Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ 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 Imfinzi® (durvalumab) approved by the Food and Drug Administration (FDA) for the treatment of certain patients with non-small cell lung cancer (NSCLC), extensive-stage small cell lung cancer (ES-SCLC), biliary tract cancer (BTC), and hepatocellular carcinoma.

Background Information

Imfinzi (durvalumab) is a programmed death-ligand 1 (PD-L1) blocking antibody.

The FDA approved indications for Imfinzi include:

- for the treatment of adult patients with unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy
- in combination with etoposide and either carboplatin or cisplatin, as first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)
- in combination with gemcitabine and cisplatin, as treatment of adults with locally advanced or metastatic biliary tract cancer (BTC)
- in combination with tremelimumab-actl (Imjudo) for the treatment of adults with unresectable hepatocellular carcinoma
- in combination with tremelimumab-actl (Imjudo) and platinum-based chemotherapy, for the treatment of adults with metastatic NSCLC, with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

The National Comprehensive Cancer Network (NCCN) provides category 1 and 2A recommendations for use in NSCLC, SCLC, and biliary tract cancer also.

NCCN also provides a 2A recommendation for use in persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) in combination with etoposide and a platinum-based chemotherapy. This recommendation cites data which is extrapolated from the studies for the use in extensive stage small cell lung cancer (Horn L, et al 2018, Luis Paz-Ares, et.al. CASPIAN 2019). Though the recommendation provides use to second-line or subsequent therapy, these studies only discuss first-line therapy.

Definitions and Measures

- Consolidation therapy: Any drug or medical treatment that is used to kill remaining cancer cells. Also called intensification therapy or post-remission therapy.

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

- 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
- Extensive-stage small cell lung cancer: Cancer has spread to other parts of the body, and could include the fluid around the lungs.
- 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.
- Limited-stage small cell lung cancer: Cancer is confined to 1 part of the chest, and radiation therapy could be an option.
- Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- 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

See background section above.

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

Other Uses

The NCCN panel provides 2A recommendations for use in Stage II NSCLC. The panel noted that a few patients in the PACIFIC trial were Stage II (Antonia SJ et al. 2018; Gray JE et.al 2020; Hui R, et.al. 2019). However, no additional trial data or studies are available to support use in this population.

NCCN provides category 2A and 2B recommendations for use of Imfinzi in several types of bladder cancer. However, their Bladder Cancer guidelines have not been updated since the manufacturer's decision in 2/2021 to withdraw this indication from the FDA label due to Imfinzi's inability to meet the overall survival primary outcome measures in the phase 3 DANUBE confirmatory trials (Powles 2020). The FDA had granted Imfinzi with its bladder cancer indication through the accelerated approval program in 2017, with continued approval contingent upon verification of clinical benefit in confirmatory trials. In the current NCCN compendia, NCCN no longer provides these bladder cancer recommendations.

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
J9173	Injection, durvalumab, 10 mg [Imfinzi]

ICD-10	Description
C22.0	Liver cell carcinoma
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C34.00-C34.92	Malignant neoplasm of bronchus and lung
Z85.110-Z85.118	Personal history of malignant neoplasm of bronchus and lung
Z92.21	Personal history of antineoplastic chemotherapy
Z92.3	Personal history of irradiation

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

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.

Imfinzi® (durvalumab)

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 Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**

A. Disease type is one of the following:

1. Disease is confirmed (histologically or cytologically) stage III locally advanced, unresectable NSCLC disease; **OR**
2. Disease is confirmed (histologically or cytologically) stage II, unresectable NSCLC;

AND

B. Disease has not progressed after definitive chemoradiation; **AND**

C. Individual is using as consolidation therapy; **AND**

D. Individual is using until disease progression or a maximum of 12 months of treatment (NCCN 2A); **AND**

E. Individual has not previously received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**

F. Individual has a current ECOG performance status of 0-2; **AND**

G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

ii. Individual has a diagnosis of NSCLC (Label, NCCN 1, NCCN 2A); **AND**

A. Individual has advanced or metastatic NSCLC disease with no prior chemotherapy or any other systemic therapy; **AND**

B. Individual is using in combination with Imjudo (tremelimumab-actl) and platinum-based chemotherapy;

AND

C. Individual has no sensitizing epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genetic tumor aberrations (molecular testing should be submitted); **AND**

