3. Existing codes can be reported.	MarrowStim™ PAD Kit
XRG00F3	Fusion of occipital-cervical joint using radiolucent porous interbody fusion device, open approach, new technology group 3	0	NO	0	NO	0	NO	1	NO	1	Option 3. Existing Index entries under "Fusion, bodypart, radiolucent porous" are also being proposed for deletion. Existing codes in Tables 0RG and 0SG can be reported that indicate an anterior interbody fusion was performed.	Vertera Spine's COHERE Interbody Fusion Device
XRG10F3	Fusion of cervical vertebral joint using radiolucent porous interbody fusion device, open approach, new technology group 3	15	NO	17	NO	21	NO	10	NO	63		
XRG20F3	Fusion of 2 or more cervical vertebral joints using radiolucent porous interbody fusion device, open approach, new technology group 3	46	NO	94	NO	65	NO	59	NO	264		
XRG40F3	Fusion of cervicothoracic vertebral joint using radiolucent porous interbody fusion device, open approach, new technology group 3	5	NO	1	NO	3	NO	1	NO	10		
XRG60F3	Fusion of thoracic vertebral joint using radiolucent porous interbody fusion device, open approach, new technology group 3	3	NO	1	NO	1	NO	2	NO	7		
XRG70F3	Fusion of 2 to 7 thoracic vertebral joints using radiolucent porous interbody fusion device, open approach, new technology group 3	0	NO	2	NO	0	NO	1	NO	3		
XRG80F3	Fusion of 8 or more thoracic vertebral joints using radiolucent porous interbody fusion device, open approach, new technology group 3	0	NO	0	NO	0	NO	0	NO	0		
XRGA0F3	Fusion of thoracolumbar vertebral joint using radiolucent porous	3	NO	1	NO	0	NO	0	NO	4		

	interbody fusion device, open approach, new technology group 3											
XRGB0F3	Fusion of lumbar vertebral joint using radiolucent porous interbody fusion device, open approach, new technology group 3	41	NO	129	NO	94	NO	103	NO	367		
XRGC0F3	Fusion of 2 or more lumbar vertebral joints using radiolucent porous interbody fusion device, open approach, new technology group 3	18	NO	57	NO	57	NO	73	NO	205		
XRGD0F3	Fusion of lumbosacral joint using radiolucent porous interbody fusion device, open approach, new technology group 3	21	NO	59	NO	42	NO	50	NO	172		
XW033A3	Introduction of bezlotoxumab monoclonal antibody into peripheral vein, percutaneous approach, new technology group 3	8	YES	23	YES	16	NO	28	NO	75	Option 4. Create new codes in Table 3E0 with qualifier "monoclonal antibody" to identify the administration of monoclonal antibodies for non-neoplastic/non-COVID indications.	ZINPLAVA™ (Bezlotoxumab)
XW043A3	Introduction of bezlotoxumab monoclonal antibody into central vein, percutaneous approach, new technology group 3	3	YES	5	YES	5	NO	5	NO	18		
XW033B3	Introduction of cytarabine and daunorubicin liposome antineoplastic into peripheral vein, percutaneous approach, new technology group 3	214	NO	202	YES	167	YES	165	NO	748	Option 1. Leave the code in Section X.	VYXEOS™ (Cytarabine and Daunorubicin Liposome for Injection)
XW043B3	Introduction of cytarabine and daunorubicin liposome antineoplastic into central vein, percutaneous approach, new technology group 3	418	NO	415	YES	367	YES	345	NO	1,545		
XW033C3	Introduction of engineered autologous chimeric antigen receptor t-cell immunotherapy into peripheral vein, percutaneous approach, new technology group 3	19	NO	37	YES	55	YES	0	NO	111	Deleted effective October 1, 2021	KYMRIAH® (Tisagenlecleucel) and YESCARTA® (Axicabtagene Ciloleucel)
XW043C3	Introduction of engineered autologous chimeric antigen receptor t-cell immunotherapy into central vein, percutaneous approach, new technology group 3	94	NO	208	YES	354	YES	0	NO	656		

XW033F3	Introduction of other new technology therapeutic substance into peripheral vein, percutaneous approach, new technology group 3	13	YES	34	YES	295	NO	91	NO	433	Option 1. Leave the code in Section X.	Stelara® (Ustekinumab)
XW043F3	Introduction of other new technology therapeutic substance into central vein, percutaneous approach, new technology group 3	4	YES	6	YES	39	NO	5	NO	54		
XY0VX83	Extracorporeal introduction of endothelial damage inhibitor to vein graft, new technology group 3	74	NO	78	NO	48	NO	47	NO	247	Option 3. The intraoperative preparation of vein graft material is not coded separately.	DuraGraft® Endothelial Damage Inhibitor

Topic # 5 - Computer-Assisted Transcranial Magnetic Stimulation of the Prefrontal Cortex

Issue: There are currently no unique ICD-10-PCS codes to describe computer-assisted transcranial magnetic stimulation of the prefrontal cortex.

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. On July 2, 2021, FDA granted Breakthrough Device designation for the Magnus Neuromodulation System (MNS) with SAINT technology with the indication of treatment of major depressive disorder (MDD) in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

Background: According to the U.S. National Institutes of Mental Health (NIMH), major depression is one of the most common mental disorders in the United States. For some individuals, major depression can result in severe impairments that interfere with or limit their ability to carry out major life activities. Per NIMH 2019 data, an estimated 19.4 million U.S. adults aged 18 or older had at least one major depressive episode (7.8% of all U.S. adults) and an estimated 13.1 million U.S. adults aged 18 or older had at least one major depressive episode with severe impairment in the past year (5.3% of all U.S. adults).

In the U.S., about 50% of the individuals with at least one major depressive episode with severe impairment responded to medications if they remained in treatment, leaving more than 5.5 million adults in 2017 and now more than 6.5 million adults (calculating from NIMH 2019 data) with severe and impairing major depression.[1] The proportion of individuals responding to subsequent pharmacotherapy trials is progressively smaller until the remission rate after a fourth antidepressant trial is between 10 and 15%.[2] This subset of individuals that fail to respond to multiple regimens of antidepressant medications are referred to as having treatment-resistant depression (TRD).[3] TRD is a chronic condition, which when left untreated is persistent, recurrent, and associated with a substantial and debilitating effect on day-to-day functioning.

Technology
The Magnus Neuromodulation System (MNS) encompasses a TMS device capable of delivering intermittent theta burst stimulation (iTBS) pulses according to the specific SAINT pattern; a neuronavigation device; and custom software that receives patient-specific structural and functional MRI data, uses a novel and proprietary algorithm to generate an individualized, focal target for stimulation, facilitates review of the targeting output, and transmits the targeting output to the physician and to the neuronavigation device. The MNS technology uses magnetic resonance imaging (MRI) of brain activity to locate the subpart of the brain that is most optimal for neuromodulation and that is most strongly functionally connected with the network (functional connectivity) that causes depression symptoms.

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[1] Gaynes BN, Rush AJ, Trivedi MH et al. The STAR*D study: treating depression in the real world. Cleveland Clinic Journal of Medicine 2008;75(1):57-66.
[2] Aaronson S, Sears P, Ruvana FA et al. 5-Year Observational Study of Patients with Treatment-Resistant Depression Treated with Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality. https://ajp.psychiatryonline.org.
[3] Fava M. Diagnosis and definition of treatment-resistant depression. Biol Psychiatry 2003;53(8):649-59.

Planning and delivering the SAINT treatment requires use of a 3T (3 Tesla) or greater MRI machine to collect functional and structural MRI imagery, which is then fed to the Magnus Target Identification Software. Target Identification for delivery of the SAINT treatment is achieved via this proprietary computer software algorithm that utilizes individual MRI data to identify the specific area of the brain that should be treated with TMS.

According to the requestor, outcomes of three published clinical studies conducted at Stanford University[4] demonstrate that the three-prong procedure implemented by the Magnus Neuromodulation System (combination of targeting, stimulation dose, and stimulation procedure) yields a clinical remission rate of up to 90%, which is more than double that of conventional TMS. Compared to conventional TMS, the clinical data indicate that treatment with the MNS procedure has a much more rapid onset of effect, substantially greater effect size, and requires fewer treatment days.

Procedure Description
The MNS utilizes magnetic pulses delivered to the prefrontal cortex in order to treat major depressive disorder (MDD). This procedure is based on the extensive historical experience with FDA-cleared transcranial magnetic TMS devices but has redesigned each aspect of those treatments in order to personalize the procedure and optimize the individual patient response. The key aspects of the MNS procedure are (1) identification of an individualized focal target area for stimulation, (2) dose (i.e., amount) of stimulation, and (3) stimulation procedure. This three-prong procedure, cumulatively, yields breakthrough effectiveness.

1) Target Identification for delivery of the SAINT treatment is achieved via a proprietary computer software algorithm that utilizes individual MRI data to identify the specific area of the brain that should be treated with TMS.
2) Dose of stimulation includes both the number of pulses delivered and the amplitude of the pulses. (18,000 pulses per day are delivered over five days at 90% of resting motor threshold amplitude, whereas in conventional iTBS 600 pulses per day are delivered over six weeks at 120% of resting motor threshold amplitude).
3) Stimulation Procedure to stimulate the individualized target area includes consideration of the grouping and spacing of pulses as well as the intersession interval. The MNS therapy uses a proprietary, optimized procedure pattern with intersession spacing of 50 minutes to accelerate and enhance the effects of iTBS.
    a. The procedure lasts five consecutive days in an inpatient hospital setting. At the start of each treatment day, a fiducial marker is placed on the patient's head and the neuronavigation system is registered to the individual patient's structural MRI data.
    b. Each procedure day consists of 10 ten-minute sessions of neurostimulation with a 50-minute break ("inter-session interval") between each session and the next, lasting over approximately 10 hours per day. Importantly, this inter-session interval optimizes the effects of consecutive sessions of neurostimulation.

        At the start of a session, the patient is seated in a treatment chair and the neuronavigation system is used to locate the stimulating coil over the patient's

[4] Cole EJ, Stimpson KH, Bentzley BS et al. Stanford accelerated intelligent neuromodulation therapy for treatment resistant depression. Am J Psychiatry 2020; Aug 177(8):716-26.

individualized target. The neurostimulator hardware is activated and begins to deliver the SAINT pulse pattern for 10 minutes; during this time, the coil position must be monitored to ensure that the coil remains over the patient's target location. After 10 minutes of stimulation, the neurostimulator turns off. A 50-minute intersession interval occurs before the start of the next treatment; that is, the ten sessions are initiated at 60-minute intervals during the day. During the inter-session interval, the patient is free to leave the treatment chair and can participate in other activities while keeping the fiducial marker on their head.

Current Coding: There are no unique ICD-10-PCS codes to describe computer-assisted transcranial magnetic stimulation. Facilities can report the procedure using the following codes:

6A221ZZ	Electromagnetic therapy, central nervous, multiple
	and
8E09XBH	Computer assisted procedure of head and neck region, with magnetic resonance imaging

Facilities can also report the MRI of the brain using the appropriate code from the table below.

Section	**B** Imaging		
Body System	**0** Central Nervous 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*
0 Brain **9** Sella Turcica/Pituitary Gland **B** Spinal Cord **C** Acoustic Nerves	**Y** Other Contrast	**0** Unenhanced and Enhanced **Z** None	**Z** None
0 Brain **9** Sella Turcica/Pituitary Gland **B** Spinal Cord **C** Acoustic Nerves	**Z** None	**Z** None	**Z** None

Coding Options

Option 1. Do not create new ICD-10-PCS codes for computer-assisted transcranial magnetic stimulation of the prefrontal cortex. Continue coding as listed in current coding.

Option 2. In table 6A2, Extracorporeal or Systemic Therapies, create new sixth character qualifier value B Computer-assisted, and new seventh character qualifier value 0 Prefrontal Cortex applied to the body system value 2 Central Nervous and the duration value 1 Multiple to identify computer-assisted transcranial magnetic stimulation of the prefrontal cortex. Continue coding the MRI procedure using the appropriate code in table B03, Magnetic Resonance Imaging (MRI) of Central Nervous System.

Section	**6** Extracorporeal or Systemic Therapies		
Body System	**A** Physiological Systems		
Operation	**2** Electromagnetic Therapy: Extracorporeal treatment by electromagnetic rays		
Body System	*Duration*	*Qualifier*	*Qualifier*
1 Urinary **2** Central Nervous	**0** Single **1** Multiple	**Z** No Qualifier	**Z** No Qualifier
2 Central Nervous	**1** Multiple	**ADD B** Computer-assisted	**ADD 0** Prefrontal Cortex

Option 3. Create a new section X table X0Z, Other Procedures, Nervous System, with new body part value 0 Prefrontal Cortex and new technology value 1 Computer-assisted Transcranial Magnetic Stimulation, to identify computer-assisted transcranial magnetic stimulation of the prefrontal cortex. Continue coding the MRI procedure using the appropriate code in table B03, Magnetic Resonance Imaging (MRI) of Central Nervous System

Section	**X** New Technology
Body System	**0** Nervous System
Operation	**ADD Z** Other Procedures: Methodologies which attempt to remediate or cure a disorder or disease

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
ADD 0 Prefrontal Cortex	**X** External	**ADD 1** Computer-Assisted Transcranial Magnetic Stimulation	**8** New Technology Group 8

CMS Recommendation: Option 3, as described above.

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

Topic # 6 - Computer-Aided Analysis for the Detection and Classification of Epileptic Events

Issue: There are currently no unique ICD-10-PCS codes to describe the analysis of epilepsy associated semiologic data using artificial intelligence (AI) software to aid in the detection and classification of epileptic events.

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 Nelli® Seizure Monitoring System was granted a Breakthrough Device designation by the FDA on October 9, 2020 for the automated analysis of audio and video data to identify seizure events with a positive motor component in children and adults. The FDA is currently reviewing the 510(k) premarket application the requestor submitted in August 2021.

Background: Epilepsy is a common neurological disorder that affect approximately 65 million people globally, and over half of seizures in patients with epilepsy present with a loss of awareness.[1] The Centers for Disease Control (CDC) reported that 1.2% of the US population had active epilepsy in the United States in 2015. This included 3 million adults and 470,000 children.[2] Inaccurate recognition of seizure types and their frequency is a major challenge in the diagnosis and treatment of epilepsy. While inpatient long-term video-EEG (electro-encephalograph) is the gold standard for electroclinical characterization of epileptic seizures, especially when there is diagnostic uncertainty in classifying seizure types or epilepsy syndrome, 20 to 30% of patients assessed by video-EEG have nonepileptic conditions.[3,4] According to the requestor, prompt diagnosis is of primary importance since patients younger than 30 years of age and those diagnosed with psychogenic nonepileptic seizures (PNES) on video-EEG have an 8-fold higher risk of death than the general population, with a similar mortality rate comparable to those with drug-resistant epilepsy.[5]

Technology

The Nelli® Seizure Monitoring System is designed to be used as an adjunct to seizure monitoring in a hospital inpatient or home setting for adults and children 6 years of age and older. The Nelli System's software is designed to automate the analysis of audio and video data to identify seizure events with a positive motor component. The software provides objective summaries of semiological components of identified events (including velocity and acceleration of movements, seizure frequency, seizure duration, heart rate, and respiratory rate) to enable the detection and classification of epileptic events using pre-trained artificial intelligence (AI). The Nelli System

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[1] Moshé SL, Perucca E, Ryvlin P, Tomson T. Epilepsy: new advances. Lancet 2015;385:884– 98. https://doi.org/10.1016/S0140-6736(14)60456-6.

[2] Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy — United States, 2015. MMWR. 2017;66:821–825. DOI: 10.15585/mmwr.mm6631a1.

[3] LaFrance Jr WC, Baker GA, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. Epilepsia 2013;54:2005–18. https://doi.org/10.1111/epi.12356

[4] Syed TU, LaFrance Jr WC, Loddenkemper T, Benbadis S, Slater JD, El-Atrache R, et al. Outcome of ambulatory video-EEG monitoring in a 10,000 patient nationwide cohort. Seizure 2019;66:104–11. https://doi.org/S1059-1311(18)30780-5 [pii].

[5] Nightscales R, McCartney L, Auvrez C, Tao G, Barnard S, Malpas CB, et al. Mortality in 16 patients with psychogenic nonepileptic seizures. Neurology 2020;95:e643–52. https://doi.org/10.1212/WNL.0000000000009855

records, processes, and provides physicians secure access to raw audiovisual recordings of patients to assist with the characterization of seizures and peri-ictal events.

Nelli offers advantages over other types of monitoring systems. EEG-based systems are only practical for short monitoring periods, can be expensive, and have low yield. Wearable systems are limited to only the more severe seizure types. As a video-based system, Nelli can monitor for additional seizure types over weeks or months.

Procedure Description
The Nelli Seizure Monitoring System is used in conjunction with standard video EEG monitoring. An EEG is performed to identify the location of the seizure activity in the brain, an important objective for patients admitted to an epilepsy monitoring unit, as well as for conducting pre-surgical evaluations. Nelli provides automatized, objective semiology information about seizures which is not possible with EEGs while also identifying seizure time stamps in real time, reducing the time and work required to both monitor and assess the patient.

Data is collected while the patient is 'observed' using the Nelli System's hardware (Personal Recording Unit [PRU]). The PRU, which includes a computer, camera, and microphone, is placed over the bed, at the patient's home or at the hospital. The camera allows for sub-millimeter accuracy. No wearables are involved and the patient can behave as usual during the examination which can last for 24 hours to 28 days. The view (receptive field) of the device is restricted to prevent the capture of other individuals in the same room. In a hospital environment, the PRU is activated by hospital staff following a prescriber-defined data collection schedule. Raw media data is temporarily stored on the PRU, where it is pre-processed to extract only periods likely to contain clinically relevant activity. Data is transmitted via a secure internet connection to the Nelli System's software running on a remote server where it is processed using the Nelli System's analysis algorithms which register and categorize media samples that may be indicative of epileptic seizure events.

Current Coding: The use of software to aid in the detection and classification of epileptic events is not reported separately for inpatient hospital coding. Facilities can report EEG (electro-encephalograph) monitoring with the following ICD-10-PCS code:

4A10X4Z Monitoring of central nervous electrical activity, external approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify the use of software to aid in the detection and classification of epileptic events. Continue coding as listed in current coding.

Option 2. Create new codes in section X table XXE, Measurement of Physiological Systems, to identify the use of software to aid in the detection and classification of epileptic events.

Section **X** New Technology *Body System* **X** Physiological Systems *Operation* **E** Measurement: Determining the level of a physiological or physical function at a point in time			
Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
0 Central Nervous	**X** External	**ADD 4** Brain Electrical Activity, Computer-aided Behavioral Analysis	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 7 - Insertion of a Posterior Spinal Motion Preservation Device

Issue: There are currently no unique ICD-10-PCS codes to describe the insertion of a posterior spinal motion preservation device.

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 TOPS™ System has not yet received FDA approval. The TOPS™ System received Breakthrough Device Designation from the FDA October 26, 2020, for patients between 35 and 80 years of age suffering from neurogenic claudication resulting from degenerative spondylolisthesis up to Grade I with moderate to severe lumbar spinal stenosis and either thickening of the ligamentum flavum or scarring of the facet joint capsule at one level from L2 to L5.

Background: Lumbar spinal stenosis is a common spinal disorder with symptoms that consist of leg and buttock pain with or without back pain caused by the narrowing of spaces around neural elements. This narrowing is often caused by degenerative spondylolisthesis and lumbar facet joint osteoarthritis both which are irreversible debilitating diseases. The prevalence of these conditions, as reported in the literature, vary widely however it is the most common reason that patients >65 years old undergo spinal surgery that often involves lumbar spinal fusion. Between 2002 to 2007 the rate of lumbar surgery for these conditions among Medicare beneficiaries was 136 for every 100,000 and in 2009, hospital charges to Medicare for these surgeries was $1.65 billion.

According to the requestor, the TOPS™ System offers an alternative to spinal fusion surgery for patients, addressing two critical functions of the spine; maintaining stability and preserving motion.

Technology and Procedure
The TOPS™ System is a mechanical device that is intended to maintain flexion, extension, lateral bending and axial rotation. It is designed as a motion preserving device comprised of a titanium construct with an interlocking polycarbonate urethane articulating core. During the procedure, which is performed via an open posterior approach, a decompression is performed to relieve neural impingement. This includes removal of the lamina (laminectomy) and removal of some or all of the facet joint (facetectomy). Following the decompression, the TOPS™ System is inserted into the lumbar vertebral joint and anchored using standard pedicle screws providing stabilization. The internal articulating surfaces along with the polycarbonate urethane articulating core allow relative movement in axial rotation, lateral bending, flexion, and extension, but blocks sagittal translation thus stabilizing the segment.

Current Coding: There are no unique ICD-10-PCS codes to describe the insertion of a posterior spinal motion preservation device. Code the procedure using the appropriate body part value in table 0SH, Insertion of Lower Joints, with approach value 0 Open and the device value D Spinal Stabilization Device, Facet Replacement.

Section	**0** Medical and Surgical
Body System	**S** Lower Joints
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device*	*Qualifier*
0 Lumbar Vertebral Joint **3** Lumbosacral Joint	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**3** Infusion Device **4** Internal Fixation Device **8** Spacer **B** Spinal Stabilization Device, Interspinous Process **C** Spinal Stabilization Device, Pedicle-Based **D** Spinal Stabilization Device, Facet Replacement	**Z** No Qualifier

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the insertion of a posterior spinal motion preservation device. Continue coding as listed in current coding.

Option 2. Create new codes in section X table XRH, Insertion of Joints, to identify the insertion of a posterior spinal motion preservation device.

Section	**X** New Technology
Body System	**R** Joints
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
B Lumbar Vertebral Joint **D** Lumbosacral Joint	**0** Open	**ADD 1** Posterior Spinal Motion Preservation Device	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 8 - Insertion of Fenestrated Sacropelvic Fixation System

Issue: There are currently no unique ICD-10-PCS codes to describe insertion of a fenestrated sacropelvic fixation system for the treatment of spinal instabilities or deformities.

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 iFuse Bedrock™ Granite Implant System received Breakthrough Device Designation from the FDA on November 23, 2021, for sacropelvic fixation and as an adjunct for sacroiliac joint fusion (when used with commercially available sacroiliac joint fusion promoting devices) in conjunction with commercially available posterior pedicle screw systems that are intended for the treatment of acute and chronic instabilities or deformities of the thoracic, lumbar, and sacral spine:

• Degenerative disc disease (DDD) as defined by back pain of discogenic origin with degeneration of the disc confirmed by patient history and radiographic studies
• Severe spondylolisthesis (Grades 3 and 4) of the L5-S1 vertebra in skeletally mature patients
• Patients receiving fusions by autogenous bone graft having implants attached to the lumbar and sacral spine (L3 to sacrum) with removal of the implants after the attainment of a solid fusion
• Spondylolisthesis
• Trauma (i.e., fracture or dislocation)
• Spinal stenosis
• Deformities or curvatures (i.e., scoliosis, kyphosis and/or lordosis)
• Spinal tumor
• Pseudarthrosis
• Failed previous fusion

Background: Adult spinal deformity (ASD) refers to malalignment of the spine resulting from congenital deformities or acquired degeneration related to osteoarthritis. Malalignment can cause back, radicular pain in arms, torso or legs, and altered balance, all of which limit the ability to perform activities of daily living and increase the risk of falls. Surgery for ASD is commonly performed to correct spinal deformity, reduce deformity progression, and to decompress neural structures. Surgical treatment typically involves decompression of neural elements, correction of sagittal, coronal and rotational (if present) spine deformities, and fusion of involved spinal motion segments. Typically, pedicle screw systems (PSS) are used. When the spinal deformity surgical procedure extends to the sacrum, it is standard of care to extend the pedicle screw instrumentation to the pelvis. This involves placement of fixation screws either directly into the ilium or through the sacral ala, across the sacroiliac (SI) joint and into the ilium. Screws are then attached to the most caudal ends of the rods. These pelvic screws provide additional biomechanical stability to the overall construct, decreasing the rate of catastrophic failure of the caudal end of the construct and increasing fusion rate of the L5-S1 spine motion segment. Currently available pelvic fixation screws (placed in either the iliac or SAI trajectories) are not designed to fuse the SI joint.

Technology and Procedure
According to the requestor, the iFuse Bedrock™ Granite implant has surface characteristics that promote biological fixation and fusion of the sacroiliac (SI) joint. The device's shape and design

are functionally equivalent to screws that are indicated for augmenting stabilization of the construct via insertion into the pelvis (iliac or sacroalar-iliac trajectories). This combination of features is designed to reduce the rate of failure of the caudal end of the spinal instrumentation construct and in addition, lower the rate of postoperative SI joint pain and reduce the rate of failure of the pelvic fixation screws.

The iFuse Bedrock™ Granite implant is a sterile, single-use permanent implant that combines features of a porous fusion device and the threaded length and posterior rod connection features of a typical pedicle fixation screw. Joint fusion occurs as a result of the device's porous surface and interstices. Fixation occurs through the device's helical threaded design and traditional posterior fixation rod connection. The device can be placed into the pelvis in two trajectories: sacroalar-iliac trajectory (i.e., into the sacrum, across the SI joint and into the ilium) or directly into the ilium. Joint fusion occurs only when the SAI trajectory is used.

The iFuse Bedrock™ Granite implant is typically placed in the SAI trajectory, bilaterally, and oftentimes "stacked" to achieve two points of fusion and fixation/stabilization across each SI joint. Currently, this two-point SI joint fixation/stabilization is achieved with bilateral traditional pedicle screws (S2AI trajectory) alongside bilateral iFuse Bedrock™ implants (S1AI trajectory). The iFuse Bedrock™ Granite implant can replace both the traditional pedicle screws.

The iFuse Bedrock ™ Granite implant may also be used in a single, but bilateral configuration, where only two implants may be required when replacing traditional pedicle screws in either an SAI trajectory or iliac trajectory.

Current Coding: There are no unique ICD-10-PCS codes to describe the insertion of a self-harvesting sacropelvic fixation device in the context of spinal fusion. If the device is placed directly into the ilium as a fixation device, code the procedure using the appropriate sacroiliac joint body part value in table 0SH, Insertion of Lower Joints, with approach value 0 Open and device value 4 Internal Fixation Device. If the device is placed in the SAI trajectory as a fusion device, code the procedure using the appropriate sacroiliac joint body part in table 0SG, Fusion of Lower Joints, with approach value 0 Open and device value 4 Internal Fixation Device.

Section	**0** Medical and Surgical
Body System	**S** Lower Joints
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device*	*Qualifier*
0 Lumbar Vertebral Joint **3** Lumbosacral Joint	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**3** Infusion Device **4** Internal Fixation Device **8** Spacer **B** Spinal Stabilization Device, Interspinous Process **C** Spinal Stabilization Device, Pedicle-Based **D** Spinal Stabilization Device, Facet Replacement	**Z** No Qualifier
2 Lumbar Vertebral Disc **4** Lumbosacral Disc	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**3** Infusion Device **8** Spacer	**Z** No Qualifier

5 Sacrococcygeal Joint **6** Coccygeal Joint **7** Sacroiliac Joint, Right **8** Sacroiliac Joint, Left	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**3** Infusion Device **4** Internal Fixation Device **8** Spacer	**Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**S** Lower Joints
Operation	**G** Fusion: Joining together portions of an articular body part rendering the articular body part immobile

Body Part	*Approach*	*Device*	*Qualifier*
5 Sacrococcygeal Joint **6** Coccygeal Joint **7** Sacroiliac Joint, Right **8** Sacroiliac Joint, Left	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**4** Internal Fixation Device **7** Autologous Tissue Substitute **J** Synthetic Substitute **K** Nonautologous Tissue Substitute	**Z** No Qualifier

Coding Options

Option 1. Do not create new ICD-10-PCS codes for the insertion of a fenestrated sacropelvic fixation device. Continue coding as listed in current coding.

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Option 2. Create new codes in section X table XRH, Insertion of Joints, to identify the insertion of a self-harvesting sacropelvic fixation device. If the device is placed directly into the ilium as a fixation device, code the procedure using the appropriate sacroiliac joint body part value in table XRH, Insertion of Joints, with approach value 0 Open and device value 5 Internal Fixation Device, Self-Harvesting. If the device is placed in the SAI trajectory as a fusion device, code the procedure using the appropriate sacroiliac joint body part in table XRG, Fusion of Joints, with approach value 0 Open and device value 5 Internal Fixation Device, Self-Harvesting.

Section	**X** New Technology
Body System	**R** Joints
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
ADD E Sacroiliac Joint, Right **ADD F** Sacroiliac Joint, Left	**0** Open	**5** Internal Fixation Device, Self-Harvesting	**8** New Technology Group 8

Section	**X** New Technology
Body System	**R** Joints
Operation	**G** Fusion: Joining together portions of an articular body part rendering the articular body part immobile

Body Part	*Approach*	*Device*	*Qualifier*
ADD E Sacroiliac Joint, Right **ADD F** Sacroiliac Joint, Left	**0** Open **3** Percutaneous	**ADD 5** Internal Fixation Device, Self-Harvesting	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 9 - ICD-10-PCS Index Addenda

Lttr	C	
Main	Add	CARVYKTI (tm) use Ciltacabtagene Autoleucel
Main	Add	Cavoatrial junction use Superior Vena Cava

Lttr	F	
Main		FlowSense Noninvasive Thermal Sensor 4B00XW0
	Delete	see Measurement, Central Nervous Cerebrospinal Fluid Shunt

Lttr	H	
Main		Hyperbaric oxygenation
		Decompression sickness treatment see Decompression, Circulatory 6A15
	Delete	Wound treatment see Assistance, Circulatory 5A05
	Add	Other treatment see Assistance, Circulatory 5A05

Lttr	P	
Main	Add	Perianal skin use Skin, Perineum

ICD-10-PCS Body Part Key Addenda

Section 0		Medical and Surgical
Axis 4		Body Part
Row	Add	
Term	Add	Skin, Perineum
Includes	Add	Perianal skin

Axis 4		Body Part
Term		Superior Vena Cava
Includes	Add	Cavoatrial junction

ICD-10-PCS Device Key Addenda

Axis 6		Device
Row		
Term		Spinal Stabilization Device, Interspinous Process for Insertion in Lower Joints
Includes	Add	X-Spine Axle Cage
Row		
Term		Spinal Stabilization Device, Interspinous Process for Insertion in Upper Joints
Includes	Add	X-Spine Axle Cage

ICD-10-PCS Substance Key Addenda

Section X		New Technology
Axis 6		Device / Substance / Technology
Row		
Term		Ciltacabtagene Autoleucel
Includes	Add	CARVYKTI (tm)

ICD-10-PCS Table Addenda

Medical and Surgical Section

Axis 4 Body Part
Ultrasonic Surgical Aspiration of Brain

Source	Description	Code specification
2021, public request with CMS internal review	In the Medical and Surgical section table 00D, Extraction of Central Nervous System and Cranial Nerves, add the body part value C Cerebellum to identify procedures such as cerebellum tumor extraction performed using cavitron ultrasonic surgical aspiration (CUSA).	Add: 00DC[034]ZZ (3 codes)

EXAMPLE

Section **0** Medical and Surgical
Body System **0** Central Nervous System and Cranial Nerves
Operation **D** Extraction: Pulling or stripping out or off all or a portion of a body part by the use of force

Body Part	*Approach*	*Device*	*Qualifier*
0 Brain **1** Cerebral Meninges **2** Dura Mater **7** Cerebral Hemisphere **ADD C** Cerebellum **F** Olfactory Nerve **G** Optic Nerve **H** Oculomotor Nerve **J** Trochlear Nerve **K** Trigeminal Nerve **L** Abducens Nerve **M** Facial Nerve **N** Acoustic Nerve **P** Glossopharyngeal Nerve **Q** Vagus Nerve **R** Accessory Nerve **S** Hypoglossal Nerve **T** Spinal Meninges	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**Z** No Qualifier

Axis 5 Approach
Drainage of the Parapharyngeal Space and Retropharyngeal Space

Source	Description	Code specification
2021, public request with CMS internal review	In the body system Anatomical Regions, General of the Medical and Surgical section, add the approach values 7 Via Natural or Artificial Opening and 8 Via Natural or Artificial Opening Endoscopic to root operation table Drainage 0W9, for the body part value 6 Neck, to enable capture of procedures such as the drainage of retropharyngeal/parapharyngeal abscesses using a fiberoptic laryngoscope.	Add: 0W96[78]0Z (2 codes) 0W96[78]Z[XZ] (4 codes)

EXAMPLES

Section	**0** Medical and Surgical		
Body System	**W** Anatomical Regions, General		
Operation	**9** Drainage: Taking or letting out fluids and/or gases from a body part		
Body Part	*Approach*	*Device*	*Qualifier*
6 Neck	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic **ADD 7** Via Natural or Artificial Opening **ADD 8** Via Natural or Artificial Opening Endoscopic	**0** Drainage Device	**Z** No Qualifier
6 Neck	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic **ADD 7** Via Natural or Artificial Opening **ADD 8** Via Natural or Artificial Opening Endoscopic	**Z** No Device	**X** Diagnostic **Z** No Qualifier

Administration Section
Axis 6 Substance

Introduction of bone-substitute material

Source	Description	Code specification
2021, public request with CMS internal review	In the Administration section root operation Introduction table 3E0, add approach values 0 Open and 4 Percutaneous Endoscopic, applied to the body part value V Bones for the substance value G Other Therapeutic Substance and qualifier value C Other Substance. These changes enable capture of additional detail for the introduction of bone-substitute material (e.g. calcium phosphate) into subchondral bone defects.	Add: 3E0V[04]GC (2 codes)

EXAMPLE

Section	**3** Administration
Body System	**E** Physiological Systems and Anatomical Regions
Operation	**0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body System / Region	*Approach*	*Substance*	*Qualifier*
V Bones	**ADD 0** Open **3** Percutaneous **ADD 4** Percutaneous Endoscopic	**G** Other Therapeutic Substance	**C** Other Substance

Topic # 10 - Paired Vagus Nerve Stimulation Therapy Using an External Controller

Issue: There are currently no unique ICD-10-PCS codes to describe paired vagus nerve stimulation using an external controller.

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. The Vivistim® Paired VNS System received FDA approval August 27, 2021. Breakthrough Device Designation was received from the FDA on February 10, 2021.

Background: An ischemic stroke occurs when blood flow to part of the brain is interrupted, causing brain cells to die from a lack of oxygen and nutrients contained in the blood. There are different types of stroke, but the most common type is ischemic stroke, meaning the blood vessels to the brain become clogged, which blocks blood flow from reaching the brain. Depending on how long the brain is deprived of blood and where in the brain the stroke occurs, stroke can lead totemporary or permanent disabilities, and in some cases, death. Disabilities resulting from stroke may include, but are not limited to, total or partial paralysis or difficulty with muscle movement.

The Vivistim® Paired VNS System is intended to be used to stimulate the vagus nerve during rehabilitation therapy to reduce upper extremity motor deficits and improve motor function in chronic ischemic stroke patients with moderate to severe arm impairment. It should not be used in patients with vagotomy, which is surgical removal of part of the vagus nerve.

According to the requestor, the clinical efficacy of the Vivistim® Paired VNS System is supported by 4 peer-reviewed clinical study publications, all of which were randomized, blinded, sham-controlled studies. The VNS-REHAB study was a pivotal, randomized, triple-blind, sham-controlled trial enrolling 108 participants with moderate to severe upper limb impairment.[1] Participants were assigned to receive rehab paired with VNS (Treatment n=53) or rehabilitation paired with sham stimulation (Control n=55). All participants were implanted with a VNS device and received six weeks of in-clinic therapy followed by a home exercise program. At 90 days, patients who received rehabilitation with VNS showed a 2-3X improvement over controls on the Fugl-Meyer Upper Extremity (FMA-UE) and Wolf Motor Function Test (WMFT). The FMA-UE score increased by 5.8 points (±6.0) from baseline with VNS and by 2.8 points (±5.2) in controls (p=0.008, between group difference 2.96, 95% CI 0.83 to 5.08). There was one serious adverse event related to surgery (paresis of the vocal cord) in the control group.

Technology

The Vivistim® Paired VNS System consists of three main components:

1. Paired VNS Implantable Pulse Generator (IPG)
2. Paired VNS Stimulation Lead
3. External Paired Stimulation Controller:
    - Paired VNS Stroke Application and Programming Software (SAPS)

[1] Dawson J, Liu CY, Francisco GE, et al. Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial. Lancet. 2021 Apr 24;397(10284):1545-1553.

- Paired VNS Wireless Transmitter (WT)

Procedure Description
The insertion of the Vivistim® Paired VNS System is similar to that of other cranial nerve insertion procedures and is performed under general anesthesia. An incision is made on the left side of the neck at the C5-6 level and dissection is made to expose the vagus nerve. Stimulator electrodes are coiled around the left vagus nerve. Electrodes are tested and results are visualized. A second incision is made above the left axilla. Using blunt dissection, a pocket is created in the subcutaneous tissue in the left pectoral region for placement of the pulse generator which is sutured into place. The electrode is tunneled subcutaneously and connected to the neurostimulator pulse generator. The stimulator system is tested again prior to wound closure.

Once implanted, the patient undergoes traditional rehabilitation therapy. While the patient is performing a rehabilitative exercise, the physical therapist triggers a wireless transmitter to send a signal to the implanted device to deliver a small burst of electrical stimulation to the vagus nerve. Each time the vagus nerve is stimulated, it sends a signal up to the brain, which triggers the release of neurotransmitters broadly across the brain including the motor cortex, enabling neuroplasticity to increase motor function and increasing the relevance of the physical therapy.

Current Coding: There are no unique ICD-10-PCS codes to describe paired VNS therapy using an external controller. Facilities report the insertion of the neurostimulator generator and lead using the following ICD-10-PCS codes:

0JH60MZ	Insertion of single array stimulator generator into chest subcutaneous tissue and fascia, open approach
	and
00HE3MZ	Insertion of neurostimulator lead into cranial nerve, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify paired VNS therapy using an external controller. Continue coding as listed in current coding.

Option 2. Create new codes in section X table X0H Insertion of Nervous System, to identify paired VNS therapy using an external controller. Continue coding the coding the implantation of the neurostimulator generator as listed in current coding

Section	**X** New Technology		
Body System	**ADD 0** Nervous System		
Operation	**H** Insertion: Putting in a nonbiological appliance that monitors, assists, performs, or prevents a physiological function but does not physically take the place of a body part		
Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
ADD Q Vagus Nerve	**3** Percutaneous	**ADD R** Neurostimulator Lead with Paired Stimulation	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 11 - Ex Vivo Autologous Hematopoietic Stem Cell Gene Therapy

Issue: Currently, there are no unique ICD-10-PCS codes to describe the administration of genetically modified *ex vivo* autologous hematopoietic stem/progenitor cells.

New Technology Application? No.

Food & Drug Administration (FDA) Approval? No.

- Submission of OTL-200 to the FDA is expected to begin in Quarter 4 of 2022. Rare Pediatric Disease designation for OTL-200 was granted on May 3, 2018.
- Submission of OTL-103 to the FDA is expected to begin in the second half of 2023. Regenerative Medicine Advanced Therapy (RMAT) designation was granted to OTL - 103 on July 29, 2019 and Rare Pediatric Disease designation on August 18, 2019.

Background: Metachromatic leukodystrophy (MLD) is a rare and life-threatening inherited disease of the body's metabolic system occurring in approximately one in every 100,000 live births, characterized by severe motor and cognitive impairment. MLD is caused by a mutation in the arylsulfatase A (*ARSA*) gene that results in massive accumulation of sulfatides in the brain, peripheral nervous system, causing progressive neurodegeneration of the central and peripheral nervous systems. Over time, the nervous system is damaged, leading to neurological problems such as motor, behavioral and cognitive regression, severe spasticity, and seizures.
MLD is classified by the age at which symptoms first develop into early onset disease (<7 years old) or later onset disease (7 years of age or older). Currently, there are no approved treatments for MLD in the US.

Wiskott Aldrich Syndrome (WAS) is a rare, X-linked primary immunodeficiency disorder characterized by mutations in the *WAS* gene encoding the WAS protein (WASP), responsible for maintaining cellular architecture integral to intracellular and cell-substrate interactions and signaling. WAS is a spectrum disorder that may progress over time and is characterized by microthrombocytopenia, eczema, recurrent or severe life-threatening infections, and malignancy or autoimmunity. Clinical management of WAS is based on supportive care for infections, manifestations of autoimmunity, and microthrombocytopenia. The approximate survival of WAS patients is 15 years with supportive treatment.

Allogeneic hematopoietic stem cell transplant (HSCT) is a treatment that is considered for eligible WAS and MLD patients. Allogeneic HSCT-limiting complications are common, affecting up to half of all patients, and include side effects of conditioning regimens, graft-vs-host disease (GVHD), graft rejection, and autoimmune complications. Additionally, allogeneic HSCT is restricted by the availability of a human-leukocyte antigen (HLA)-matched donor and the risk of morbidity and mortality. The success and accompanying morbidity are largely based upon the degree of human leukocyte antigen (HLA)-matching between the donor and the patient. HLA-matched donors are only available for a minority of patients, meaning alternative donor sources such as mismatched donors, haploidentical donors, or umbilical cord blood must be used, which increase the risk of morbidity.

Description of OTL-200
OTL-200 is an autologous $CD34^+$ cell-enriched population that contains hematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the *ARSA* gene for the treatment of patients diagnosed with MLD. OTL-200 can be given in presymptomatic or early symptomatic MLD, depending on the MLD subtype. If approved by the FDA, OTL-200 would be the first *ex vivo* autologous HSC-GT available for use in the US intended for the treatment of patients diagnosed with MLD.

Description of OTL-103
OTL-103 is an autologous $CD34^+$ cell-enriched population that contains HSPCs transduced *ex vivo* using a lentiviral vector encoding the human *WAS* gene for the treatment of patients diagnosed with WAS. OTL-103 is a durable treatment that can provide comprehensive immune reconstitution across stem cell progeny in this phenotypically heterogenous population of patients characterized by autoimmunity. As an *ex vivo* autologous hematopoietic stem cell gene therapy (HSC-GT) approach, OTL-103 has not exhibited the significant mortality and morbidity known to be associated with allogeneic HSCT therapy, such as GVHD. If approved by the FDA, OTL-103 would be the first *ex vivo* autologous HSC-GT available for use in the US intended for the treatment of patients diagnosed with WAS.

Mechanism of Action
OTL-200 and OTL-103 are investigational autologous HSPC-enriched cell fractions that contain CD34+ HSPCs genetically modified *ex vivo* using a lentiviral vector encoding specific genetic sequences.

- OTL-200 contains CD34+ HSPCs genetically modified *ex vivo* using a lentiviral vector encoding the *ARSA* complementary deoxyribonucleic acid (cDNA) sequence with constitutive expression driven by the human phosphoglycerate kinase (PGK) promoter leading to expression of ARSA in all stem cell progeny (Sessa 2016). As an *ex vivo* autologous HSC-GT approach, OTL-200 is a durable treatment that does not require the donor matching needed for allogeneic HSCT and can provide comprehensive benefit, including in infantile-onset disease. OTL-200 cells, which are able to cross the blood-brain barrier, are reinfused into patients following a conditioning regimen, which reduces defective cells and favors the engraftment of genetically modified cells expressing *ARSA*. OTL-200 has been evaluated in prospective, non-randomized phase I/II clinical trials and expanded access programs. According to the requestor, no serious adverse events or mortality related to OTL-200 have been reported to date. The most commonly reported adverse events were potentially related to busulfan conditioning and included febrile neutropenia, infections, liver disorders, stomatitis, and mucosal inflammation. During clinical development, anti-ARSA antibodies (AAA) were reported in 5 patients (antibodies against ARSA), which resolved spontaneously or after treatment with rituximab.

- OTL-103 contains CD34+ HSPCs genetically modified *ex vivo* using a lentiviral vector encoding the *WAS* complementary deoxyribonucleic acid (cDNA) sequence with expression driven by the endogenous WAS promoter, leading to physiological expression in stem cell progeny. As an *ex vivo* autologous HSC-GT approach, OTL-103 has not exhibited the significant mortality and morbidity known to be associated with allogeneic HSCT therapy,

such as GVHD. OTL-103 was evaluated in clinical trials and expanded access programs. According to the requestor, there were no reported adverse events related to OTL-103. In patients that did experience mild or moderate adverse events, investigator assessment concluded they were related to the conditioning regimen.

Inpatient Administration of OTL-200 and OTL-103
The gene therapy treatment includes five steps:

1. Autologous HSPCs are harvested from the patient through leukapheresis or bone marrow harvest.
2. The harvested sample is selected and purified to a CD34+ enriched cell fraction.
3. In an *ex vivo* process, a lentiviral vector is utilized to insert a working copy of the missing or faulty gene into the cells (the gene is disease-specific) and the product is cryopreserved, ensuring that the drug product can be released following quality-control testing. The genetically corrected HSPCs are transported to the treatment site.
4. The patient undergoes a conditioning regimen (selected regimen is disease-dependent).
5. The genetically corrected HSPCs are thawed and then infused into the patient intravenously as a single, durable treatment. These cells engraft in the patient's bone marrow and begin to self-renew to produce healthy stem cell progeny containing the functional gene.

Current Coding: Facilities can report the administration of genetically modified *ex vivo* autologous hematopoietic stem/progenitor cells with 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 administration of OTL-200 and OTL-103. Continue coding as listed in current coding.

Option 2. Create new codes in section X New Technology, table XW1 Transfusion, to identify intravenous transfusion of OTL-200 and OTL-103.

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 D** OTL-103 **ADD E** OTL-200	**ADD 8** New Technology Group 8

Option 3. Create new codes in section X New Technology, table XW0 Introduction, to identify intravenous administration of OTL-200 and OTL-103.

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 E** OTL-103 **ADD F** OTL-200	**ADD 8** New Technology Group 8

Option 4. In the Administration Section, table 302 Transfusion, revise existing substance value C:

Revised from -

C Hematopoietic Stem/Progenitor Cells, Genetically Modified;

Revised to -

C Hematopoietic Stem/Progenitor Cells, Genetically Modified Ex Vivo

Section	**3** Administration
Body System	**0** Circulatory
Operation	**2** Transfusion: Putting in blood or blood products

Body System / Region	*Approach*	*Substance*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**A** Stem Cells, Embryonic	**Z** No Qualifier
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**REVISE FROM C** Hematopoietic Stem/Progenitor Cells, Genetically Modified **REVISE TO C** Hematopoietic Stem/Progenitor Cells, Genetically Modified Ex Vivo	**0** Autologous

CMS Recommendation: CMS is seeking input from the audience.

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

Topic # 12 - Quantitative Flow Ratio for Non-invasive Analysis of Coronary Angiography

Issue: There are currently no unique ICD-10-PCS codes to describe the non-invasive qualitative measurement of lesions in coronary vessels.

New Technology Application? No.

Food & Drug Administration (FDA) Approval? Yes. QAngio XA® 3D received 510(k) clearance May 30, 2019 (K182611) for use in clinical settings where validated and reproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

Background: Coronary catheterization and percutaneous coronary intervention (PCI) procedures require measurement of physiologic and anatomical characteristics to determine the extent of a patient's coronary artery disease. According to the requestor, quantitative flow ratio (QFR®) is a non-invasive approach that uses angiographic images and applies advanced three-dimensional (3D) mathematical modelling to facilitate physician treatment decisions prior to, during and after PCI procedures.

Currently, a patient who presents to a catheterization laboratory with ischemic heart disease for a PCI procedure is assessed to determine whether a vessel needs to be treated or not (e.g. angioplasty or stenting). To perform this assessment, the physician may insert a fractional flow reserve (FFR) pressure wire into the coronary artery to be analyzed. Next, administration of a vasodilator, such as adenosine, is required for maximal hyperemia of the artery. The use of FFR is a class IIA recommendation in the United States guidelines for assessment of angiographic intermediate coronary lesions and for guiding revascularization decisions.[1]

Technology
The requestor stated QFR® is a proprietary software solution delivering image-based functional assessment of coronary obstructions from standard coronary X-ray angiograms. The requestor also stated that, as an alternative to FFR, it is non-invasive in that QFR® does not require insertion of a pressure wire or use of a vasodilator. Physiologic measures are available to the operator, that include fixed flow QFR® using a default fixed flow velocity, and contrast QFR® based on the actual contrast frame count derived from the angiograms. Results from the mathematical modeling produce 3D anatomic information for stent sizing, and a residual QFR® value that predicts the QFR® value after intervention.

According to the requestor, QFR® has several advantages over the use of FFR, including:
• Proven Accuracy: Proven to have excellent correlation and agreement with FFR
• Time and Cost Efficiency: No pressure wire and the need for adenosine being eliminated reduces treatment costs and procedure time
• Patient benefit: No unpleasant side-effect from adenosine since not administered and no risk of damaged vessels due to the insertion of a pressure wire
• Clinical Benefits: Can be used for the assessment of results post-PCI, thereby facilitating quality control of the procedure.

[1] https://www.jacc.org/doi/10.1016/j.jacc.2011.08.007

Procedure Description
During the cardiac catheterization procedure, two standard X-ray angiographic image runs are acquired, between 25 and 40 degrees apart. These images are sent immediately to the QFR workstation for subsequent processing. The user indicates a beginning point of the vessel to be analyzed and an end point. Next, the contours of the vessel segment are detected automatically, and edited by the user if needed. Based on the contours, a three-dimensional (3D) representation of the vessel is calculated and visualized. The QFR-values along the vessel are calculated from the 3D anatomy and the flow velocity, which is determined by frame counting. A QFR curve is created along the coronary segment for visual identification of pressure drops. In addition, different QFR indices along the analyzed coronary segment are provided, including vessel QFR (the QFR value at the distal location of the analyzed vessel segment) and delta QFR, the local pressure drop over a selected narrowing alone.

Current Coding: The performance of QFR® analysis of coronary angiography is not reported separately for inpatient hospital coding. Facilities report the coronary angiography using the appropriate code from the table below.

Section	**B** Imaging
Body System	**2** Heart
Type	**1** Fluoroscopy: Single plane or bi-plane real time display of an image developed from the capture of external ionizing radiation on a fluorescent screen. The image may also be stored by either digital or analog means

Body Part	*Contrast*	*Qualifier*	*Qualifier*
0 Coronary Artery, Single **1** Coronary Arteries, Multiple **2** Coronary Artery Bypass Graft, Single **3** Coronary Artery Bypass Grafts, Multiple	**0** High Osmolar **1** Low Osmolar **Y** Other Contrast	**1** Laser	**0** Intraoperative
0 Coronary Artery, Single **1** Coronary Arteries, Multiple **2** Coronary Artery Bypass Graft, Single **3** Coronary Artery Bypass Grafts, Multiple	**0** High Osmolar **1** Low Osmolar **Y** Other Contrast	**Z** None	**Z** None
4 Heart, Right **5** Heart, Left **6** Heart, Right and Left **7** Internal Mammary Bypass Graft, Right **8** Internal Mammary Bypass Graft, Left **F** Bypass Graft, Other	**0** High Osmolar **1** Low Osmolar **Y** Other Contrast	**Z** None	**Z** None

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify QFR® analysis of coronary angiography. Continue coding as listed in current coding.

Option 2. Create new codes in section X table XXE, Measurement of Physiological Systems, to identify QFR® analysis of coronary angiography. Continue coding the coronary angiography as listed in current coding.

Section	**X** New Technology
Body System	**X** Physiological Systems
Operation	**E** Measurement: Determining the level of a physiological or physical function at a point in time

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
3 Arterial	**X** External	**ADD 5** Coronary Artery Flow, Quantitative Flow Ratio Analysis	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 13 - Application of Allogeneic Thymus Derived Tissue

Issue: There are currently no unique ICD-10-PCS codes to describe the application of human allogeneic (donor-derived) thymus tissue.

New Technology Application? No.

Food & Drug Administration (FDA) Approval? Yes. FDA approval was obtained on October 8, 2021.

Background: Congenital athymia is an ultra-rare disease characterized by the absence of a functioning thymus with an estimated incidence in the U.S. of 17 to 24 live births each year.[1] Patients with the condition are born without a thymus, a condition that causes profound immunodeficiency, life-threatening immune dysregulation, and high susceptibility to potentially fatal infections.[2] The clinical manifestations are a direct result of the absence of the thymus and the inability to produce immunocompetent T cells, leading to increased susceptibility to infection. There is no safe and effective treatment for congenital athymia, and most patients die by three years of age. RETHYMIC® is a regenerative therapy used for immune reconstitution for these patients.[3]

Technology
RETHYMIC® is a one-time engineered regenerative human thymus tissue-based therapy for immune reconstitution in pediatric patients with congenital athymia. RETHYMIC® is designed to regenerate the thymic function missing in these patients and does not require donor-recipient matching. RETHYMIC® is not for use in patients who have been diagnosed with severe combined immunodeficiency (SCID).

The most common side effects with RETHYMIC® are hypertension (high blood pressure), cytokine release syndrome, rash, hypomagnesemia (low magnesium), renal impairment / failure (decrease of kidney function), thrombocytopenia (low platelets), and graft versus host disease. Because RETHYMIC® is derived from human tissue, it carries a risk of transmitting infectious disease. Based on effective donor screening procedures and product manufacturing processes, the risk of infectious disease transmission is mitigated – but not completely eliminated.

Procedure Description
RETHYMIC® is a thymus tissue-derived product that consists of yellow to brown slices of processed tissue with varying thickness and shape that is administered in an open surgical procedure between the furrows of the quadriceps muscle in one or both legs. The recommended dose range is 5,000 to 22,000 mm^2 of RETHYMIC® surface area/m^2 recipient BSA. The manufacturer calculates the dose in advance for the specific patient; the amount of product provided is adjusted at the manufacturing facility to ensure the maximum dose for the patient cannot be exceeded. The portion of the product that represents the minimum dose is communicated to the surgical team at the time of surgery. RETHYMIC® requires a healthy bed of muscle tissue. Each individual slice of RETHYMIC® (up to 42 slices) is implanted between the furrows of the

[1] Hsieh, E.W.Y., Kim-Chang, J.J., Kulke, S. et al. Defining the Clinical, Emotional, Social, and Financial Burden of Congenital Athymia. Adv Ther (2021). https://doi.org/10.1007/s12325-021-01820-9
[2] Collins et al, Journal of Clinical Immunology (2021) 41:881–895
[3] Markert et al. J Allergy Clin Immunol. 2021 Aug 3: S0091-6749 (21) 01056-3.

quadriceps muscle and a single stich closes the pocket holding the RETHYMIC® slice. This process is repeated until all slices of RETHYMIC® have been implanted into pockets in one or both of the quadriceps muscles. The open surgical procedure takes approximately 2 hours to complete, and the patient is typically hospitalized for a minimum of two days for pain control secondary to swelling in one or both legs. Surgical implantation of allogeneic processed thymus tissue product (RETHYMIC®) should be done by a qualified surgeon.

Current Coding: There are no unique ICD-10-PCS codes to describe the open intramuscular application of allogeneic thymus derived tissue. Facilities can report intramuscular application of allogeneic thymus derived tissue with the following ICD-10-PCS percutaneous code:

3E023GC	Introduction of other therapeutic substance into muscle, percutaneous approach

Coding Options

Option 1. Do not create new ICD-10-PCS codes for intramuscular application of allogeneic thymus derived tissue. Continue coding as listed in current coding.

Option 2. Create new codes in section X, New Technology, to identify intramuscular application of allogeneic thymus derived tissue.

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*
2 Muscle	**0** Open	**ADD D** Engineered Allogeneic Thymus Tissue	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 14 - Cardiac Perfusion with Intra-arterial Supersaturated Oxygen

Issue: The existing ICD-10-PCS codes used to describe cardiac perfusion with intra-arterial supersaturated oxygen do not accurately describe the procedure.

New Technology Application? No.

Food & Drug Administration (FDA) Approval? Supersaturated Oxygen Therapy (SSO_2) was most recently approved by the FDA in 2019.

Background: SSO_2 therapy is a FDA-approved treatment for the management of ST-segment elevation myocardial infarction (STEMI). SSO_2 therapy delivers an infusion of the patient's blood carrying supersaturated oxygen to the left main coronary artery (LMCA) following successful percutaneous coronary intervention (PCI) with stenting that has been completed within 6 hours after the onset of anterior acute myocardial infarction (AMI) symptoms caused by a left anterior descending artery infarct lesion. SSO_2 therapy improves impaired blood flow in the capillary beds and at-risk myocardium with no toxicity to the coronaries, myocardium, or end organs. SSO_2 therapy has been clinically evaluated in a series of FDA-approved IDE clinical trials demonstrating safety and effectiveness.[1]

SSO_2 therapy is performed to reduce infarct size after successful PCI/stenting in STEMI patients. The SSO_2 therapy's mechanism of action targets residual endothelial edema, neutrophil blockage and other physiologic responses, such as obstructing or blocking blood flow. SSO_2 therapy addresses these challenges by perfusing supersaturated oxygen into myocardial microvasculature and endothelial tissue to relieve swelling and restore blood flow. The reduction in infarct size is intended to improve myocardial function and reduce short- and long-term complications, including heart failure and mortality.[2]

The topic of "SuperOxygenation Therapy" was originally presented at the ICD-9 Coordination and Maintenance Committee Meeting in September 2007. The Committee approved ICD-9-CM code 00.49 (Supersaturated Oxygen Therapy).

In the transition to ICD-10-PCS, the closest translations available for ICD-9-CM code 00.49 were codes 5A0512C and 5A0522C from the following table:

5A0512C	Extracorporeal supersaturated oxygenation, intermittent and
5A0522C	Extracorporeal supersaturated oxygenation, continuous

[1] Stone GW, et al. Circ Cardiovasc Interv; 2; 366-375. Sep 2009. O'Neill WW, et al. J Am Coll Cardiol. 2007;50; No.5. 397-405
[2] Kloner et al., "Update on Carioprotective Strategies for STEMI, Focus on Supersaturated Oxygen Delivery", *JACC: BASIC TO TRANSLATIONAL SCIENCE*, 2021

Section	**5** Extracorporeal or Systemic Assistance and Performance
Body System	**A** Physiological Systems
Operation	**0** Assistance: Taking over a portion of a physiological function by extracorporeal means

Body System	*Duration*	*Function*	*Qualifier*
2 Cardiac	**1** Intermittent **2** Continuous	**1** Output	**0** Balloon Pump **5** Pulsatile Compression **6** Other Pump **D** Impeller Pump
5 Circulatory	**1** Intermittent **2** Continuous	**2** Oxygenation	**1** Hyperbaric **C** Supersaturated

Concerns with current coding:

- Code placement: Confusion exists due to location within the ICD-10-PCS placement tables.
- Percutaneous SSO_2 perfusion is not accurately classified with extracorporeal hyperbaric oxygenation.
- Hospital perspectives: At times, SSO_2 has been wrongly interpreted by hospitals as Extracorporeal Membrane Oxygenation (ECMO).

According to the requestor, a revision to current coding will significantly contribute to uniform hospital reporting and enable better collection of clinical data.

Technology

The SSO_2 therapy procedure utilizes a closed loop, arterial to arterial circuit, through a console enabling perfusion of supersaturated oxygen infusate directly to the infarct, reducing endothelial edema in the microvasculature and reversing myocardial infarct damage. The console contains a blood-supersaturated oxygen mixing chamber and a pump, with sheath and coronary infusion catheters.

SSO_2 therapy assists the heart, removing blood from the body and delivering the blood to an SSO_2 cartridge, where arterial blood is mixed with oxygen-rich saline in a low-priming volume (50 ml) blood loop to achieve high levels of oxygen (pO_2=1000mmHg). The newly oxygenated blood is then pumped back to the patient through radial or femoral artery access. According to the requestor, studies have demonstrated that the effect of this high level of oxygen transfer to the ischemic myocardium is to resolve endothelial cell edema and restore capillary patency, improving microcirculatory flow and tissue level perfusion. Ultimately, this improvement leads to significant reductions in infarct size. Since SSO_2 therapy is an adjunctive treatment performed in the operating room after successful PCI, it complements the current standard of care, without delays in treatment or door-to-balloon time.[3]

Procedure Description

SSO_2 therapy is a one-time, 60-minute infusion/perfusion performed in an operating room, typically the cardiac catherization laboratory, immediately following successful PCI. Autologous arterial blood is mixed with oxygen-rich saline in a low-priming volume (50 ml) blood loop to achieve high levels of oxygen (pO_2=1000mmHg). The superoxygenated infusate is returned to the patient via a 5F angiographic style delivery catheter placed in the ostium of the left main coronary

[3] SuperSaturated Oxygen (SSO2) Therapy: A Data Continuum, ZOLL Medical Corporation, 2020.

artery. The high level of dissolved oxygen (7-10x normal) creates a large concentration gradient for oxygen to perfuse and diffuse into ischemic tissue even when blood flow is compromised.

After a brief neurologic assessment (degree of arousal to verbal stimuli, percent of O_2 saturation, etc.) and documentation of hemodynamic status, moderate sedation is continued uninterrupted from the end of the PCI/stenting procedure to completion of the SSO_2 therapy.

Upon completion of the 60 minutes of SSO_2 therapy, the draw and delivery tubings are disconnected from the patient lines. The SSO_2 catheter is withdrawn to beyond the aortic arch and removed over a guidewire after disconnection from the return tubing. An EKG is obtained, vascular closure device(s) applied, moderate sedation discontinued, and the patient's clinical status is re-evaluated post-sedation. A normal saline IV infusion is continued, depending on hemodynamics and renal function.

Current Coding: Facilities report cardiac perfusion with intra-arterial supersaturated oxygen using the appropriate code from the table below.

Section **5** Extracorporeal or Systemic Assistance and Performance *Body System* **A** Physiological Systems *Operation* **0** Assistance: Taking over a portion of a physiological function by extracorporeal means			
Body System	*Duration*	*Function*	*Qualifier*
2 Cardiac	**1** Intermittent **2** Continuous	**1** Output	**0** Balloon Pump **5** Pulsatile Compression **6** Other Pump **D** Impeller Pump
5 Circulatory	**1** Intermittent **2** Continuous	**2** Oxygenation	**1** Hyperbaric **C** Supersaturated

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify cardiac perfusion with intra-arterial supersaturated oxygen. Continue coding as listed in current coding.

Option 2. In section 5 table 5A0, Assistance of Physiological Systems, add existing body part value 2 Cardiac, applied to the duration value 2 Continuous, the function value 2 Oxygenation and the qualifier value C Supersaturated to identify cardiac perfusion with intra-arterial supersaturated oxygen. Delete codes in table 5A0 that identify cardiac perfusion with intra-arterial supersaturated oxygen.

Section **5** Extracorporeal or Systemic Assistance and Performance *Body System* **A** Physiological Systems *Operation* **0** Assistance: Taking over a portion of a physiological function by extracorporeal means			
Body System	*Duration*	*Function*	*Qualifier*
2 Cardiac	**1** Intermittent **2** Continuous	**1** Output	**0** Balloon Pump **5** Pulsatile Compression **6** Other Pump **D** Impeller Pump
5 Circulatory	**1** Intermittent **2** Continuous	**2** Oxygenation	**1** Hyperbaric **DELETE C** Supersaturated
ADD 2 Cardiac	**2** Continuous	**2** Oxygenation	**C** Supersaturated

Option 3. Create new codes in Administration Section table 3E0 to identify cardiac perfusion with intra-arterial supersaturated oxygen. Delete codes in table 5A0 that identify cardiac perfusion with intra-arterial supersaturated oxygen.

Section **3** Administration *Body System* **E** Physiological Systems and Anatomical Regions *Operation* **0** Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products			
Body System/Region	*Approach*	*Substance*	*Qualifier*
7 Coronary Artery	**3** Percutaneous	**G** Other Therapeutic Substance	**C** Other Substance **ADD R** Supersatured Oxygen

Section **5** Extracorporeal or Systemic Assistance and Performance *Body System* **A** Physiological Systems *Operation* **0** Assistance: Taking over a portion of a physiological function by extracorporeal means			
Body System	*Duration*	*Function*	*Qualifier*
2 Cardiac	**1** Intermittent **2** Continuous	**1** Output	**0** Balloon Pump **5** Pulsatile Compression **6** Other Pump **D** Impeller Pump
5 Circulatory	**1** Intermittent **2** Continuous	**2** Oxygenation	**1** Hyperbaric **DELETE C** Supersaturated

Option 4. Create new codes in Other Procedures Section table 8E0 to identify cardiac perfusion with intra-arterial supersaturated oxygen. Delete codes in table 5A0 that identify cardiac perfusion with intra-arterial supersaturated oxygen.

Section **8** Other Procedures *Body System* **E** Physiological Systems and Anatomical Regions *Operation* **0** Other Procedures: Methodologies which attempt to remediate or cure a disorder or a disease			
Body Region	*Approach*	*Method*	*Qualifier*
2 Circulatory System	**3** Percutaneous	**ADD F** Cardiac Perfusion with Supersatured Oxygen	**Z** No Qualifier

Section **5** Extracorporeal or Systemic Assistance and Performance *Body System* **A** Physiological Systems *Operation* **0** Assistance: Taking over a portion of a physiological function by extracorporeal means			
Body System	*Duration*	*Function*	*Qualifier*
2 Cardiac	**1** Intermittent **2** Continuous	**1** Output	**0** Balloon Pump **5** Pulsatile Compression **6** Other Pump **D** Impeller Pump
5 Circulatory	**1** Intermittent **2** Continuous	**2** Oxygenation	**1** Hyperbaric **DELETE C** Supersaturated

CMS Recommendation: CMS is interested in hearing input.

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

Topic # 15 – Simulation for Assessment of Coronary Obstruction Risk

Issue: There are currently no unique ICD-10-PCS codes to describe the use of simulation software for assessment of coronary obstruction risk in structural heart valve interventions.

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. An application for 510(k) clearance of the Precision TAVI™ Coronary Obstruction Module has been submitted to the FDA.

Background: Coronary obstruction, as defined by the 2011 American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions guidelines for percutaneous coronary intervention, is considered as a >50% obstruction of the left main coronary artery, >70% in any other coronary artery, or both.[1,2] Transcatheter aortic valve replacement (TAVR) represents a major advance in the treatment of patients with aortic stenosis, which is a narrowing of the aortic valve opening. Despite the overall effectiveness of TAVR, complications can limit the realization of mortality and quality of life benefits. Among these is coronary obstruction, a fatal complication which can occur upon transcatheter valve deployment, and most often affects the left coronary artery.

The requestor stated that the Precision TAVI™ Coronary Obstruction Module utilizes intelligent decision support that may assist physicians in the evaluation of patients with severe aortic stenosis who are being considered for surgical replacement versus transcatheter replacement. The module was developed to help physicians better assess potential coronary obstructions and further consider the need for coronary protection measures or other interventional measures.

Technology and Procedure
According to the requestor, Precision TAVI™ enables the visualization of transcatheter aortic valve placement and deployment for preoperative planning, coronary obstruction risk biomarker, and implant valve sizing for TAVR procedures.

General functionalities include:
· Visualization of CT scan images for 2D review and 3D reconstruction
· Segmentation of cardiovascular structures
· Measurements/dimensions of vessels and structures
· Aortic valve model (AVM) generation
· Simulation of transcatheter valve deployment

The Precision TAVI™ software operates in 3 distinct stages. In the first dimensions stage, patient computerized tomography (CT) data is uploaded to a secure server, which also includes patient-specific selections on which device and size combinations will be used in the procedure.

[1] Maddox TM, Stanislawski MA, Grunwald GK, Bradley SM, Ho PM, Tsai TT, et al. Nonobstructive coronary artery disease and risk of myocardial infarction. *JAMA*. 2014;312;1754-63.
[2] Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl SR, Cercek B, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/Ameican Heart Association task force on practice guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol.* 2011;58:e44-122

In the second stage, image processing and simulation occurs. A segmentation module creates a 3D file containing the patient specific AVM, which contains surface and volume meshes of the AVM configured for the simulation module. The coronary obstruction module analyzes the simulation results and outputs a coronary obstruction risk biomarker.

In the visualization stage, a report is generated containing images and videos of the device placement and simulated valve deployment into the patient specific AVM from the simulation module, and the coronary obstruction risk biomarker (DLC/d). The report is made available for download via a secure portal.
The requestor stated that the information provided by the software is not intended to eliminate, replace, or substitute for, in whole or in part, the healthcare provider's judgement and analysis of the patient's condition.

Current Coding: The use of simulation software for assessment of coronary obstruction risk is not reported separately for inpatient hospital coding. Facilities report the CT angiogram using the appropriate code from the table below.

Section	**B** Imaging
Body System	**2** Heart
Type	**2** Computerized Tomography (CT Scan): Computer reformatted digital display of multiplanar images developed from the capture of multiple exposures of external ionizing radiation

Body Part	*Contrast*	*Qualifier*	*Qualifier*
1 Coronary Arteries, Multiple **3** Coronary Artery Bypass Grafts, Multiple **6** Heart, Right and Left	**0** High Osmolar **1** Low Osmolar **Y** Other Contrast	**0** Unenhanced and Enhanced **Z** None	**Z** None
1 Coronary Arteries, Multiple **3** Coronary Artery Bypass Grafts, Multiple **6** Heart, Right and Left	**Z** None	**2** Intravascular Optical Coherence **Z** None	**Z** None

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify the use of simulation software for assessment of coronary obstruction risk. Continue coding as listed in current coding.

Option 2. Create new codes in section X table XXE, Measurement of Physiological Systems, to identify the use of simulation software for assessment of coronary obstruction risk. Continue coding the CT angiogram as listed in current coding

Section	**X** New Technology
Body System	**X** Physiological Systems
Operation	**E** Measurement: Determining the level of a physiological or physical function at a point in time

Body Part	*Approach*	*Device / Substance / Technology*	*Qualifier*
0 Central Nervous	**X** External	**0** Intracranial Vascular Activity, Computer-aided Assessment	**7** New Technology Group 7
3 Arterial	**X** External	**2** Pulmonary Artery Flow, Computer-aided Triage and Notification	**7** New Technology Group 7
3 Arterial	**X** External	**ADD 6** Coronary Artery Flow, Computer-aided Analysis and Notification	**8** New Technology Group 8

CMS Recommendation: Option 2, as described above.

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

Topic # 16 - Laser Interstitial Thermal Therapy (LITT)

Issue: There are currently no unique ICD-10-PCS codes to describe laser interstitial thermal therapy (LITT) for ablation.

New Technology Application? No.

Food & Drug Administration (FDA) Approval? Yes. Bio Tex, Inc. initially received 510(k) approval for the first system, the Visualase® Thermal Therapy System in 2007. Medtronic Navigation Inc. subsequently acquired Bio Tex, Inc. and the technology in 2014. On January 7, 2022, Medtronic received FDA clearance for updated labeling: The Visualase™ MRI-Guided Laser Ablation System is a neurosurgical tool and is indicated for use to ablate, necrotize, or coagulate intracranial soft tissue including brain structures (for example, brain tumor, radiation necrosis and epileptic foci as identified by non-invasive and invasive neurodiagnostic testing, including imaging) through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 800nm through 1064nm lasers.

Monteris Medical, Inc. initially received 510(k) approval for the AutoLITT® System in 2009 and its next generation system, NeuroBlate™, received 510(k) approval in 2013. The Monteris Medical NeuroBlate™ System is a neurosurgical tool and is indicated for use to ablate, necrotize, or coagulate intracranial soft tissue, including brain structures (e.g., brain tumor, radiation necrosis, and epileptogenic foci as identified by non-invasive and invasive neurodiagnostic testing, including imaging), through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 1064 nm lasers. The Monteris Medical NeuroBlate System is intended for planning and monitoring thermal therapies under MRI visualization. It provides MRI-based trajectory planning assistance for the stereotaxic placement of MRI compatible (conditional) NeuroBlate Laser Delivery Probes. It also provides near real-time thermographic analysis of selected MRI images in medicine and surgery in the discipline of neurosurgery with 1064 nm lasers.

Background: Laser Interstitial Thermal Therapy (LITT) has been uniquely identified in the encoded data for over 10 years, first in ICD-9-CM and now in ICD-10-PCS. However, LITT is misclassified to section D-Radiation Therapy in ICD-10-PCS possibly because, borrowing terminology used for predicate devices, FDA indications have included the phrase "interstitial irradiation or thermal therapy" in describing LITT's method of action. LITT is thermal therapy, destroying soft tissue using heat generated by a laser probe at the target site. The LITT procedure does not use ionizing radiation, which is what the term "radiation" commonly refers to in the general medical sense.

By itself, radiation is a broad term. The spectrum of electromagnetic radiation technically encompasses low energy non-ionizing radio waves, microwaves, and infrared to high energy ionizing X-rays and gamma rays. Ionizing radiation creates ions in the cells it passes through by removing electrons, a process which kills or alters the cells over time.

Only certain medical uses of radiation are classified to section D-Radiation Therapy. Specifically, section D-Radiation Therapy categorizes treatments using ionizing radiation, including beam radiation, brachytherapy, and stereotactic radiosurgery. All of these deliver concentrated ionizing radiation to eradicate abnormal cells, most commonly neoplasms. Other

treatments classified to section D-Radiation Therapy, such as hyperthermia, are used as adjuncts to ionizing radiation. While LITT eradicates abnormal cells, it does so with heat, not ionizing radiation.

Technology
Visualase™ and NeuroBlate® are minimally invasive, robotic, laser thermotherapy tools that use MRI-guided surgical ablation technology to deliver light energy to the target area. As the temperature in the target rises, it is observed under real-time MRI imaging. This allows the surgeon precise control and enables maximal tumor reduction without an open neurosurgical procedure.

Procedure Description
The patient undergoes creation of a burr hole in the skull through which the laser probe is introduced and advanced to the target site. The probe is quite thin and displaces brain tissue along its path rather than cutting through it. After raising the temperature of the target via laser energy sufficiently to destroy the abnormal tissue under MRI guidance, the probe is withdrawn and the burr hole is closed.

Current Coding: There are no unique ICD-10-PCS codes to describe LITT for ablation of various body parts. Facilities report LITT procedures using the appropriate code from section D Radiation Therapy, tables D0Y, DBY, DDY, DFY, DGY, DMY, DVY, using the modality qualifier K, Laser Interstitial Thermal Therapy. An example of table D0Y is provided below to illustrate LITT of central and peripheral nervous system sites.

Section	**D** Radiation Therapy
Body System	**0** Central and Peripheral Nervous System
Modality	**Y** Other Radiation

Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Brain **1** Brain Stem **6** Spinal Cord **7** Peripheral Nerve	**7** Contact Radiation **8** Hyperthermia **C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Coding Options

Option 1. Do not create new ICD-10-PCS codes to identify LITT for ablation of various body parts. Continue coding as listed in current coding.

Option 2. In section 0 table 005, Destruction of Central Nervous System and Cranial Nerves, create new qualifier value 3 Laser Interstitial Thermal Therapy, to identify LITT for ablation of brain or spinal cord tissue.

Section	**0** Medical and Surgical
Body System	**0** Central Nervous System and Cranial Nerves
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
0 Brain **W** Cervical Spinal Cord	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

X Thoracic Spinal Cord **Y** Lumbar Spinal Cord			

In addition, create new qualifier value 3 Laser Interstitial Thermal Therapy, to identify LITT for ablation of tissue in the root operation Destruction tables below.

Section	**0** Medical and Surgical
Body System	**B** Respiratory System
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
C Upper Lung Lobe, Right **D** Middle Lung Lobe, Right **F** Lower Lung Lobe, Right **G** Upper Lung Lobe, Left **H** Lung Lingula **J** Lower Lung Lobe, Left **K** Lung, Right **L** Lung, Left **M** Lungs, Bilateral	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**D** Gastrointestinal System
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
1 Esophagus, Upper **2** Esophagus, Middle **3** Esophagus, Lower **4** Esophagogastric Junction **5** Esophagus **6** Stomach **7** Stomach, Pylorus **8** Small Intestine **9** Duodenum **A** Jejunum **B** Ileum **C** Ileocecal Valve **E** Large Intestine **F** Large Intestine, Right **G** Large Intestine, Left **H** Cecum **J** Appendix **K** Ascending Colon **L** Transverse Colon **M** Descending Colon **N** Sigmoid Colon **P** Rectum	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier
Q Anus	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**F** Hepatobiliary System and Pancreas
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
0 Liver **1** Liver, Right Lobe **2** Liver, Left Lobe	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy

			F Irreversible Electroporation **Z** No Qualifier
4 Gallbladder	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier
5 Hepatic Duct, Right **6** Hepatic Duct, Left **7** Hepatic Duct, Common **8** Cystic Duct **9** Common Bile Duct **C** Ampulla of Vater **D** Pancreatic Duct **F** Pancreatic Duct, Accessory	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier
G Pancreas	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **F** Irreversible Electroporation **Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**G** Endocrine System
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
0 Pituitary Gland **1** Pineal Body **2** Adrenal Gland, Left **3** Adrenal Gland, Right **4** Adrenal Glands, Bilateral **6** Carotid Body, Left **7** Carotid Body, Right **8** Carotid Bodies, Bilateral **9** Para-aortic Body **B** Coccygeal Glomus **C** Glomus Jugulare **D** Aortic Body **F** Paraganglion Extremity **G** Thyroid Gland Lobe, Left **H** Thyroid Gland Lobe, Right **K** Thyroid Gland **L** Superior Parathyroid Gland, Right **M** Superior Parathyroid Gland, Left **N** Inferior Parathyroid Gland, Right **P** Inferior Parathyroid Gland, Left **Q** Parathyroid Glands, Multiple **R** Parathyroid Gland	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**H** Skin and Breast
Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent

Body Part	*Approach*	*Device*	*Qualifier*
T Breast, Right **U** Breast, Left **V** Breast, Bilateral	**0** Open **3** Percutaneous	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

Section	**0** Medical and Surgical
Body System	**V** Male Reproductive System

Operation	**5** Destruction: Physical eradication of all or a portion of a body part by the direct use of energy, force, or a destructive agent		
Body Part	*Approach*	*Device*	*Qualifier*
0 Prostate	**0** Open **3** Percutaneous **4** Percutaneous Endoscopic	**Z** No Device	**ADD 3** Laser Interstitial Thermal Therapy **Z** No Qualifier

Delete modality qualifier value K, Laser Interstitial Thermal Therapy, from the tables below in section D Radiation Therapy, Other Radiation.

Section	**D** Radiation Therapy		
Body System	**0** Central and Peripheral Nervous System		
Modality	**Y** Other Radiation		
Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Brain **1** Brain Stem **6** Spinal Cord **7** Peripheral Nerve	**7** Contact Radiation **8** Hyperthermia **C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy		
Body System	**B** Respiratory System		
Modality	**Y** Other Radiation		
Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Trachea **1** Bronchus **2** Lung **5** Pleura **6** Mediastinum **7** Chest Wall **8** Diaphragm	**7** Contact Radiation **8** Hyperthermia **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy		
Body System	**D** Gastrointestinal System		
Modality	**Y** Other Radiation		
Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Esophagus	**7** Contact Radiation **8** Hyperthermia **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None
1 Stomach **2** Duodenum **3** Jejunum **4** Ileum **5** Colon **7** Rectum	**7** Contact Radiation **8** Hyperthermia **C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None
8 Anus	**C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy		
Body System	**F** Hepatobiliary System and Pancreas		
Modality	**Y** Other Radiation		
Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*

0 Liver **1** Gallbladder **2** Bile Ducts **3** Pancreas	**7** Contact Radiation **8** Hyperthermia **C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy
Body System	**G** Endocrine System
Modality	**Y** Other Radiation

Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Pituitary Gland **1** Pineal Body **2** Adrenal Glands **4** Parathyroid Glands **5** Thyroid	**7** Contact Radiation **8** Hyperthermia **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy
Body System	**M** Breast
Modality	**Y** Other Radiation

Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Breast, Left **1** Breast, Right	**7** Contact Radiation **8** Hyperthermia **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

Section	**D** Radiation Therapy
Body System	**V** Male Reproductive System
Modality	**Y** Other Radiation

Treatment Site	*Modality Qualifier*	*Isotope*	*Qualifier*
0 Prostate	**7** Contact Radiation **8** Hyperthermia **C** Intraoperative Radiation Therapy (IORT) **F** Plaque Radiation **DELETE K** Laser Interstitial Thermal Therapy	**Z** None	**Z** None

CMS Recommendation: Option 2, as described above.

