STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Imjudo (tremelimumab-actl)
PAM-058

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	04/01/2023
Revision Number:	2	**Last Rev Date:**	01/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	01/17/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/21/2023

Overview

Medication:[1]	tremelimumab-actl
Brand Name:	Imjudo®
Pharmacologic Category:	Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) blocking antibody
FDA-Approved Indication(s):	• **Unresectable hepatocellular carcinoma (uHCC):** Indicated in combination with durvalumab (Imfinzi®), for the treatment of adult patients with uHCC. • **Metastatic non-small cell lung cancer (mNSCLC):** Indicated in combination with Imfinzi® and platinum-based chemotherapy for the treatment of adult patients with mNSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
How Supplied:	Single-dose vial (containing 20 mg/mL) as either: 25 mg/1.25 mL or 300 mg/15 mL
Administration:	Administer via intravenous (IV) infusion; follow dosing schedule in below tables.
Benefit Category:	Medical

uHCC	**Recommended Dosage & Regimen**
	Patients with a body weight of 30 kg and more: • A **single dose** of Imjudo® 300 mg followed by durvalumab (Imfinzi®)1,500 mg at Day 1 of Cycle 1; • Continue durvalumab (Imfinzi®) 1,500 mg as a single agent every 4 weeks. Patients with a body weight of less than 30 kg: • A **single dose** of Imjudo® 4 mg/kg followed by durvalumab (Imfinzi®) 20 mg/kg at Day 1 of Cycle 1; • Continue durvalumab (Imfinzi®) 20 mg/kg as a single agent every 4 weeks.
	Duration of Therapy
	After Cycle 1 of combination therapy, administer durvalumab (Imfinzi®) as a single agent every 4 weeks until disease progression or unacceptable toxicity.

NSCLC: Recommended Regimen and Dosage (see next table for dosing schedule)				
Tumor Histology	**Patient Weight**	**Imjudo® Dosage**	**Imfinzi® Dosage** [a]	**Platinum-based chemotherapy regimen** [a]
Non-Squamous	≥ 30 kg	75 mg	1,500 mg	• carboplatin & nabpaclitaxel (Abraxane®) OR • carboplatin or cisplatin & pemetrexed (Alimta®)
	< 30 kg	1 mg/kg	20 mg/kg	
Squamous	≥ 30 kg	75 mg	1,500 mg	• carboplatin & nabpaclitaxel (Abraxane®) OR • carboplatin or cisplatin & gemcitabine
	< 30 kg	1 mg/kg	20 mg/kg	

[a] Refer to prescribing information for dosing information.

NSCLC: Recommended Dosage Schedule																									
Week [b, c]	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Cycle:	1			2			3			4			5				6				7				8
Imjudo [d]	X			X			X			X							X								
Imfinzi [b]	X			X			X			X			X				X				X				X
Chemotherapy	X			X			X			X			X[e]				X[e]				X[e]				X[e]

[b] Continue Imfinzi until disease progression.
[c] Dosing interval change from every 3 weeks to every 4 weeks starting at cycle 5.
[d] If patients receive fewer than 4 cycles of platinum-based chemotherapy, the remaining cycles of IMJUDO (up to a total of 5) should be given after the platinum-based chemotherapy phase, in combination with durvalumab, every 4 weeks.
[e] 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.

Descriptive Narrative

Hepatobiliary cancers are highly lethal cancers including a spectrum of invasive carcinomas arising in the liver (hepatocellular carcinoma; HCC), gall bladder, and bile ducts (intrahepatic and extrahepatic cholangiocarcinoma [CCA]). Gallbladder cancer and CCAs are collectively known as biliary tract cancers. In 2022, it was estimated that 41,260 people in the United States would be diagnosed with liver cancer and intrahepatic bile duct cancer and an additional 12,130 people would be diagnosed with gallbladder cancer or other biliary tract cancer. Approximately 30,520 deaths from liver or intrahepatic bile duct cancer, and 4,400 deaths due to gallbladder cancer or other biliary tract cancer were anticipated.[2]

Lung cancer is the leading cause of cancer death in the United States. In 2023, an estimated 238,340 new cases (117,550 in males and 120,790 in females) of lung and bronchial cancer will be diagnosed, and 127,070 deaths (67,160 in males and 59,910 in females) are estimated to occur because of the disease. During the COVID pandemic, the diagnosis and treatment of lung cancer have been hampered; however, this has not been reflected in the 2023 estimates for incidence and mortality because of the typical delays in collecting and reporting the data. Only 22.9% of all patients with lung cancer are alive 5 years or more after diagnosis; this includes patients with non-small cell lung cancer (NSCLC) and those with small cell lung cancer (SCLC). From 2012 to 2018, the overall 5-year relative survival rate for NSCLC with adenocarcinoma histology was 29.8% in the United States. Since 2006 to 2007, the incidence of lung cancer decreased annually by 2.6% in men and 1.1% in women.

Much progress has been made recently for lung cancer, such as screening; minimally invasive techniques for diagnosis and treatment; advances in radiation therapy (RT), including stereotactic ablative radiotherapy (SABR); new targeted therapies; and new immunotherapies. These new treatments are reflected in the improved survival rates for patients with NSCLC. From 2015 to 2016, 2-year relative survival for NSCLC was 42% compared with 34% from 2009 to 2010. From 1990 to 2020, the death rate from lung cancer dropped by 58% in men; from 2002 to 2020, the death rate dropped by 36% in women. Patients with NSCLC who are eligible for targeted therapies or immunotherapies are now surviving longer; 5-year survival rates range from 15% to 50%, depending on the biomarker. Thus, death rates for lung cancer have been declining, although there are still more deaths from lung cancer than from breast, prostate, colorectal, and brain cancers combined.[3]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[4]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Hepatocellular Carcinoma (Version 2.2023 – September 14, 2023)[5]
- NCCN Guidelines® for Non-Small Cell Lung Cancer (Version 5.2023 – November 8, 2023)[6]

Recommendation(s) for tremelimumab-actl (Imjudo®) in hepatocellular carcinoma
(1) First-line systemic therapy A. Imjudo® + Imfinzi®: Category 1, preferred regimen

Recommendation(s) for tremelimumab-actl (Imjudo®) in non-small cell lung cancer (NSCLC)
(I) Molecular and biomarker-directed therapy for advanced or metastatic disease A. First-line therapy: PD-L1 ≥ 50% i. Adenocarcinoma, large cell, NSCLC NOS 1. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 2B, other recommended 2. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + pemetrexed: Category 2B, other recommended ii. Squamous cell carcinoma 1. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 2B, other recommended 2. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + gemcitabine: Category 2B, other recommended B. First-line therapy: PD-L1 ≥ 1 % - 49 % i. Adenocarcinoma, large cell, NSCLC NOS 1. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 1, other recommended 2. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + pemetrexed: Category 1, other recommended ii. Squamous cell carcinoma 1. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 2A, other recommended 2. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + gemcitabine: Category 2A, other recommended (II) Systemic therapy for advanced or metastatic disease A. Adenocarcinoma, large cell, NSCLC NOS (PS 0–1) & no contraindications to PD-1 or PD-L1 inhibitors [a] a. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 2A, other recommended [b] b. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + pemetrexed: Category 2A, other recommended [b] B. Squamous cell carcinoma (PS 0–1) & no contraindications to PD-1 or PD-L1 inhibitors a. Imjudo® + Imfinzi® + carboplatin + albumin-bound paclitaxel: Category 2A, other recommended [b] b. Imjudo® + Imfinzi® + (carboplatin or cisplatin) + gemcitabine: Category 2A, other recommended [b] a Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (i.e., *EGFR exon 19* deletion or *L858R*, *ALK* rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors. b If progression on PD-1/PD-L1 inhibitor, using a PD-1/PD-L1 inhibitor is not recommended.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[7]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
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, e.g., 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.

Criteria

Prior authorization is required.

Unresectable Hepatocellular Carcinoma

Imjudo® is considered medically necessary when **ALL** of the following are met:

1. Confirmed diagnosis of unresectable hepatocellular carcinoma (uHCC); **AND**
2. Member is 18 years of age or older; **AND**
3. Member has not received prior immune-mediated therapy (excluding anticancer vaccines); **AND**
4. Member has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Request meets one of the following (a or b):
    a. Imjudo® is prescribed as a one-time, single-administration treatment in combination with durvalumab (Imfinzi®) (reference recommended regimen in Overview section); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in the NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen prescribed does not align with FDA-approved labeling.

Imjudo® is **NOT** considered medically necessary for continuation of therapy, as FDA-approval and NCCN recommendations support a one-time dose for uHCC.

Non-Small Cell Lung Cancer

Imjudo® is considered medically necessary when **ALL** of the following are met:

1. Confirmed diagnosis of metastatic non-small cell lung cancer (mNSCLC); **AND**
2. Tumors do **NOT** have sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations; **AND**
3. Member is 18 years of age or older; **AND**
4. Member has not received prior immune-mediated therapy (excluding anticancer vaccines); **AND**
5. Member has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
6. Prescribed by, or in consultation with, an oncologist; **AND**
7. Request meets one of the following (a or b):
    a. Imjudo® is prescribed for up to a total of 5 doses [one dose every 3 weeks in combination with durvalumab (Imfinzi®) and platinum-based chemotherapy for 4 cycles, and a fifth dose of Imjudo® in combination with Imfinzi® (dose 6) at week 16]. See overview section for dosing recommendations; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in the NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen prescribed does not align with FDA-approved labeling.

Imjudo® is considered medically necessary for continuation of therapy (mNSCLC) when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Member has received less than 5 total doses of Imjudo®. If all other continuation criteria are met, may authorize number of doses sufficient to complete total of 5 doses.
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in the NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

- Unresectable hepatocellular carcinoma (uHCC)

	Authorization Duration	Quantity Limits
Initial	30 days	one-time dose, not to exceed 4 mg/kg for body weight less than 30 kg, or 300 mg for body weight of 30 kg or more
Continuation	Not applicable	Not applicable

- Metastatic non-small cell lung cancer (mNSCLC)*

	Authorization Duration	Quantity Limits
Initial	6 months	Not to exceed total of 5 doses (dosing in Overview section)
Continuation	duration necessary to complete total of 5 doses	

* mNSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
~~C9147~~	~~Injection, tremelimumab-actl, 1 mg~~ *(code effective 4-1-2023 to 6-30-2023)*
J9347	Injection, tremelimumab-actl, 1 mg *(code effective 7-1-2023)*

ICD-10	Description
C22.0	Liver cell carcinoma
C34.00 – C34.92	Malignant neoplasm of bronchus and lung

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
00310-4505-25 (25 mg/1.25 mL)	AstraZeneca Pharmaceuticals LP	1 mg	1	EA	25
00310-4535-30 (300 mg/15 mL)	AstraZeneca Pharmaceuticals LP	1 mg	1	EA	300

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Imjudo prescribing information (06/2023). AstraZeneca Pharmaceuticals LP: Wilmington, DE. Available online at www.imfinzihcp.com. Accessed December 12, 2023.

[2] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatocellular Carcinoma (v.2.2023 – September 14, 2023). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[3] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer (v.5.2023 – November 8, 2023). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[4] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed January 19, 2023.

[5] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatocellular Carcinoma (v.2.2023 – September 14, 2023). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer (v.5.2023 – November 8, 2023). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

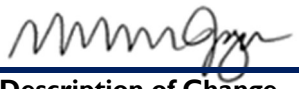
[7] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

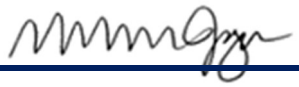
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Changed from July to January review cycle (to align with Imfinzi®). Reviewed NCCN Guidelines; no changes to recommendations. Minor formatting changes.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee