Imjudo® (tremelimumab-actl)
(Intravenous)

Document Number: EOCCO-0683

Last Review Date: 03/02/2023
Date of Origin: 12/01/2022
Dates Reviewed: 12/2022, 03/2023

I. Length of Authorization Δ [1]

- Hepatocellular Carcinoma (HCC): Coverage will be provided for one dose only and may not be renewed.
- Non-Small Cell Lung Cancer (NSCLC): Coverage will be provided for five doses only 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: 300 mg one time only
- NSCLC: 75 mg x 4 doses every 21 days, followed by 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 does not have clinically meaningful ascites requiring non-pharmacologic intervention within 6 months; **AND**
- Patient does not have main portal vein tumor thrombosis; **AND**
- Patient does not have active or recent prior history of a gastrointestinal bleed (e.g., esophageal varices, bleeding ulcer, etc.); **AND**
  - Patient has unresectable disease and is not a transplant candidate; **OR**

- Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; **OR**
- Patient has metastatic disease or extensive liver tumor burden

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

- Patient has recurrent, advanced, or metastatic disease; **AND**
  - Used as first-line therapy; **AND**
    - Used in one of the following:
      - Patients with tumors that are negative for actionable molecular biomarkers* and PD-L1 ≥ 1% to 49%
      - Patients with 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 mutations: EGFR exon 20, KRAS G12C, 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 in one of the following:
      - Patients with PS of 0-1 who are positive for one of the following molecular mutations: 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 mutations 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 exon 14 skipping mutation, RET rearrangement, and ERBB2 (HER2). If there is insufficient issue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2) repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

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

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

IV. Renewal Criteria [Δ 1]

- Coverage may NOT be renewed.

Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration (i.e., receipt of 24 months of PD-directed therapy) are eligible to re-initiate checkpoint inhibitor therapy.
- 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

Indication	Dose
Hepatocellular Carcinoma (HCC)	**STRIDE (Single Tremelimumab Regular Interval Durvalumab)** Weight ≥30 kg: – Administer a single dose of Imjudo[1] 300 mg intravenously followed by durvalumab[2] 1,500 mg at Day 1-Cycle 1 – Continue durvalumab 1,500 mg as a single agent every 4 weeks Weight <30 kg: – Administer a single dose of Imjudo[1] 4 mg/kg intravenously followed by durvalumab[2] 20 mg/kg at Day 1-Cycle 1 – Continue durvalumab[2] 20 mg/kg as a single agent every 4 weeks
Non-Small Cell Lung Cancer (NSCLC)	**In combination with Durvalumab and Platinum-Based Chemotherapy** Weight ≥30 kg: – Administer Imjudo 75 mg intravenously on Day 1 of every 3 week-cycle x 4 cycles (Cycles 1-4) in combination with durvalumab[2] followed by platinum-containing chemotherapy – Administer Imjudo 75 mg x 1 dose on Day 1 of a 4-week cycle (Cycle 6; Week 16) in combination with durvalumab[2] *(Note: the dosing interval changes from every 3 weeks to every 4 weeks starting at cycle 5)* – Continue durvalumab[2] every 4 weeks with or without platinum-based chemotherapy**§** Weight <30 kg : – Administer Imjudo 1 mg/kg intravenously on Day 1 of every 3 week-cycle x 4 cycles (Cycles 1-4) in combination with durvalumab[2] followed by platinum-containing chemotherapy – Administer Imjudo 1 mg/kg x 1 dose on Day 1 of a 4 week-cycle (Cycle 6; Week 16) in combination with durvalumab[2] *(Note: the dosing interval changes from every 3 weeks to every 4 weeks starting at cycle 5)* – Continue durvalumab[2] every 4 weeks with or without platinum-based chemotherapy**§**
1 Administer IMJUDO prior to durvalumab on the same day. *2 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-actl (up to a total of 5) should be given after the platinum-based chemotherapy phase, in combination with IMFINZI, 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:

- J9999 – Not otherwise classified, antineoplastic drugs
- C9399 – Unclassified drugs or biologicals (for hospital outpatient use ONLY)

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.; November 2022. Accessed February 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) tremelimumab. National Comprehensive Cancer Network, 2023. 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 February 2023.
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®) Hepatobiliary Cancers. Version 5.2022. National Comprehensive Cancer Network, 2023. 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 February 2023.
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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung

ICD-10	ICD-10 Description
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
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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)
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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC