Imjudo® (tremelimumab-actl)
(Intravenous)

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I. Length of Authorization Δ [1,7,8]

- Gastric, Esophageal, and Esophagogastric Junction Cancers: Coverage will be provided for one (1) dose only and may NOT be renewed.
- Hepatocellular Carcinoma (HCC): Coverage will be provided for one (1) dose only and may NOT be renewed.
- Non-Small Cell Lung Cancer (NSCLC): Coverage will be provided for up to a maximum of 16 weeks of therapy (5 doses) and may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Imjudo 25 mg/1.25 mL (20 mg/mL) solution for injection: 3 vials every 21 days x 4 doses, then 3 vials on day 112
- Imjudo 300 mg/15 mL (20 mg/mL) solution for injection: 1 vial once

B. Max Units (per dose and over time) [HCPCS Unit]:

- HCC, Gastric Cancer, and Esophageal and Esophagogastric Junction Cancers: 300 billable units (300 mg) one time only
- NSCLC: 75 billable units (75 mg) every 21 days x 4 doses, followed by 75 billable units (75 mg) x 1 dose on day 112

III. Initial Approval Criteria [1]

Coverage is provided under the following conditions:

- Patient is at least 18 years of age; **AND**

Hepatocellular Carcinoma (HCC) † ‡ Φ [1-5]

- Used as first-line therapy in combination with durvalumab; **AND**
  - Patient has unresectable disease **†**; **OR**
  - Patient has extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,2,6,9]

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used as first-line therapy; **AND**
    - Used for one of the following:
      - Patients with tumors that are negative for actionable molecular biomarkers***¥** and PD-L1 ≥ 1% to 49%
      - Patients with a performance status (PS) of 0-1 who have tumors that are negative for actionable molecular biomarkers***¥** and PD-L1 < 1%
      - Patients with PS of 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2); **AND**
        - Used in combination with durvalumab, albumin-bound paclitaxel, and carboplatin; **OR**
        - Used in combination with durvalumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology; **OR**
        - Used in combination with durvalumab, gemcitabine, and either carboplatin or cisplatin for squamous cell histology; **OR**
  - Used as subsequent therapy; **AND**
    - Used for one of the following:
      - Patients with PS of 0-1 who are positive for one of the following molecular biomarkers: BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, or RET rearrangement
      - Patients with PS of 0-1 who are positive for one of the following molecular biomarkers AND received prior targeted therapy**§**: EGFR exon 19 deletion or exon 21 L858R tumors, EGFR S768I, L861Q, and/or G719X mutation, ALK rearrangement, or ROS1 rearrangement; **AND**
        - Used in combination with durvalumab, albumin-bound paclitaxel, and carboplatin; **OR**
        - Used in combination with durvalumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology; **OR**
        - Used in combination with durvalumab, gemcitabine, and either carboplatin or cisplatin for squamous cell histology

***Note:** Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*
¥ *May also be used for patients with KRAS G12C mutation positive tumors*

Esophageal and Esophagogastric Junction Cancers ‡ [2,7]

- Used as neoadjuvant therapy in combination with durvalumab; **AND**
- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Patient has adenocarcinoma; **AND**
- Used as primary treatment for patients who are medically fit for surgery with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease

Gastric Cancer ‡ [2,8]

- Used as neoadjuvant therapy in combination with durvalumab; **AND**
- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Patient has adenocarcinoma; **AND**
- Used as primary treatment for potentially resectable locoregional disease (cT2 or higher, any N) in patients who are medically fit for surgery

❖ *If confirmed using an FDA approved assay – http://www.fda.gov/CompanionDiagnostic*

§ Genomic Aberration/Mutational Driver Targeted Therapies [9] (Note: *not all inclusive, refer to guidelines for appropriate use*)			
EGFR exon 19 deletion or exon 21 L858R tumors	*EGFR* S768I, L861Q, and/or G719X mutation positive tumors	*EGFR* exon 20 insertion mutation positive tumors	*NTRK1/2/3* gene fusion positive tumors
– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Amivantamab	– Larotrectinib – Entrectinib – Repotrectinib
ALK rearrangement-positive tumors	*ROS1* rearrangement-positive tumors	*BRAF* V600E-mutation positive tumors	*ERBB2 (HER2)* mutation positive tumors
– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib – Lorlatinib – Repotrectinib	– Dabrafenib ± trametinib – Encorafenib + binimetinib – Vemurafenib	– Fam-trastuzumab deruxtecan-nxki – Ado-trastuzumab emtansine
PD-L1 tumor expression ≥ 1%	*MET* exon-14 skipping mutations	*RET* rearrangement-positive tumors	*KRAS G12C* mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria Δ [1,7,8]

- Coverage may NOT be renewed.

Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration are eligible to re-initiate checkpoint inhibitor therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy without interruption or discontinuation.
- Patients who complete adjuvant therapy and progress ≥ 6 months after discontinuation are eligible to re-initiate checkpoint inhibitor therapy for metastatic disease.
- Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate checkpoint inhibitor therapy and will be evaluated on a case-by-case basis.

V. Dosage/Administration Δ [1,7,8]

Indication	Dose
Hepatocellular Carcinoma (HCC)	Weight ≥30 kg: – Administer a single dose of tremelimumab 300 mg intravenously (followed by durvalumab) at Day 1-Cycle 1 – Continue durvalumab as a single agent every 4 weeks Weight <30 kg: – Administer a single dose of tremelimumab 4 mg/kg intravenously (followed by durvalumab) at Day 1-Cycle 1 – Continue durvalumab as a single agent every 4 weeks
Non-Small Cell Lung Cancer (NSCLC)	Weight ≥30 kg: – Administer tremelimumab 75 mg intravenously on Day 1 of every 3 week-cycle x 4 cycles (Cycles 1-4) in combination with durvalumab followed by platinum-based chemotherapy – Administer tremelimumab 75 mg x 1 dose on Day 1 of a 4-week cycle (Cycle 6; Week 16) in combination with durvalumab *(Note: the dosing interval changes from every 3 weeks to every 4 weeks starting at cycle 5)* – Continue durvalumab every 4 weeks with or without platinum-based chemotherapy**§** Weight <30 kg: – Administer tremelimumab 1 mg/kg intravenously on Day 1 of every 3 week-cycle x 4 cycles (Cycles 1-4) in combination with durvalumab followed by platinum-based chemotherapy – Administer tremelimumab 1 mg/kg x 1 dose on Day 1 of a 4 week-cycle (Cycle 6; Week 16) in combination with durvalumab *(Note: the dosing interval changes from every 3 weeks to every 4 weeks starting at cycle 5)* – Continue durvalumab every 4 weeks with or without platinum-based chemotherapy**§**
Gastric, Esophageal, and Esophagogastric Junction Cancers	Administer tremelimumab 300 mg intravenously x 1 dose on Day 1 of a 12-week cycle in combination with durvalumab
• Administer tremelimumab prior to durvalumab on the same day.	

- Refer to the Prescribing Information for durvalumab dosing information

§ If patients receive fewer than 4 cycles of platinum-based chemotherapy, the remaining cycles of tremelimumab (up to a total of 5) should be given after the platinum-based chemotherapy phase, in combination with durvalumab, every 4 weeks. Optional pemetrexed therapy from week 12 until disease progression or intolerable toxicity for patients with non-squamous disease who received treatment with pemetrexed and carboplatin/cisplatin.

VI. Billing Code/Availability Information

HCPCS Code:

- J9347 – Injection, tremelimumab-actl, 1 mg; 1 billable unit = 1 mg

NDC(s):

- Imjudo 25 mg/1.25 mL solution for injection (single-dose vial): 00310-4505-xx
- Imjudo 300 mg/15 mL solution for injection (single-dose vial): 00310-4535-xx

VII. References

1. Imjudo [package insert]. Wilmington, DE; AstraZeneca Pharm.; July 2024. Accessed August 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) tremelimumab. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2024.
3. Abou-Alfa GK, Lam Chan S, Furuse J, et al. A randomized, multicenter phase 3 study of durvalumab (D) and tremelimumab (T) as first-line treatment in patients with unresectable hepatocellular carcinoma (HCC): HIMALAYA study. Journal of Clinical Oncology 36, no. 15_suppl. DOI: 10.1200/JCO.2018.36.15_suppl.TPS4144
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hepatocellular Carcinoma. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2024.
5. Llovet JM, Bru C, Bruix J. Prognosis of hepatocellular carcinoma: the BCLC staging classification. *Semin Liver Dis.* 1999;19:329–38.
6. Johnson ML, Cho BC, Luft A, et al; POSEIDON investigators. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. J Clin Oncol. 2022 Nov 3:JCO2200975. doi: 10.1200/JCO.22.00975.
7. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Esophageal and Esophagogastric Junction Cancers. Version 4.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN

Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2024.

8. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Gastric Cancer. Version 4.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed September 2024.
9. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Non-Small Cell Lung Cancer. Version 9.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed September 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus

ICD-10	ICD-10 Description
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC