Clinical Policy: Durvalumab (Imfinzi)

Reference Number: CP.PHAR.339
Effective Date: 07.01.17
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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 or b):
   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)*;

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. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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 Imfinzi 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 1,500 mg every 3 weeks in combination with chemotherapy for 4 cycles, 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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*).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or member has previously met initial approval criteria, or documentation supports that member is currently receiving Imfinzi for a covered indication and has received this medication for at least 30 days;
2. For 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

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

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 Imfinzi 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 Imfinzi 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
Non-Squamous	≥ 30 kg	1,500 mg	75 mg	carboplatin & nab-paclitaxel OR carboplatin or cisplatin & pemetrexed
	< 30 kg	20 mg/kg	1 mg/kg	
Squamous	≥ 30 kg	1,500 mg	75 mg	carboplatin & nab-paclitaxel OR carboplatin or cisplatin & gemcitabine
	< 30 kg	20 mg/kg	1 mg/kg	

V. 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
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	See regimen

Indication	Dosing Regimen	Maximum Dose
	single dose at Cycle 1/Day 1, followed by Imfinzi as a single agent every 4 weeks	

* 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.]*

VI. Product Availability

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

VII. 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	P& T Approval Date
2Q 2018 annual review: added new FDA indication for NSCLC with total duration of therapy of 12 months only per trial design and NCCN guideline; HIM added; references reviewed and updated.	04.24.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	12.19.19	05.19

Reviews, Revisions, and Approvals	Date	P& T Approval Date
No significant changes; revised formatting only.	07.08.19	
2Q 2020 annual review: HIM line of business added; UC stage III added to encompass NCCN recommended use for locally advanced disease; NCCN recommended use for SCLC added; references reviewed and updated.	02.11.20	05.20
FDA new indication added for ES-SCLC; references reviewed and updated.	04.27.20	
Added Commercial line of business	10.15.20	
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 to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	01.15.21	05.21
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.	02.15.22	05.22
RT4: added criteria for new FDA approved indication of BTC; added off-label criteria for hepatocellular carcinoma per NCCN 2A recommendation; for NSCLC and ES-SCLC added age ≥ 18 years to be consistent with prescribing information. Template changes applied to other diagnoses/indications.	09.09.22	
RT4: added criteria for newly FDA-approved indications for metastatic NSCLC and HCC; HCC converted from off-label to FDA approved status.	12.02.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.