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

CENTER FOR MEDICARE

ICD-10 Coordination and Maintenance Committee Meeting
September 10, 2024
ICD-10-PCS Therapeutic Agent Topics

Consistent with the requirements of section 1886(d)(5)(K)(iii) of the Social Security Act, applicants submitted requests to create a unique procedure code to describe the administration of a therapeutic agent, such as the option to create a new code in Section X within the International Classification of Diseases, 10th Revision, Procedure Coding System (ICD-10-PCS). CMS is soliciting public comments on the proposed coding options and any clinical questions for the two procedure code topics associated with new technology add-on payment (NTAP)-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent. The deadline to submit comments for topics being considered for an April 1, 2025 implementation is October 11, 2024 and the deadline to submit comments for topics being considered for an October 1, 2025 implementation is November 15, 2024. Members of the public should send any questions or comments to CMS' ICD-10-PCS mailbox at: ICDProcedureCodeRequest@cms.hhs.gov.

Prior to the September 10, 2024 virtual meeting, CMS will post a question and answer document on our website at https://www.cms.gov/medicare/coding-billing/icd-10-codes/icd-10-coordination-maintenance-committee-materials to address clinical or coding questions that members of the public have submitted related to the two therapeutic agents. At a later date, CMS will post an updated question and answer document to address any additional clinical or coding questions that members of the public may have submitted by the October 11, 2024 or November 15, 2024 deadline, respectively.

CMS will not be presenting the two NTAP-related ICD-10-PCS procedure code requests that involve the administration of a therapeutic agent at the September 10, 2024 virtual meeting. CMS will present the NTAP-related ICD-10-PCS procedure code requests that do not involve the administration of a therapeutic agent and all non-NTAP-related procedure code requests during the virtual meeting on September 10, 2024.

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

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

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

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

1. Email Address

Submit

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

Administration of emapalumab-lzsg**	Pages 11-13
Administration of tarlatamab-dlle**	Pages 14-16

** *Request is for an April 1, 2025 implementation date and the requestor intends to submit a NTAP application for FY 2026 consideration.*

The slide presentations for these procedure code topics are available at: https://www.cms.gov/medicare/coding-billing/icd-10-codes/icd-10-coordination-maintenance-committee-materials.

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

ICD-10 TIMELINE

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

September 10-11, 2024	The September 2024 ICD-10 Coordination and Maintenance Committee Meeting will be held virtually by Zoom Webinar.
September 2024	Recordings and slide presentations of the September 10-11, 2024 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the following web pages: **Diagnosis code portion of the recording and related materials–** https://www.cdc.gov/nchs/icd/icd-10-maintenance/meetings.html **Procedure code portion of the recording and related materials–** https://www.cms.gov/medicare/coding-billing/icd-10-codes/icd-10-coordination-maintenance-committee-materials
October 1, 2024	New and revised ICD-10-CM and ICD-10-PCS codes go into effect along with MS-DRG changes. Final addenda available on web pages as follows: **Diagnosis addendum –** https://www.cdc.gov/nchs/icd/icd-10-cm/files.html **Procedure addendum –** https://www.cms.gov/medicare/coding-billing/icd-10-codes
October 11, 2024	**Deadline for receipt of public comments on proposed new codes discussed at the September 10-11, 2024 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2025.**
November 2024	Any new ICD-10 codes that will be implemented on the following April 1 will be announced. Information on any new codes to be implemented April 1, 2025 will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd-10-cm/files.html https://www.cms.gov/medicare/coding-billing/icd-10-codes/latest-news
November 15, 2024	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the September 10-11, 2024**

	ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2025.
December 6, 2024	**Deadline for requestors: Those members of the public requesting that topics be discussed at the March 18-19, 2025 ICD-10 Coordination and Maintenance Committee Meeting must have their requests submitted to CMS for procedures and to NCHS for diagnoses by this date.** **Procedure code requests should be directed to CMS at:** https://mearis.cms.gov. **Diagnosis code requests should be directed to NCHS at:** nchsicd10cm@cdc.gov. Requestors should indicate if they are submitting their code request for consideration for an October 1, 2025 implementation date, or an April 1, 2026 implementation date. The ICD-10 Coordination and Maintenance Committee will make efforts to accommodate the requested implementation date for each request submitted, however, the Committee will determine which requests will be presented for consideration for an October 1, 2025 implementation date or an April 1, 2026 implementation date.
January 2025	Federal Register notice for the March 18-19, 2025 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
February 2025	Tentative agenda for the Procedure portion of the March 18, 2025 ICD-10 Coordination and Maintenance Committee Meeting posted on CMS webpage at: https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html Tentative agenda for the Diagnosis portion of the March 19, 2025 ICD-10 Coordination and Maintenance Committee Meeting posted on NCHS homepage at: https://www.cdc.gov/nchs/icd/icd-10-maintenance/meetings.html
February 1, 2025	ICD-10 MS-DRG Grouper software and related materials posted on CMS webpage at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/MS-DRG-Classifications-and-Software

