Clinical Policy: Durvalumab (Imfinzi)

Reference Number: PA.CP.PHAR.339
Effective Date: 01/2018
Last Review Date: 01/2023 Revision Log

Description
Durvalumab (Imfinzi®) is a programmed death-ligand 1 (PD-L1) blocking antibody.

FDA approved indication
Imfinzi is indicated:

- 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 tremelimumab-actl (Imjudo®) and platinum-based chemotherapy, for the treatment of adult patients with metastatic NSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
- In combination with etoposide and either carboplatin or cisplatin as first-line treatment of adults patients with extensive-stage small cell lung cancer (ES-SCLC).
- In combination with gemcitabine and cisplatin, as treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC).

In combination with tremelimumab-actl (Imjudo®) as treatment of adults patients with unresectable hepatocellular carcinoma (uHCC).

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of PA Health & Wellness® that Imfinzi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b or c):
   a. Disease is unresectable, stage II-III, and has not progressed following concurrent platinum-based chemotherapy and radiation therapy (RT);
   b. Disease is metastatic with neither sensitizing EGFR mutations or ALK genomic tumor aberrations and is prescribed in combination with tremelimumab-actl and platinum-based chemotherapy (*Appendix E)*;
   c. NCCN category 1, 2A or 2B recommendation;
5. Request meets one of the following (a, b, or c):
   a. For unresectable, stage II-III disease (i or ii):

i. For body weight < 30 kg: dose does not exceed 10 mg/kg every 2 weeks;
ii. For body weight ≥ 30 kg: dose does not exceed 10 mg/kg every 2 weeks or 1,500 mg every 4 weeks;

b. For metastatic disease (i or ii):
i. For body weight < 30 kg: dose does not exceed Imfinzi 20 mg/kg every 3 weeks in combination with tremelimumab-actl 1 mg/kg and platinum-based chemotherapy, and then Imfinzi 20 mg/kg every 4 weeks as a single agent with histology-based pemetrexed therapy every 4 weeks, and a fifth dose of Imjudo 1 mg/kg in combination with Imfinzi dose 6 at Week 16;
ii. For body weight ≥ 30 kg: dose does not exceed Imfinzi 1,500 mg every 3 weeks in combination with tremelimumab-actl 75 mg and platinum-based chemotherapy for 4 cycles, and then 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 Imjudo 75 mg in combination with Imfinzi dose 6 at Week 16;

c. For body weight ≥ 30 kg: dose does not exceed Imfinzi 1,500 mg every 3 weeks in combination with tremelimumab-actl 75 mg and platinum-based chemotherapy for 4 cycles, and then 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 Imjudo 75 mg in combination with Imfinzi dose 6 at Week 16; Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Extensive-Stage Small Cell Lung Cancer (must meet all):
1. Diagnosis of ES-SCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as first-line treatment with etoposide and either carboplatin or cisplatin followed by maintenance with Infimzi as a single agent;
5. Request meets one of the following (a, b, or c):
   a. For body weight < 30 kg, dose does not exceed 20 mg/kg every 3 weeks in combination with chemotherapy for 4 cycles, then 10 mg/kg every 2 weeks as a single agent;
   b. For body weight ≥ 30 kg, dose does not exceed 1500 mg every 3 weeks in combination with chemotherapy for 4 cycles, then 1500 mg every 4 weeks as a single agent;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Biliary Tract Cancer (must meet all)**:**
1. Diagnosis of locally advanced, unresectable, recurrent (> 6 months after surgery and/or completion of adjuvant therapy), or metastatic BTC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;

4. Prescribed in combination with gemcitabine and cisplatin;
5. Request meets one of the following (a, b, or c):
   a. For body weight < 30 kg, dose does not exceed 20 mg/kg every 3 weeks in combination with chemotherapy, then 20 mg/kg every 4 weeks as a single agent;
   b. For body weight ≥ 30 kg, dose does not exceed 1,500 mg every 3 weeks in combination with chemotherapy, then 1,500 mg every 4 weeks as a single agent;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Hepatocellular Carcinoma (must meet all)**:**
1. Diagnosis of unresectable, liver-confined, or metastatic hepatocellular carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b, or c):
   a. For body weight < 30 kg: dose does not exceed Imfinzi 20 mg/kg in combination with tremelimumab-actl 4 mg/kg as a single dose at Cycle 1/Day 1, followed by Imfinzi as a single agent every 4 weeks;
   b. For body weight ≥ 30 kg: dose does not exceed Imfinzi 1,500 mg in combination with tremelimumab-actl 300 mg as a single dose at Cycle 1/Day 1, followed by Imfinzi as a single agent every 4 weeks;
   c. Dose supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