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

Topic # 17 - 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.

Topic # 18 - 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.

Topic # 19 - 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

[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.

care for a catheter lock solution.

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** Externa**l**	**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.

Topic # 20 - 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.**Error! Bookmark not defined.**,[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.**Error! Bookmark not defined.**

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.

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[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.

Topic # 21 - 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.

Topic # 22 - 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.

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[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.

Topic # 23 - 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.

Topic # 24 - 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 tabelecleucel 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.

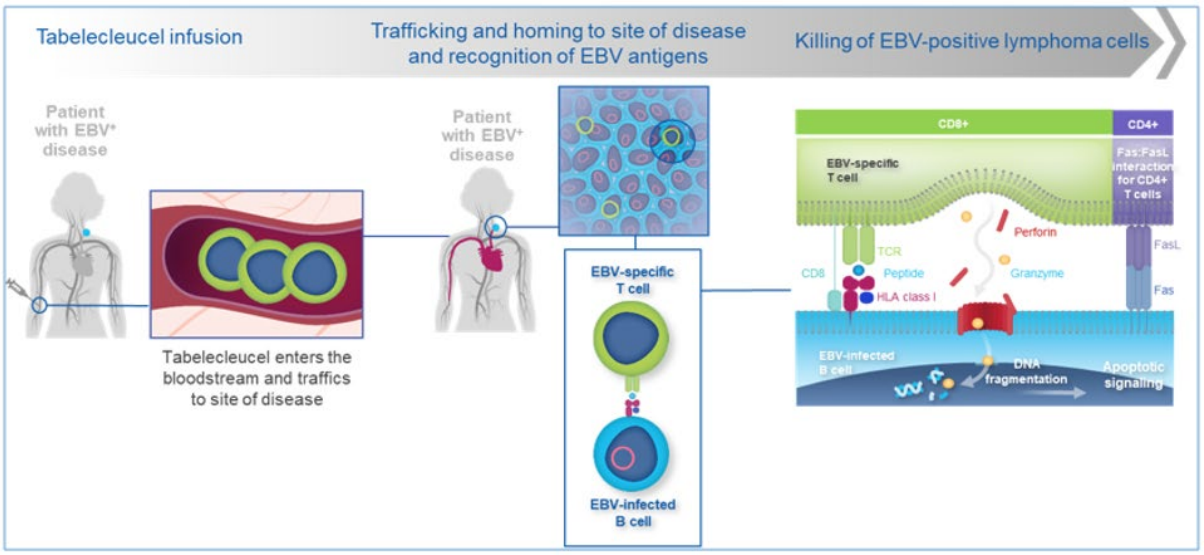
Description and Mechanism of Action for Tabelecleucel
Tabelecleucel is an allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy which targets and eliminates EBV-positive cells in a human leukocyte antigen (HLA)-restricted manner. It can be used for patients following a solid organ or allogeneic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

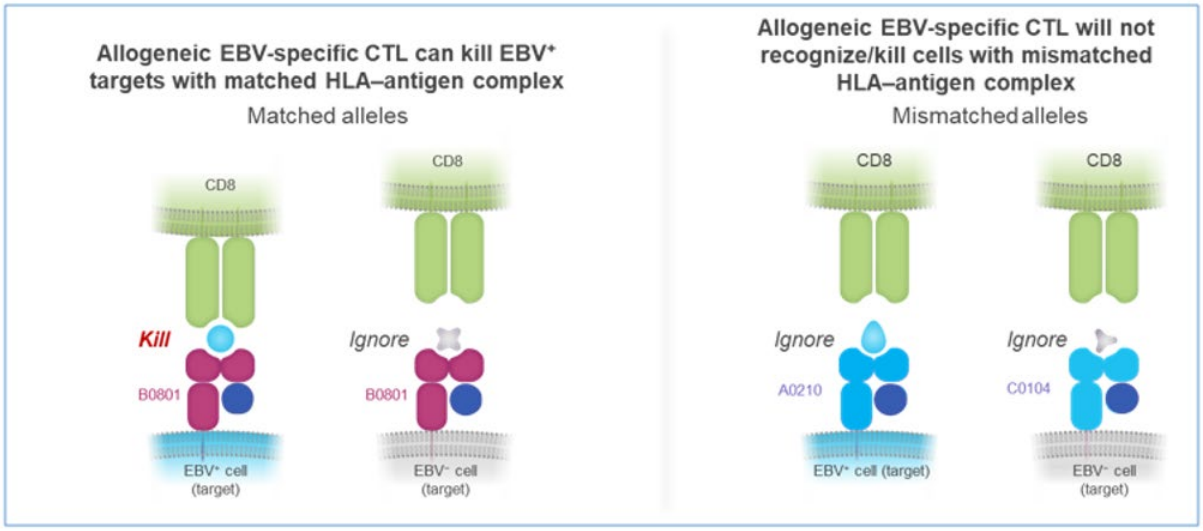
According to the requestor, the T-cell receptor of each clonal population within tabelecleucel recognizes an EBV peptide in complex with a specific HLA molecule on the surface of target cells (the restricting HLA allele) and allows tabelecleucel to exert cytotoxic activity against the EBV-infected cell. 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.

Topic # 25 - 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.

Topic # 26 - 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]
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,

[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/.

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).**Error! Bookmark not defined.**

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.

Topic # 27 - 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.

Topic # 28 - 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.**Error! Bookmark not defined.** 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.**Error! Bookmark not defined.**

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
[3] Bauer DE, Kamran SC, Orkin SH. Reawakening fetal hemoglobin: prospects for new therapies for the β-globin disorders. Blood. 2012;120(15):2945-2953. doi: 10.1182/blood-2012-06-292078.
[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}.**Error! Bookmark not defined.** Following successful engraftment and achievement of transfusion independence, the effects of beti-cel are expected to be lifelong,**Error! Bookmark not defined.** 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

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[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.

Topic # 29 - 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.

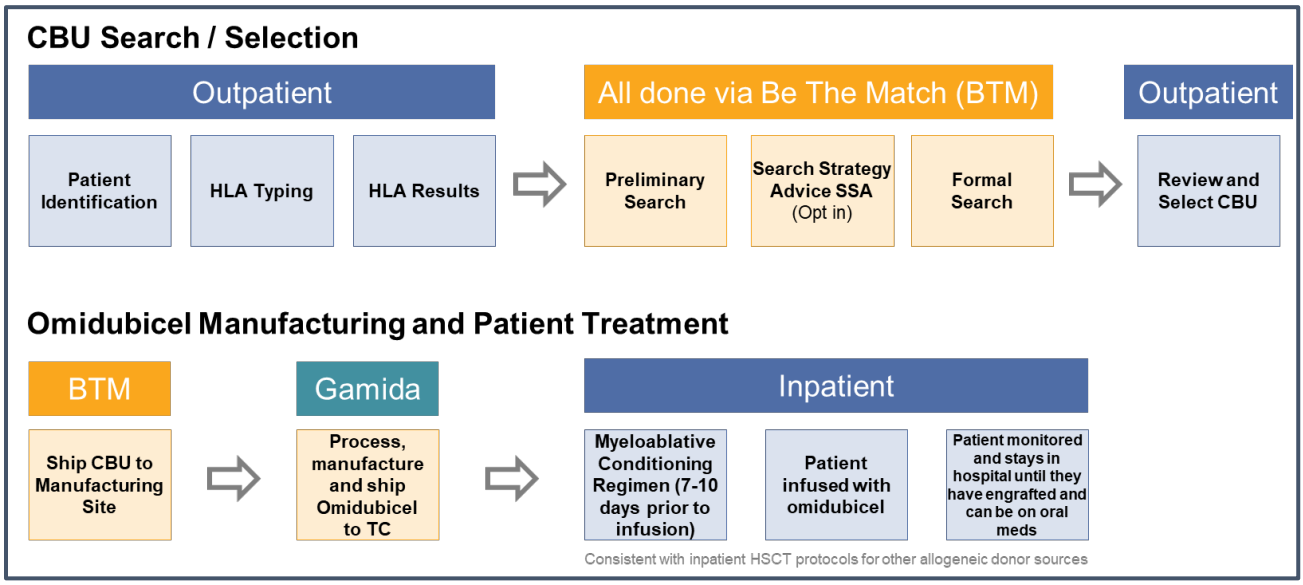
According to the requestor, the safety and efficacy of omidubicel advanced cell therapy donor source was demonstrated in an international, multi-center, randomized Phase 3 registration study (NCT02730299) designed to evaluate safety and efficacy of omidubicel (intent to treat [ITT] n=62) compared with 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.

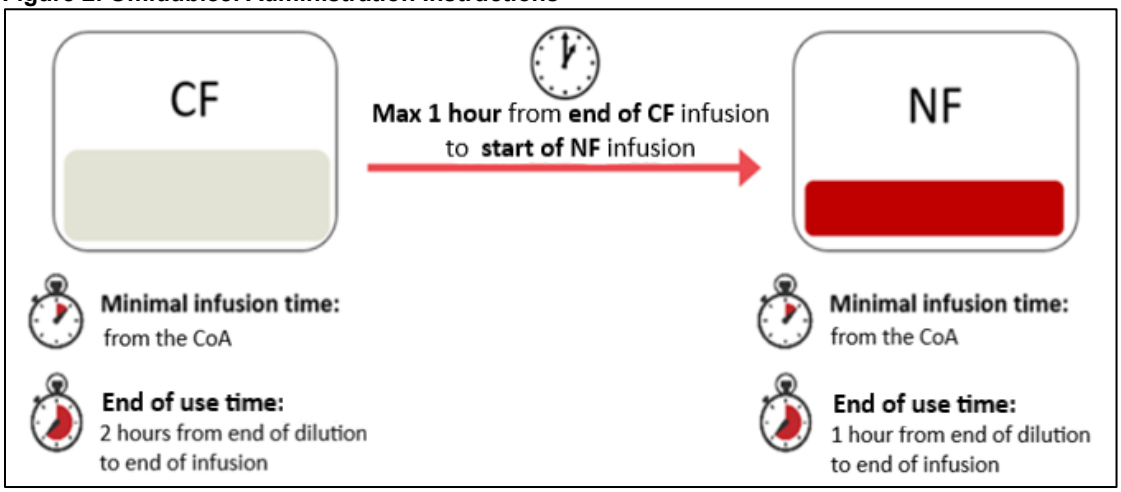
- A single dose of omidubicel contains 2 separate infusions that are prepared from 2 cryopreserved cell suspension bags that are thawed and diluted prior to infusion with their dedicated infusion solutions. The actual number of total viable cells and % of CD34+ cells in the product is reported on the 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.