February 1, 2025	Any updates to the ICD-10-CM and ICD-10-PCS Coding Guidelines will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd-10-cm/files.html https://www.cms.gov/Medicare/Coding/ICD10/
February 1, 2025	All ICD-10-CM and ICD-10-PCS code update files (includes April 1 update and full files from prior October 1) will be posted on the following websites: https://www.cdc.gov/nchs/icd/icd-10-cm/files.html https://www.cms.gov/Medicare/Coding/ICD10/
March 18-19, 2025	The ICD-10 Coordination and Maintenance Committee Meeting is anticipated to be fully virtual by zoom and dial-in. Those who wish to attend must participate via Zoom Webinar or by dialing in.
March 2025	Recordings and slide presentations of the March 18-19, 2025 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/icd-10-maintenance/meetings.html **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
April 1, 2025	Any new or revised ICD-10 codes will be implemented on April 1, 2025.
April 18, 2025	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 18-19, 2025 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2025**.
April 2025	Notice of Proposed Rulemaking to be published in the Federal Register as mandated by the Omnibus Budget Reconciliation Act of 1986, Public Law 99-509 (Pub. L. 99-509). This notice will include references to the FY 2026 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 16, 2025	**Deadline for receipt of public comments on proposed new codes and revisions discussed at the March 18-19, 2025 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on April 1, 2026.** **Deadline for receipt of public comments on proposed new diagnosis codes and revisions discussed at the March 18-19, 2025 ICD-10 Coordination and Maintenance Committee Meeting being considered for implementation on October 1, 2026**.
May/June 2025	Final addenda posted on web pages as follows: **Diagnosis addendum -** https://www.cdc.gov/nchs/icd/icd-10-cm/files.html **Procedure addendum -** https://www.cms.gov/Medicare/Coding/ICD10/index.html
June 6, 2025	**Deadline for requestors: Those members of the public requesting that topics be discussed at the September 9-10, 2025 ICD-10 Coordination and Maintenance Committee Meeting must have their requests submitted to CMS for procedures and NCHS for diagnoses.** Requestors should indicate if they are submitting their code request for consideration for an April 1, 2026 implementation date or an October 1, 2026 implementation date. The ICD-10 Coordination and Maintenance Committee will make efforts to accommodate the requested implementation date for each request submitted, however, the Committee will determine which requests will be presented for consideration for an April 1, 2026 implementation date or an October 1, 2026 implementation date.
July 2025	Federal Register notice for the September 9-10, 2025 ICD-10 Coordination and Maintenance Committee Meeting will be published. This will include the tentative agenda.
August 1, 2025	Hospital Inpatient Prospective Payment System final rule expected to be published in the Federal Register as mandated by Pub. L. 99-509. This rule will also include links to all the final codes to be implemented on October 1, 2025.

	This rule can be accessed at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/index.html
August 2025	Tentative agenda for the Procedure portion of the September 9, 2025 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 10, 2025 ICD-10 Coordination and Maintenance Committee Meeting will be posted on the NCHS webpage at – https://www.cdc.gov/nchs/icd/icd-10-maintenance/meetings.html
September 9-10, 2025	The September 2025 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 2025	Recordings and slide presentations of the September 9-10, 2025 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/icd-10-maintenance/meetings.html **Procedure code portion of the recording and related materials–** https://www.cms.gov/Medicare/Coding/ICD10/C-and-M-Meeting-Materials.html
October 1, 2025	New and revised ICD-10-CM and ICD-10-PCS codes go into effect along with MS-DRG changes. Final addenda available on web pages as follows: **Diagnosis addendum –** https://www.cdc.gov/nchs/icd/icd-10-cm/files.html **Procedure addendum –** https://www.cms.gov/Medicare/Coding/ICD10/index.html

Introductions and Overview

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

Code Proposals

- ICD-10-PCS code proposals being considered for implementation on April 1, 2025 and October 1, 2025
- No final decisions are made at the meeting
- CMS will describe options and recommendations to facilitate discussion
- Public can comment during the meeting and send written comments

Comments on Code Proposals

- Submit written comments by
  - October 11, 2024 for codes being considered for April 1, 2025 implementation
  - November 15, 2024 for codes being considered for October 1, 2025 implementation
- Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
- Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

Proposed and Final Rules

- April 2024 – Notice of Proposed Rulemaking, IPPS
  - Includes ICD-10-CM/PCS diagnosis and procedure updates approved prior to March 2024 C&M meeting

- August 2024 – Final rule with links to final codes to be implemented October 1, 2024
  - Includes any additional codes approved from March 19-20, 2024 C&M meeting
  - https://www.cms.gov/medicare/payment/prospective-payment-systems/acute-inpatient-pps

Addenda

- June/July 2024 – Final code updates and addendum posted
  - FY 2025 ICD-10-PCS (Procedures)
    https://www.cms.gov/medicare/coding-billing/icd-10-codes
  - FY 2025 ICD-10-CM (Diagnoses)
    https://www.cdc.gov/nchs/icd/icd-10-cm/files.html

Public Participation

- For this virtual meeting, the public may participate in the following ways:
  - Participate via Zoom Webinar
  - Listen to proceedings through free conference lines
  - Listen to recordings and view slide presentations
- CMS & CDC hope this provides greater opportunity for public participation

Written Comments

- No matter how you participate – please send written comments by
  - October 11, 2024 for codes being considered for April 1, 2025 implementation
  - November 15, 2024 for codes being considered for October 1, 2025 implementation
  - Procedure comments to CMS: ICDProcedureCodeRequest@cms.hhs.gov
  - Diagnosis comments to NCHS: nchsicd10cm@cdc.gov

ICD-10-PCS Codes Implementation

- ICD-10-PCS codes under consideration for April 1, 2025 or October 1, 2025 implementation

March 18-19, 2025 C&M Code Requests

- December 6, 2024 – Deadline for submitting topics for March 18-19, 2025 C&M meeting
  - Procedure requests to CMS: https://mearis.cms.gov
  - Diagnosis requests to NCHS: nchsicd10cm@cdc.gov

Topic # 01 – Administration of emapalumab-lzsg

Issue: There are no unique ICD-10-PCS codes to describe the administration of emapalumab-lzsg. An April 1, 2025 implementation date is being requested.

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

Food & Drug Administration (FDA) Approval? Yes. GAMIFANT™ (emapalumab-lzsg) was granted FDA approval on November 20, 2018, for the treatment of hemophagocytic lymphohistiocytosis (HLH) with primary HLH refractory, recurrent, or progressive disease and intolerance with conventional HLH therapy in adult and pediatric patients. The requestor intends to submit a Supplemental Biologics License Application (sBLA) in the second half of 2024, with a new indication of treatment in adult and pediatric patients with known or suspected secondary hemophagocytic lymphohistiocytosis (sHLH)/macrophage activation syndrome (MAS) in known or suspected Still's disease (including systemic juvenile idiopathic arthritis [sJIA] and adult-onset Still's disease [AOSD]) with an inadequate response or intolerance to steroids, or with recurrent MAS.

Background: HLH is a rare, frequently fatal, hyperinflammatory syndrome characterized by pathologic immune dysregulation, resulting in overproduction of proinflammatory cytokines such as IFNγ. MAS, a subtype of sHLH, occurs in the context of rheumatic disease and occurs most frequently as a life-threatening complication of Still's disease (i.e., sJIA and AOSD, both rare, autoinflammatory disorders). According to the requestor, the prevalence of sJIA is expected to be ≤8.6 per 100,000 children and the prevalence of AOSD, the adult form of sJIA, is expected to range between 0.73 to 6.77 per 100,000 adults. Additionally, the occurrence of MAS secondary to Still's disease has been reported to range between 5.0-19.5% of patients with AOSD and to be approximately 10% of patients with sJIA. MAS secondary to auto-immune diseases is generally accepted as a rare disease that affects less than 200,000 people in the United States (U.S.). Life-threatening symptoms of MAS include fever, splenomegaly, cytopenias and multiple organ failure.

Per the requestor, the diagnosis of MAS is often delayed due to the lack of awareness of the characteristic signs and complex pattern of presenting features overlap with other hyperinflammatory conditions. There are no individual laboratory or clinical findings that are unique to sHLH/MAS in Still's disease and no single set of validated criteria for diagnosis. Currently, there are no individual laboratory or clinical findings that are unique to sHLH/MAS in Still's disease and no single set of validated criteria for diagnosis. There are no FDA-approved treatments for MAS in Still's disease; and common options for initial therapy (primarily systemic glucocorticoids) are nonspecific and do not address the hyperinflammation caused by the overexpression of interferon gamma (IFNγ); recommended use is not based on robust clinical evidence. Furthermore, glucocorticoids have a low rate of response and are not recommended for long-term use due to their side effects. Given the life-threatening symptoms of MAS in Still's disease, treatments are more likely to take place in the inpatient setting, including elevated intensive care unit admission, and overall lengthy hospital stays. Affected patients are more likely to experience multiple relapses and recurrence of MAS episodes.

According to the requestor, emapalumab-lzsg can address an unmet treatment need for adult and pediatric patients with known or suspected sHLH/MAS in known or suspected Still's disease (including sJIA and AOSD) with an inadequate response or intolerance to steroids, or with recurrent MAS.

Mechanism of Action
GAMIFANT™ (emapalumab-lzsg) is a fully human IgG1 anti-IFNγ monoclonal antibody that binds free and receptor bound IFNγ, neutralizing its biological activity. Overproduction of IFNγ is present and pathogenic in animal models of MAS. In sJIA/AOSD, high IFNγ activity demonstrated by high serum levels of C-X-C motif chemokine ligand 9 (CXCL9), a chemokine selectively induced by IFNγ, is associated with MAS onset and severity.[1] The role of IFNγ in hyperinflammation can be summarized as the following: (1) patients with MAS have an increased proportion of circulating IFNγ-producing activated T cells, (2) diagnosed patients have increased serum levels of IFNγ-induced products that correlate with disease activity, and (3) the excess of cytokines leads to the signs and symptoms of MAS and adversely affects multiple organs. Overactivation of macrophages and T cells can lead to self-perpetuating, overexpression of multiple proinflammatory cytokines. Thus, T cells stimulate macrophages by releasing IFNγ and macrophages stimulate T cells with IL-18 and IL-12. Per the requestor, results of the completed Phase 2 study demonstrated that IFNγ is an important driver of MAS secondary to sJIA/AOSD and that its neutralization with emapalumab-lzsg leads to remission of MAS in patients who failed high-dose glucocorticoids.[1]

Inpatient Administration of emapalumab-lzsg
For the indication of primary HLH, the recommended starting dose for emapalumab-lzsg is 1mg/kg administered via an intravenous infusion utilizing an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2-micron inline filter, over 1 hour twice per week (every three to four days). For patients diagnosed with known or suspected sHLH/MAS in Still's disease, the recommended starting dose in the completed Phase 2 study was 6mg/kg, followed by 3mg/kg every 3 days for 5 doses, then 3mg/kg twice per week. Based on clinical response, the dose can be increased, or intervals can be shortened to daily infusions. In the completed Phase 2 study, the median treatment duration was 27 days (range, 7-39), with the number of infusions ranging from 3 to 17 per patient. GAMIFANT™ (emapalumab-lzsg) is supplied as a solution in single-dose vials of 10 mg/2 mL, 50 mg/2 mL and 100 mg/2 mL; it must be stored in a refrigerator at 2ºC to 8ºC (36ºF to 46ºF) in the original carton to protect from light.

Per the requestor, adverse events frequently associated with the administration of emapalumab-lzsg were infections and asymptomatic positive viral tests. All infectious events were of viral origin and were mild or moderate in intensity; no bacterial or opportunistic infections were reported. One cytomegalovirus (CMV) reactivation was reported as serious. In total, there were five CMV events (three reactivations, one infection and one positive test with no symptoms). All

[1] De Benedetti, F., Grom, A. A., Brogan, P. A., Bracaglia, C., Pardeo, M., Marucci, G., Eleftheriou, D., Papadopoulou, C., Schulert, G. S., Quartier, P., Antón, J., Laveille, C., Frederiksen, R., Asnaghi, V., Ballabio, M., Jacqmin, P., & de Min, C. (2023). Efficacy and safety of emapalumab in macrophage activation syndrome. *Annals of the rheumatic diseases*, *82*(6), 857–865. https://doi.org/10.1136/ard-2022-223739

viral events resolved spontaneously or with standard treatment. Two mild infusion-related reactions (pruritic rash) occurred during a total of 128 infusions. Additionally, there was an incidence of cardiopulmonary failure and neutropenia, not directly related to use of GAMIFANT™ (emapalumab-lzsg). No instances of death were reported during the trial or in the long-term follow-up.

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

3E033GR Introduction of other therapeutic monoclonal antibody into peripheral vein, percutaneous approach

3E043GR Introduction of other therapeutic monoclonal antibody into central vein, percutaneous approach

Coding Options

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

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

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 D** Emapalumab-lzsg Anti-IFNy Monoclonal Antibody	**A** New Technology Group 10

CMS Recommendation: Option 2, as described above.

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

Topic # 02 – Administration of tarlatamab-dlle

Issue: There are no unique ICD-10-PCS codes to describe the administration of tarlatamab-dlle. An April 1, 2025 implementation date is being requested.

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

Food & Drug Administration (FDA) Approval? Yes. The requestor was granted accelerated Biologics License Application (BLA) approval for tarlatamab-dlle by the FDA on May 16, 2024. IMDELLTRA™ (tarlatamab-dlle) is indicated for the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy. Breakthrough Therapy Designation was granted in October 2023 and priority review was granted on December 12, 2023. The indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). The FDA set a Prescription Drug User Fee Act (PDUFA) date of June 12, 2024.

Background: SCLC is one of the most aggressive and devastating solid tumors, with a median survival of approximately 12 months following initial therapy and a 7% five-year relative survival rate when all stages are combined.[2,3,4,5,6] In 2024, it is estimated that there will be approximately 30,000 to 35,000 new cases of SCLC in the United States.[7] Despite initial high response rates to platinum-based first-line chemotherapy, SCLC patients quickly relapse and require subsequent treatment options.[8] In addition, SCLC has a high rate of molecular alterations and no actionable biomarkers exist currently. Approximately 85% to 96% of SCLC patients have expression of delta-like ligand 3 (DLL3) on the cell surface of SCLC cells, with minimal expression in normal cells.[9,10,11,12]

[2] Amgen Press Release, "FDA approves IMDELLTRA (tarlatamab-dlle), the first and only t-cell engager therapy for the treatment of extensive-stage small cell lung cancer," (May 16, 2024). Available at: https://wwwext.amgen.com/newsroom/press-releases/2024/05/fda-approvesimdelltra-tarlatamabdlle-the-first-and-only-tcell-engager-therapy-for-thetreatment-of-extensivestage-small-cell-lung-cancer. Accessed May 17, 2024.
[3] Amgen Press Release, "FDA grants priority review to Amgen's Tarlatamab application," (December 13, 2023). Available at: https://wwwext.amgen.com/newsroom/press-releases/2023/12/fda-grantspriority-review-to-amgens-tarlatamab-application-for-advanced-small-cell-lungcancer. Accessed June 7, 2024.
[4] Paz-Ares L, et al. ESMO Open. 2022;7:100408.
[5] American Cancer Society. Lung Cancer Survival Rates. 2023. Available at: https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosisstaging/survival-rates.html. Accessed June 7, 2024.
[6] Liu SV, et al. J Clin Oncol. 2021;39:619-630.
[7] American Cancer Society, "Cancer Facts & Figures 2024," (January 14, 2024). Available at: https://www.cancer.org/content/dam/cancerorg/research/cancer-facts-and-statistics/annual-cancer-facts-andfigures/2024/2024-cancer-facts-and-figures-acs.pdf. Accessed June 7, 2024.
[8] Oronsky B, et al. J Cancer. 2022;13:2945-2953.
[9] Giffin MJ, et al. Clin Cancer Res. 2021;27:1526-1537.
[10] Rojo F, et al. Lung Cancer. 2020;147:237-243.
[11] Paz-Ares L, et al. J Clin Oncol. 2023;41:2893-2903.
[12] Ahn M-J, et al. N Engl J Med. 2023;389:2063-2075.

Mechanism of Action
IMDELLTRA™ (tarlatamab-dlle) is a bispecific DLL3-directed CD3 T-cell engager that binds to DLL3 expressed on the surface of cells, including tumor cells, and CD3 expressed on the surface of T cells. Per the requestor, tarlatamab-dlle causes T-cell activation, release of inflammatory cytokines, and lysis of DLL3-expressing cells.

Inpatient Administration of tarlatamab-dlle
In clinical studies, tarlatamab-dlle has been administered in the inpatient setting; however, the requestor stated its clinical profile supports both hospital inpatient and hospital outpatient administration. The treatment is administered by a qualified healthcare provider in an appropriate healthcare setting, via a 1-hour intravenous (IV) infusion through the central or peripheral vein. Appropriate medical support is recommended to manage severe reactions such as cytokine release syndrome (CRS) and neurologic toxicity including immune effector cell-associated neurotoxicity syndrome (ICANS). According to the prescribing information, tarlatamab-dlle is administered in cycles primarily as a standalone procedure. However, there are doses that will require concomitant medications. Cycle 1 consists of a step-up dosing schedule of 1 mg on Day 1 followed by 10 mg on Days 8 and 15. During cycle 1, patients should be monitored for 22 to 24 hours from the start of the first and second infusions (Day 1 and Day 8) in an appropriate healthcare setting, and for 6 to 8 hours after the third infusion (Day 15). Additionally, patients are recommended to remain within a 1-hour distance of an appropriate healthcare setting for a total of 48 hours from the start of the infusion and be accompanied by a caregiver. An inpatient stay could be necessary due to the minimum recommended monitoring time and administration of concomitant medications before and after infusions.

For cycles 2 to 5 and subsequent infusions, the recommended dosing of tarlatamab-dlle is 10 mg every 2 weeks unless there is disease progression or there are unacceptable levels of toxicity. During cycle 2 patients should be monitored for 6-8 hours after infusions. During cycles 3 and 4, patients should be monitored for 3-4 hours after infusions. For cycle 5 and any subsequent infusions, patients should be monitored for 2 hours after infusions. After the step-up dosing schedule, extended monitoring in a healthcare setting is not required unless the patient experiences grade 2 or higher CRS, ICANS, or neurological toxicity during prior treatments. Patients that experience grade 2 or 3 CRS, neurological toxicity or ICANS should be monitored for 22 to 24 hours following the next dose. If a patient experiences grade 2 or higher CRS, hospitalization is recommended. If a patient experiences grade 3 CRS, neurological toxicity including ICANS, monitoring in the intensive care unit is recommended. For grade 4 CRS, neurological toxicity including ICANS, patients must be managed in the intensive care unit. In the occurrence of severe adverse events, tarlatamab-dlle should be withheld or permanently discontinued.

According to the requestor, 58% of patients who received IMDELLTRA™ (tarlatamab-dlle) in clinical studies experienced serious adverse reactions. Serious adverse reactions in >3% of patients included CRS, pneumonia, pyrexia, and hyponatremia. CRS occurred in 55% of patients and 1.6% of treated patients developed grade 3 or 4 CRS. Recurrent CRS occurred in 24% of patients. Neurologic toxicity including ICANS occurred in 47% of patients and ICANS alone occurred in 9%, respectively. Additionally, the most common (≥20%) adverse reactions were CRS, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, and constipation.

The most common (≥2%) grade 3 or 4 laboratory abnormalities were decreased lymphocytes, decreased sodium, increased uric acid, decreased total neutrophils, decreased hemoglobin, increased activated partial thromboplastin time, decreased potassium, increased aspartate aminotransferase, decreased white blood cells, decreased platelets and increased alanine aminotransferase. Permanent discontinuation of tarlatamab-dlle due to an adverse reaction occurred in 7% of patients, with 1.6% of patients permanently discontinuing due to CRS and 1.1% of patients discontinuing due to tumor lysis syndrome. A *boxed warning* for CRS and neurological toxicities with ICANS is included in the prescribing information for IMDELLTRA™ (tarlatamab-dlle).

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

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

Coding Options

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

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

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 C** Tarlatamab-dlle Antineoplastic	**A** New Technology Group 10

CMS Recommendation: Option 2, as described above.

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