D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 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 NSCLC (NCCN 2A); **AND**

A. Individual is using as continuation maintenance therapy in one of the following ways:

1. As a single agent for recurrent, advanced, or metastatic disease after initial systemic therapy with durvalumab/tremelimumab-actl plus chemotherapy; **OR**
2. In combination with pemetrexed for recurrent, advanced, or metastatic disease after initial systemic therapy with durvalumab/tremelimumab-actl and platinum-based chemotherapy; **AND**
3. Individual is using until disease progression or unacceptable toxicity following positive tumor response or stable disease following initial systemic therapy; **AND**
4. Individual has a ECOG performance status of 0-2;

OR

iv. Individual has a diagnosis of extensive stage Small Cell Lung Cancer; **AND**
   A. Individual is using as first line therapy in combination with etoposide and either cisplatin or carboplatin for four (4) cycles (followed by maintenance Imfinzi monotherapy); **AND**
   B. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

v. Individual has a diagnosis of locally advanced or metastatic biliary tract cancer (Label, NCCN 1); **AND**
   A. Individual is using in combination with gemcitabine and cisplatin; **AND**
   B. Individual has a current ECOG performance status of 0-2; **AND**
   C. Individual has not previously received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

vi. Individual has a diagnosis of unresectable hepatocellular carcinoma (uHCC) (Label, NCCN 1, 2A); **AND**
   A. Individual is using in one of the following ways:
      1. Individual is using in combination with tremelimumab-actl (Imjudo) for initial therapy; **OR**
      2. Individual is using as a single agent after initial therapy with tremelimumab-actl (Imjudo) until disease progression or unacceptable toxicity; **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;

OR

vii. Individual has a diagnosis of persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) (NCCN 2A); **AND**
   A. Individual is using as first-line therapy; **AND**
   B. Individual is using in combination with etoposide and either cisplatin or carboplatin for four (4) cycles (followed by maintenance Imfinzi monotherapy); **AND**

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Imfinzi (durvalumab) 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, and the recommended duration of therapy has not been exceeded. 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. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

Approved Indication	Initial Approval Duration	Reauthorization Approval Duration	Treatment Duration
Single Agent			
Unresectable, Stage III non-small cell lung cancer (NSCLC)	Up to 6 months	Up to six months, to complete a total duration of therapy of 12 months.	Until disease progression, unacceptable toxicity, or a maximum of 12 months.
In combination with other therapeutic agents			
Metastatic non-small cell lung cancer (NSCLC)	Up to 3 months	Up to 6 months	Until disease progression or unacceptable toxicity
Extensive-stage small cell lung cancer (ES-SCLC)	Up to 3 months	Up to 6 months	Until disease progression or unacceptable toxicity
Locally advanced or metastatic biliary tract cancer (BTC)	Up to 6 months	Up to 6 months	Until disease progression or unacceptable toxicity
Unresectable hepatocellular carcinoma (uHCC)	Up to 6 months	Up to 6 months	Until disease progression or unacceptable toxicity

D. **Conditions Not Covered**

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

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

i. Requests for Imfinzi (durvalumab) may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Limits or Restrictions

