CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Tarlatamab-dlle (Imdelltra®)

Version: 1.0

EFFECTIVE DATE: 1/1/2025

NantHealth® | Eviti®

Please note the following:

Tarlatamab-dlle (Imdelltra®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Tarlatamab-dlle (Imdelltra): Discussion

Small cell lung cancer (SCLC) is a heterogeneous disease including extremely chemosensitive and chemoresistant clones. For this reason, a high percentage of patients respond to first-line chemotherapy but rapidly succumb to the disease. SCLC is generally divided into two stages, limited and extensive. Common mutations in SCLC include loss of retinoblastoma 1 (RB1) tumor suppressor gene and TP53(17p13) mutations which decrease the pro-apoptotic activity of cancer cells.[1]

In the United States, there are over 200,000 new cases per year and over 150,000 deaths per year attributed to lung cancer. SCLC comprises about 15% of cases. There is a higher incidence of SCLC in males.[2] In the DeLLphi-301 phase I trial multinational, open-label, dose-escalation study, the primary endpoint was safety, including dose-limiting toxicities. Secondary endpoints included pharmacokinetics (PK), antitumor activity including objective response per modified RECIST 1.1 by investigator assessment, duration of response (DOR), time to response, progression-free survival (PFS), and overall survival (OS). The confirmed overall response rate (ORR) was 23.4% including two complete and 23 partial responses by modified RECIST 1.1 per investigator assessment. The disease control rate was 51.4%. At least 30% tumor shrinkage in target lesions at postbaseline assessment was observed in 39 patients (36.4%). The median time of response was 1.8 months (range, 1.2-7.4), and the DOR was 12.3 months. The longest DOR was 14.9 months, and 11 patients (44% of responders) had an ongoing response at the data cutoff. The median PFS was 3.7 months, and the median OS was 13.2 months, respectively. Out of 77 progressive disease events, eight were in the brain (10.4%).[3]

Between December 2021 and May 2023, a total of 222 patients were enrolled in 56 sites in 17 countries in the DeLLphi-301 phase II trial. The primary endpoint was a confirmed objective response. Secondary endpoints included duration of objective response, disease control, duration of disease control, progression-free survival, overall survival, adverse events during the treatment period, serum concentration of tarlatamab-dlle, and formation of the anti-tarlatamab antibody. An objective response occurred in 40%.[4]

Tarlatamab-dlle works by binding to delta-like ligand 3 (DLL3) on tumor cells and a cluster of differentiation 3 (CD3) on T cells, which triggers T cell-dependent antitumor immunity which is why it's a therapeutic target in SCLC. DLL3 is an inhibitory notch ligand, highly expressed in small cell lung cancer and other neuroendocrine tumors.[5]

Cytokine release syndrome (CRS) is a systemic inflammatory response that can be triggered by a variety of factors such as infections and certain drugs. The incidence of CRS in patients receiving cancer immunotherapy varies widely depending on the type of immunotherapeutic agent. The onset of CRS can occur within a few days, and in the case of CAR-T cell therapy, up to several weeks after the drug infusion.[6]

Immune effector cell associated neurotoxicity syndrome (ICANS) is a potentially life-threatening neurotoxicity. Patients at greater risk for ICANs include those with younger age, pre-existing neurological/medical conditions, high tumor burden, high-intensity lymphodepleting therapy, cytopenia, and early or severe CRS. ICANS can appear in various ways, ranging from mild symptoms like confusion, headaches, attention deficits, and difficulty finding words, to more severe issues such as focal neurological deficits, and encephalopathy. In extreme cases, it can lead to life-threatening conditions like cerebral edema, transient coma, or seizures. Although the precise mechanisms of ICANS are not identified, disruption of the blood-brain barrier, cytokines, myeloid cells, and T cells have all been suggested to be a factor.[7]

Tarlatamab-dlle has several adverse reactions which include CRS, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, constipation, anemia, and nausea. Neurologic toxicities are serious or life-threatening and can be caused by tarlatamab-dlle. Patients receiving tarlatamab-dlle are at risk of neurologic adverse reactions and ICANS resulting in depressed levels of consciousness. The most frequent neurologic toxicities were headache (14%), peripheral neuropathy (7%), dizziness (7%), insomnia (6%), muscular weakness (3.7%), delirium (2.1%), and syncope (1.6%).

Tarlatamab-dlle is approved by the Food and Drug Administration (FDA) for extensive stage small cell lung cancer (ES-SCLC).[8]

The National Comprehensive Cancer Network (NCCN) endorses tarlatamab-dlle for the following cancer types: small cell lung.[9]

Tarlatamab-dlle: Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Risk Evaluation and Mitigation Strategy (REMS) -** A drug safety program that the U.S. FDA can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks. REMS is designed to reinforce medication adherence for safe use. The focus of REMS is on prevention, monitoring, and managing serious risks by informing, educating, and reinforcing actions to reduce the frequency and severity of adverse risks.[10]

Tarlatamab-dlle: Policy

Note: Coverage of tarlatamab-dlle will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Tarlatamab-dlle will be considered for coverage when the following criteria are met:

Small Cell Lung Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Extensive stage disease with progression on or after platinum-based chemotherapy[8]; OR

For **NCCN** required criteria coverage:

4. Single agent as a subsequent systemic therapy for extensive stage disease with disease progression on or after platinum-based chemotherapy with a performance status 0-2 for one of the following:
   a) Relapse following complete or partial response or stable disease with primary treatment
   b) Primary progressive disease.[9]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Tarlatamab-dlle: References

1. Bernhardt EB et al. Small Cell Lung Cancer. https://pubmed.ncbi.nlm.nih.gov/27535400/. Accessed January 15, 2025.
2. Basumallik N. Small Cell Lung Cancer. https://www.ncbi.nlm.nih.gov/books/NBK482458/. Accessed January 15, 2025.
3. Paz-Ares L et al. Tarlatamab, a First-in-Class DLL3-Targeted Bispecific T-Cell Engager, in Recurrent Small-Cell Lung Cancer: An Open-Label, Phase I Study. https://ascopubs.org/doi/10.1200/JCO.22.02823. Accessed January 15, 2025.
4. Ahn M et al. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. https://www.nejm.org/doi/10.1056/NEJMoa2307980. Accessed January 15, 2025.
5. Tang D et al. Tarlatamab: the promising immunotherapy on its way from the lab to the clinic. https://pmc.ncbi.nlm.nih.gov/articles/PMC10326778/. Accessed January 15, 2025.
6. Shimabukuro-Vornhagen A et al. Cytokine release syndrome. https://pubmed.ncbi.nlm.nih.gov/29907163/. Accessed January 15, 2025.

7. Sterner RC et al. Immune effector cell associated neurotoxicity syndrome in chimeric antigen receptor-T cell therapy. https://pubmed.ncbi.nlm.nih.gov/36081506/. Accessed January 15, 2025.
8. Tarlatamab-dlle Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761344s000lbl.pdf. Accessed January 15, 2025.
9. National Comprehensive Cancer Network. Small Cell Lung Cancer. https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed January 15, 2025.
10. Risk Evaluation and Mitigation Strategies (REMS). https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems. Accessed January 15, 2025.

Tarlatamab-dlle: Coding (CPT®, ICD 10, and HCPCS)*

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C34.90	Small cell lung cancer
J9026	Tarlatamab-dlle

Tarlatamab-dlle: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	1/24/2025
6	Revision Changes:	