E. Other diagnoses/indications:
1. Refer to PA.CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via of PA Health & Wellness benefit or member has previously met initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. For unresectable NSCLC requests, member has not received more than 12 months of Imfinzi therapy;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a, b, c, d, e, or f):*
   a. For stage II-II NSCLC (i or ii):
      i. For body weight < 30 kg: new dose does not exceed 10 mg/kg every 2 weeks;
      ii. For body weight ≥ 30 kg: new dose does not exceed 10 mg/kg every 2 weeks or 1,500 mg every 4 weeks
   b. For metastatic NSCLC (i or ii):
      i. For body weight < 30 kg: new dose does not exceed Imfinzi 20 mg/kg every 3 weeks in combination with tremelimumab-actl and platinum-based

chemotherapy for 4 cycles, then Imfinzi 20 mg/kg every 4 weeks with histology-based pemetrexed maintenance therapy;

ii. For body weight ≥ 30 kg, new dose does not exceed Imfinzi 1,500 mg every 3 weeks in combination with tremelimumab-actl and platinum based chemotherapy for 4 cycles, then Imfinzi 1,500 mg every 4 weeks with histology-based pemetrexed maintenance therapy;

c. For ES-SCLC (i or ii):
   i. For body weight < 30 kg, new dose does not exceed 20 mg/kg every 3 weeks in combination with chemotherapy for 4 cycles, then 10 mg/kg every 2 weeks as a single agent;
   ii. For body weight ≥ 30 kg, new dose does not exceed 1,500 mg every 3 weeks in combination with chemotherapy for 4 cycles, and then 1,500 mg every 4 weeks as a single agent;
d. For BTC (i or ii):
   i. For body weight < 30 kg, new dose does not exceed 20 mg/kg every 3 weeks in combination with chemotherapy, then 20 mg/kg every 4 weeks as a single agent;
   ii. For body weight ≥ 30 kg, new dose does not exceed 1,500 mg every 3 weeks in combination with chemotherapy, then 1,500 mg every 4 weeks as a single agent;
e. uHCC (i or ii):
   i. For body weight < 30 kg, new dose does not exceed 20 mg/kg in combination with tremelimumab-actl, then 20mg/kg every 4 weeks;
   ii. For body weight ≥ 30 kg, new dose does not exceed, 1,500 mg in combination with tremelimumab-actl, then 1,500 mg every 4 weeks;
f. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
NSCLC: up to a total duration of 12 months
All other indications: 12 months

B. Other diagnoses/indications:

1. Currently receiving medication via of PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALK: anaplastic lymphoma kinase
BTC: biliary tract cancer
ES-SCLC: extensive-stage small cell lung cancer
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

RT: radiotherapy
uHCC: unresectable hepatocellular carcinoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
NSCLC (examples of concurrent platinum-containing/radiotherapy regimens)		
cisplatin, etoposide, RT	Varies	Varies
Carboplatin/cisplatin, pemetrexed, RT		
paclitaxel, carboplatin, RT		
ES-SCLC (regimen examples as included in the NCCN SCLC guidelines)		
(carboplatin or cisplatin) and etoposide and Imfinzi	Carboplatin AUC 5-6 day 1 and etoposide 80-100 mg/m^2 days 1, 2, 3 and Imvinzi 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance Imfinzi 1,500 mg day 1 every 28 days Cisplatin 75-80 mg/m^2 day 1 and etoposide 80-100 mg/m^2 days 1, 2, 3 and Imvinzi 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance Imfinzi 1,500 mg day 1 every 28 days	See dosing regimens

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
On February 22, 2021, AstraZeneca announced the voluntary withdrawal of the indication for Imfinzi for second-line treatment of locally advanced or metastatic bladder cancer. Imfinzi was approved for this indication under the accelerated pathway in 2017, based on study results that showed positive tumor response rates and duration of response. In its announcement, AstraZeneca pointed to results from the DANUBE confirmatory trial, in which Imfinzi failed to meet its key primary endpoint of overall survival.

Appendix E: Recommended Combination Regimens

Tumor Histology	Patient Weight	Imfinzi Dosage	Tremelimumab-actl Dosage	Platinum-based Chemotherapy Regimen
	≥ 30 kg	1,500 mg	75 mg	carboplatin & nab-paclitaxel

Non-Squamous	< 30 kg	20 mg/kg	1 mg/kg	OR carboplatin or cisplatin & pemetrexed
Squamous	≥ 30 kg	1,500 mg	75 mg	carboplatin & nab-paclitaxel OR carboplatin or cisplatin & gemcitabine
	< 30 kg	20 mg/kg	1 mg/kg	

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC	Stage II-III: • Weight ≥ 30 kg: 10 mg/kg IV every 2 weeks or 1,500 mg every 4 weeks • Weight < 30 kg: 10 mg/kg IV every 2 weeks Metastatic: • 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, 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*	Stage II-III See regimen; maximum duration of 12 months Metastatic: See regimen
ES-SCLC	• Weight ≥ 30 kg: 1,500 mg IV 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 IV in combination with chemotherapy* every 3 weeks (21 days) for 4 cycles, following by 10 mg/kg every 2 weeks as a single agent	See regimen
BTC	• Weight ≥ 30 kg: 1,500 mg IV every 3 weeks in combination with chemotherapy †, then 1,500 mg every 4 weeks as a single agent • Weight < 30 kg: 20 mg/kg IV every 3 weeks in combination with chemotherapy †, then 20 mg/kg every 4 weeks as a single agent	See regimen

Indication	Dosing Regimen	Maximum Dose
uHCC	• Weight ≥ 30 kg: Imfinzi 1,500 mg in combination with tremelimumab-actl (Imjudo) 300 mg as a single dose at Cycle 1/Day 1, followed by Imfinzi as a single agent every 4 weeks • Weight < 30 kg: Imfinzi 20 mg/kg in combination with tremelimumab-actl (Imjudo) 4 mg/kg as a single dose at Cycle 1/Day 1, followed by Imfinzi as a single agent every 4 weeks	See regimen

* Optional pemetrexed therapy may be initiated from week 12 until disease progression or intolerable toxicity for patients with nonsquamous disease who received treatment with pemetrexed and carboplatin/cisplatin. †Administer Imfinzi prior to chemotherapy on the same day. Refer to the Prescribing Information for the agent administered in combination with Imfinzi for recommended dosage information, as appropriate. *[For ES-SCLC, see also Appendix B. Therapeutic Alternatives for NCCN regimens as carboplatin, cisplatin, and etoposide are off-label for this indication.]*

V. Product Availability

Single-dose vials: 120 mg/2.4 mL, 500 mg/10 mL

VI. References

1. Imfinzi Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022. Available at: https://www.imfinzi.com. Accessed December 1, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed September 9, 2022.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 6.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed December 2, 2022.
4. National Comprehensive Cancer Network. Small Cell Lung Cancer Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 15, 2022.
5. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed December 2, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9173	Injection, durvalumab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: added new FDA indication for NSCLC; references reviewed and updated.	02/2018	
2Q 2019 annual review: references reviewed and updated.	04/2019	
2Q 2020 annual review: UC stage III added to encompass NCCN recommended use for locally advanced disease; NCCN recommended use for SCLC added; references reviewed and updated.	04/2020	
2Q 2021 annual review: removed criteria for bladder cancer as the FDA labeled indication was withdrawn by the manufacturer based on confirmatory trial results; added coverage for stage II NSCLC per NCCN 2A recommendation; revised dosing for all indications per updated FDA label; references reviewed and updated.	04/2021	
2Q 2022 annual review: per prescribing information, for continued therapy, added the following requirement to reemphasize the NSCLC approval duration: "For NSCLC requests, member has not received more than 12 months of Imfinzi therapy"; updated HCPCS code; references reviewed and updated.	04/2022	
RT4: added criteria for new FDA approved indication of BTC; for NSCLC and ES-SCLC added age ≥ 18 years to be consistent with prescribing information; added criteria for newly FDA-approved indications for metastatic NSCLC and HCC.	01/2023	