A. 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.

Approved Indication	Combination Therapy	Recommended Dosing
Unresectable, Stage III non-small cell lung cancer (NSCLC)	Single agent	• Weight ≥ 30 kg: 10 mg/kg every 2 weeks **or** 1,500 mg every 4 weeks • Weight < 30 kg: 10 mg/kg every 2 weeks
Metastatic non-small cell lung cancer (NSCLC)	In combination with tremelimumab-actl and platinum-based chemotherapy	• Weight ≥ 30 kg: 1,500 mg every 3 weeks in combination with tremelimumab-actl 75 mg and platinum-based chemotherapy for 4 cycles, and then administer Imfinzi 1,500 mg every 4 weeks as a single agent with histology-based pemetrexed maintenance therapy every 4 weeks, and a fifth dose of tremelimumab-actl 75 mg in combination with Imfinzi dose 6 at week 16. • Weight < 30 kg: 20 mg/kg every 3 weeks in combination with tremelimumab-actl 1 mg/kg and platinum-based chemotherapy for 4 cycles, and then administer imfinzi 20 mg/kg every 4 weeks as a single agent with histology-based pemetrexed therapy every 4 weeks, and a fifth dose of tremelimumab-actl 1 mg/kg in combination with Imfinzi dose 6 at week 16
Extensive-stage small cell lung cancer (ES-SCLC)	In combination with etoposide and either carboplatin or cisplatin	• Weight ≥ 30 kg: 1,500 mg in combination with chemotherapy every 3 weeks (21 days) for 4 cycles, followed by 1,500 mg every 4 weeks as a single agent • Weight < 30 kg: 20 mg/kg in combination with chemotherapy every 3 weeks (21 days) for 4 cycles, followed by 10 mg/kg every 2 weeks as a single agent.

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

Approved Indication	Combination Therapy	Recommended Dosing
Locally advanced or metastatic biliary tract cancer (BTC)	In combination with gemcitabine and cisplatin	• Patients with a body weight of ≥ 30 kg: 1,500 mg in combination with chemotherapy every 3 weeks (21 days) up to 8 cycles followed by 1,500 mg every 4 weeks as a single agent. • Patients with a body weight of < 30 kg: 20 mg/kg in combination with chemotherapy every 3 weeks (21 days) up to 8 cycles followed by 20 mg/kg every 4 weeks as a single agent.
Unresectable hepatocellular carcinoma (uHCC)	In combination with tremelimumab-actl	• Patients with a body weight of ≥ 30 kg: Imfinzi 1,500 mg following a single dose of tremelimumab-actl 300 mg at Day 1 of Cycle 1. Continue Imfinzi 1,500 mg as a single agent every 4 weeks thereafter. • Patients with a body weight of < 30 kg: Initiate Imfinzi 20 mg/kg following a single dose of tremelimumab-actl 4 mg/kg at Day 1 of Cycle 1. Continue Imfinzi 20 mg/kg as a single agent every 4 weeks thereafter.
Exceptions		
None		

- Patients should be weighted prior to each infusion. For most indications Imfinzi's frequency of administration and co-administered medications change after the first cycle.

Policy Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

Reference Information

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2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 18, 2022.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Gray JE, Villegas A, Daniel D, et.al. Three-Year Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC-Update from PACIFIC. J Thorac Oncol 2020; 15: 288-293.
6. Hui R, Ozguroglu M, Villegas A., et al. Patient-reported outcomes with durvalumab after chemoradiotherapy in stage III, unresectable non-small cell lung cancer (PACIFIC): a randomized, controlled, phase 3 study. Lancet Oncol 2019:20:1670-1680.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
8. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on February 26, 2021.
    a. Non-Small Cell Lung Cancer. V1.2022. Revised December 7, 2021.
    b. Small Cell Lung Cancer. V2.2022. Revised November 24, 2021.
    c. Hepatobiliary Cancers. V2.2022. Revised July 15, 2022.
9. Powles T, van der Heijden MS, Castellano D, et al; DANUBE study investigators. Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): a randomised, open-label, multicentre, phase 3 trial. Lancet Oncol. 2020;21(12):1574-1588. doi:10.1016/S1470-2045(20)30541-6.

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 Name	Policy Number	Scope
Durvalumab (Imfinzi®)	MP-RX-FP-39-23	☒ MMM MA ☒ MMM Multihealth

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023
Select Review	Update statement for 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.	3/25/2024	5/9/2024

Revised: 10/16/2023