Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Tremelimumab-actl (Imjudo®)	MP-RX-FP-150-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Tremelimumab-actl (Imjudo®),* a cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) blocking antibody, approved by the Food and Drug Administration (FDA) for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC) in combination with durvalumab and 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 in combination with durvalumab and platinum-based chemotherapy.

Background Information

Tremelimumab-actl 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 approved by the FDA in combination with durvalumab, for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC) and 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.

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

Policy Name	Policy Number	Scope
Tremelimumab-actl (Imjudo®)	MP-RX-FP-150-24	☒ MMM MA ☒ MMM Multihealth

- 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).

Approved Indications

A. In combination with durvalumab, for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC).
B. 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.

Other Uses

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

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

Policy Name	Policy Number	Scope
Tremelimumab-actl (Imjudo®)	MP-RX-FP-150-24	☒ MMM MA ☒ MMM Multihealth

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

ICD-10	Description
C22.0-C22.9	Malignant neoplasm of liver and intrahepatic bile ducts
C34.00-C34.92	Malignant neoplasm of bronchus and lung

Medical Necessity Guidelines

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.

Tremelimumab-actl (Imjudo®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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 not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.; **AND**
   - F. 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**

Policy Name	Policy Number	Scope
Tremelimumab-actl (Imjudo®)	MP-RX-FP-150-24	☒ MMM MA ☒ MMM Multihealth

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
   A. Individual is using as neoadjuvant therapy; **AND**
   B. Individual is using in combination with durvalumab (Imfinzi); **AND**
   C. Individual has microsatellite instability-high/deficient mismatch repair (MSI-H/dMMR) tumors.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Tremelimumab-actl (Imjudo®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:
   A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
   B. A current oncology note documenting the patient's response to treatment showing no evidence of intolerable toxicity.
   C. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Imjudo (tremelimumab-actl) may not be approved when the above criteria (section A: Criteria for Initial Approval) are not met and for all other indications.

Policy Name	Policy Number	Scope
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Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Tremelimumab-actl (Imjudo®) 25 mg/1.25 mL (20 mg/mL) SDV; 300 mg/15 mL (20 mg/mL) SDV

Imjudo in combination with Durvalumab		
Indication	**Recommended Dosage**	**Duration of Therapy**
uHCC	Patients with a body weight of 30 kg and more: • A single dose of IMJUDO1 300 mg followed by durvalumab2 1,500 mg at Day 1 of Cycle 1; • Continue durvalumab 1,500 mg as a single agent every 4 weeks Patients with a body weight of less than 30 kg: • A single dose of IMJUDO1 4 mg/kg followed by durvalumab2 20 mg/kg at Day 1 of Cycle 1; • Continue durvalumab 20 mg/kg as a single agent every 4 weeks	After Cycle 1 of combination therapy, administer durvalumab as a single agent every 4 weeks until disease progression or unacceptable toxicity
Exceptions		
• Treatment regimen should be withheld for severe (Grade 3) immune-mediated adverse reactions. • Permanently discontinue treatment regimen for life threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids.		

Policy Name	Policy Number	Scope
Tremelimumab-actl (Imjudo®)	MP-RX-FP-150-24	☒ MMM MA ☒ MMM Multihealth

Imjudo in combination with Durvalumab and Platinum-Based Chemotherapy for NSCLC

Recommended Dosage Schedule

	Week[1,2]																							
	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[3,4]	X			X			X			X							X								
Durvalumab[1,3]	X			X			X			X			X				X				X				X
Chemotherapy	X			X			X			X			X[5]				X[5]				X[5]				X[5]

Recommended Regimen and Dosage

Tumor Histology	Patient Weight	Imjudo Dosage	Durvalumab Dosage	Platinum-based Chemotherapy regimen
Non-Squamous	≥ 30 kg	75 mg	1,500 mg	• carboplatin & nabpaclitaxel OR • carboplatin or cisplatin & **pemetrexed**
	< 30 kg	1 mg/kg	20 mg/kg	
Squamous	≥ 30 kg	75 mg	1,500 mg	• carboplatin & nabpaclitaxel OR • carboplatin or cisplatin & **gemcitabine**
	< 30 kg	1 mg/kg	20 mg/kg	

Exceptions

- Calculate the appropriate dose based on the patient's weight and tumor histology.
- Dosing intervals change from every 3 weeks to every 4 weeks starting at cycle 5.
- 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 4weeks.
- 5 optional pemetrexed therapy from week 12 until disease progression or intolerable toxicity for patients with nonsquamous disease who received treatment with pemetrexed and carboplatin/cisplatin.
- Treatment regimen should be withheld for severe (Grade 3) immune-mediated adverse reactions.
- Permanently discontinue treatment regimen for life threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids.

Policy Name	Policy Number	Scope
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Reference Information

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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, 2023.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; 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™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on September 29, 2023.
    a. Esophageal and Esophagogastric Junction Cancers. V3.2023. Revised August 29, 2023.
    b. Gastric Cancer. V2.2023. Revised August 29, 2023.
    c. Hepatocellular Cancer. V2.2023. Revised September 14, 2023.
    d. Non-Small Cell Lung Cancer. V3.2023. Revised April 13, 2023.

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.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/20/2024	Added dosage form and strenght to quantity limit table. Minor wording and formatting changes. Coding reciewed: no changes.	3/20/2025	4/2/2025
Policy Inception 01/26/2024	New Medical Policy creation	4/18/2024	6/28/2024