Medical Drug Clinical Criteria

Subject:	Imjudo (tremelimumab-actl)		
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Overview

This document addresses the use of Imjudo (tremelimumab-actl). Imjudo is a monoclonal antibody that binds to CTLA-4 and blocks the interaction with its ligands CD80 and CD86, releasing CTLA-4 mediated inhibition of T-cell activation.

The FDA approved indication for Imjudo (tremelimumab-actl)

- in combination with durvalumab, for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC)
- in combination with durvalumab and platinum-based chemotherapy for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with no sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

Imjudo is an intravenous infusion as a weight based single dose in combination with durvalumab. Immune-mediated adverse reactions, which may be severe or fatal, can potentially occur with this combination.

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations for the following uses:

- Non-Small Cell Lung Cancer (NCCN 1, 2A)
- Esophageal and Esophagogastric Junction Cancers (NCCN 2A)
- Hepatocellular Carcinoma (NCCN 1)
- Gastric Cancer (NCCN 2A)

Definitions and Measures

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Immune checkpoint inhibitor: A type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. When these proteins are blocked, the "brakes" on the immune system are

released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include programmed death (PD)-1, PD-ligand 1 (PD-L1), and cytotoxic T-lymphocyte–associated antigen (CTLA)-4/B7-1/B7-2.

Programmed death (PD)-1 proteins: PD-1 proteins are found on T-cells and attach to PD ligands (PD-L1) found on normal (and cancer) cells (see immune checkpoint inhibitor above). Normally, this process keeps T-cells from attacking other cells in the body. However, this can also prevent T-cells from attacking cancer cells in the body. Examples of FDA approved anti-PD-1 agents include Keytruda (pembrolizumab), Opdivo (nivolumab), and Libtayo (cemiplimab).

Programmed death ligand (PD-L)-1: The ligands found on normal (and cancer) cells to which the PD-1 proteins attach (see immune checkpoint inhibitor above). Cancer cells can have large amounts of PD-L1 on their surface, which helps them to avoid immune attacks. Examples of FDA approved anti-PD-L1 agents include Bavencio (avelumab), Tecentriq (atezolizumab), and Imfinzi (durvalumab).

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Imjudo (tremelimumab-actl)

Requests for Imjudo (tremelimumab-actl) may be approved if the following criteria are met:

I. Individual has a diagnosis of unresectable hepatocellular carcinoma (uHCC) (Label, NCCN 1); **AND**
   - A. Individual is using in combination with durvalumab (Imfinzi) for initial therapy; **AND**
   - B. Individual has Child-Pugh Class A; **AND**
   - C. Individual has a current ECOG performance status of 0-1; **AND**
   - D. Individual has not received treatment with another anti-PD-1 or anti-PDL1 agent; **AND**
   - E. Individual is ineligible for transplant; **AND**
   - F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.; **AND**
   - G. Individual is using as a one-time, single-administration treatment.

OR

II. Individual has a diagnosis of Non-small cell lung cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
   - A. Individual has recurrent, advanced, or metastatic NSCLC disease with no prior chemotherapy or any other systemic therapy; **AND**
   - B. Individual is using in combination with durvalumab (Imfinzi) and platinum-based chemotherapy; **AND**
   - C. Negative for actionable molecular biomarkers (including but not limited to EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET and ERBB2 (HER2); **AND**
   - D. Individual has not received treatment with another anti-PD-1 or anti-PDL1 agent; **AND**
   - E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

III. Individual has a diagnosis of Esophageal and esophagogastric junction cancers or Gastric cancer (NCCN 2A); **AND**
   - F. Individual is using as neoadjuvant therapy; **AND**
   - G. Individual is using in combination with durvalumab (Imfinzi); **AND**
   - H. Individual has microsatellite instability-high ordeficient mismatch repair (MSI-H ordMMR) tumors.

Requests for Imjudo (tremelimumab-actl) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member

coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J9347	Injection, tremelimumab-actl, 1 mg [Imjudo]

ICD-10 Diagnosis	
C15.3-C15.9	Malignant neoplasm of esophagus
C16.0-C16.9	Malignant neoplasm of stomach
C22.0-C22.9	Malignant neoplasm of liver and intrahepatic bile ducts
C34.00-C34.92	Malignant neoplasm of bronchus and lung

Document History

Revised: 11/15/2024
Document History:

- 11/15/2024 – Annual Review: Update existing criteria to ensure use in uHCC is in those transplant ineligible. Clarify criteria within Esophageal or Gastric cancer to allow use in either those individuals with MSI-H or dMMR mutations. Removed the slash to avoid confusion of requiring both mutations. Coding Reviewed: Added ICD-10-CM: C15.3-C15.9, C16.0-C16.9.
- 11/19/2023 – Annual Review: Add criteria to NSCLC criteria from NCCN regarding biomarkers. Add NCCN 2A criteria for use in Esophageal and esophagogastric junction cancers and Gastric cancer. Coding Reviewed: No changes.
- 12/12/2022 – Select Review: Add new clinical criteria for FDA approved use in metastatic NSCLC in combination with Imfinzi and platinum-based chemotherapy. Coding Reviewed. No changes. Effective 4/1/2023 Added HCPCS C9147. Effective 7/1/2023 Added HCPCS J9347. Deleted HCPCS J3590, J3490, J9999, C9147. Added ICD-10-CM C22.0-C22.9, C34.00-C34.92.
- 11/18/2022 – Select Review: Add new clinical criteria document for Imjudo (tremelimumab-actl). Coding reviewed: Added HCPCS J9999, J3590, J3490. Added ICD-10-CM All diagnosis pend.

References

1. Abou-Alfa GK, Lau G, Kudo M, et al. Tremelimumab plus Durvalumab in Unresectable Hepatocellular Carcinoma. [published online ahead of print, 2022 June 6]. NEJM. Available at: https://evidence.nejm.org/doi/full/10.1056/EVIDoa2100070
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 29, 2024.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. NCT03298451. ClinicalTrials.gov. U.S. National Library of Medicine. Available: https://www.clinicaltrials.gov/ct2/show/NCT03298451.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on September 29, 2024.
    a. Esophageal and Esophagogastric Junction Cancers. V4.2024. Revised July 30, 2024.
    b. Gastric Cancer. V4.2024. Revised August 12, 2024.
    c. Hepatocellular Cancer. V3.2024. Revised September 24, 2024.
    d. Non-Small Cell Lung Cancer. V10.2024. Revised September 23, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.