Clinical Policy: Durvalumab (Imfinzi)

Reference Number: CP.PHAR.339
Effective Date: 07.01.17
Last Review Date: 05.25
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:

- In combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by Iminfzi continued as a single agent as adjuvant treatment after surgery, for the treatment of adult patients with resectable (tumors ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.
- As a single agent for the treatment of adult patients with unresectable, stage III 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 EGFR mutations or ALK genomic tumor aberrations.
- As a single agent for the treatment of adult patients with limited-stage small cell lung cancer (LS-SCLC) 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 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) for the treatment of adults patients with unresectable hepatocellular carcinoma (HCC).
- In combination with carboplatin and paclitaxel followed by Imfinzi as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR) as determined by an FDA-approved test.

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, b, c, or d):
   a. Disease is unresectable, stage II-III, and all of the following (i, ii, and iii):
      i. Disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy (RT);
      ii. Prescribed as a single agent;
      iii. Disease does not have EGFR exon 19 deletion or exon 21 L858R mutation;
   b. Disease is recurrent, advanced, or metastatic, and Imfinzi is prescribed in combination with Imjudo and platinum-based chemotherapy as one of the following (i-ix):
      i. First-line therapy for disease without EGFR exon 19 deletion, EGFR exon 21 L858R mutation, ALK, RET, or ROS1 rearrangement, or other actionable molecular biomarkers (e.g., KRAS, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, ERBB2 (HER2) – note: may be KRAS G12C mutation positive) (see *Appendix E)*;
      ii. First-line therapy for EGFR exon 20 mutation positive disease;
      iii. First-line or subsequent therapy for BRAF V600E mutation positive tumors;
      iv. First-line or subsequent therapy for NRTK1/2/3 gene fusion positive tumors;
      v. First-line or subsequent therapy for MET exon 14 skipping mutation positive tumors;
      vi. First-line or subsequent therapy for RET rearrangement positive tumors;
      vii. First-line therapy for ERBB2 (HER2) mutation positive tumors;
      viii. First-line therapy for NRG1 gene fusion positive tumors;
      ix. Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy;
   c. Prescribed as continuation maintenance therapy for recurrent, advanced, or metastatic disease that is negative for actionable molecular biomarkers (may be KRAS G12C mutation positive), and no contraindications to PD-1 or PD-L1 inhibitors (see *Appendix D*) and performance status 0-2, that achieved tumor response or stable disease following initial systemic therapy with one of the following (i or ii):
      i. Imfinzi/Imjudo/pemetrexed with either carboplatin or cisplatin for nonsquamous cell histology, and Imfinzi for maintenance therapy is prescribed in combination with pemetrexed (off-label);
      ii. Imfinzi/Imjudo plus chemotherapy, and Imfinzi for maintenance therapy is prescribed a single agent (off-label);
   d. Prescribed as neoadjuvant therapy in combination with platinum-containing chemotherapy, followed by use as adjuvant therapy as a single agent after surgery for disease that meets both of the following (a and b):
      i. Resectable (tumors ≥ 4 cm and/or node positive);

ii. No known EGFR or ALK mutations;

5. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a, b, c, or d):*
   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 Imjudo 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 Imjudo 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 resectable disease (i and ii):
      i. Neoadjuvant therapy (1 or 2):
         1) For body weight < 30 kg: Dose does not exceed Imfinzi 20 mg/kg every 3 weeks in combination with chemotherapy for up to 4 cycles prior to surgery;
         2) For body weight ≥ 30 kg: Dose does not exceed Imfinzi 1,500 mg every 3 weeks in combination with chemotherapy for up to 4 cycles prior to surgery;
      ii. Adjuvant therapy (1 or 2):
         1) For body weight < 30 kg: Dose does not exceed 20 mg/kg every 4 weeks as a single agent for up to 12 cycles after surgery;
         2) For body weight ≥ 30 kg: Dose does not exceed 1,500 mg every 4 weeks as a single agent for up to 12 cycles after surgery;
   d. 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. Limited-Stage Small Cell Lung Cancer (must meet all):
1. Diagnosis of LS-SCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as a single agent;
5. Disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy;

6. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*
   a. For body weight < 30 kg: Dose does not exceed 20 mg/kg every 4 weeks;
   b. For body weight ≥ 30 kg: Dose does not exceed 1,500 mg every 4 weeks;
   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. 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. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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

D. Biliary Tract Cancer (must meet all)**:**
1. Diagnosis of locally advanced, unresectable, resected gross residual (R2), recurrent (> 6 months after surgery with curative intent 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. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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

E. Hepatocellular Carcinoma (must meet all)**:**

1. Diagnosis of unresectable, liver-confined, or extrahepatic/metastatic HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. 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 Imjudo 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 Imjudo 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

F. Endometrial Cancer (must meet all)**:**

1. Diagnosis of primary advanced, recurrent, metastatic, stage III, or stage IV endometrial cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with carboplatin and paclitaxel for the first 6 cycles;
5. Disease is dMMR;
6. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*
   a. For body weight < 30 kg: Dose does not exceed 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles, then 20 mg/kg every 4 weeks as a single agent;
   b. For body weight ≥ 30 kg: Dose does not exceed 1,120 mg every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles, then 1,500 mg every 4 weeks as a single agent;
   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

G. Cervical Cancer (off-label) (must meet all)**:**
1. Diagnosis of persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with etoposide and either cisplatin or carboplatin, then continued as a single agent for maintenance therapy;
5. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed the FDA approved maximum recommended dose;
   b. 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

H. Gastric, Esophageal, and Esophagogastric Junction Cancer (off-label) (must meet all)**:**
1. Diagnosis of gastric, esophageal, or esophagogastric junction adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Imjudo as neoadjuvant therapy;
5. Disease is microsatellite instability-high (MSI-H) or dMMR;
6. Provider attestation that member is medically fit for surgery;
7. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed the FDA approved maximum recommended dose;
   b. 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

I. Ampullary Adenocarcinoma (off-label) (must meet all)**:**
1. Diagnosis of ampullary adenocarcinoma (pancreatobiliary or mixed type);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with gemcitabine and cisplatin;
5. Disease is metastatic;
6. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed the FDA approved maximum recommended dose;
   b. 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

J. 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 unresectable, stage II-III NSCLC requests, member has not received more than 12 months of Imfinzi therapy;
3. For resectable NSCLC requests, member has not received more than 12 cycles of Iminfzi therapy following surgery;
4. For LS-SCLC requests, member has not received more than 24 months of Imfinzi therapy;
5. Member is responding positively to therapy;
6. For brand Imfinzi requests, member must use generic durvalumab, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. If request is for a dose increase, request meets one of the following (a, b, c, d, e, f, g, h, or i):*
   a. For unresectable, stage II-III 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 20 mg/kg every 3 weeks in combination with Imjudo and platinum-based chemotherapy for 4 cycles, then 20 mg/kg every 4 weeks with histology-based pemetrexed maintenance therapy;

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

c. For resectable NSCLC (i and ii):
   i. Neoadjuvant therapy (1 or 2):
      1) For body weight < 30 kg: Dose does not exceed Imfinzi 20 mg/kg every 3 weeks in combination with chemotherapy for up to 4 cycles prior to surgery;
      2) For body weight ≥ 30 kg: Dose does not exceed Imfinzi 1,500 mg every 3 weeks in combination with chemotherapy for up to 4 cycles prior to surgery;
   ii. Adjuvant therapy (1 or 2):
      1) For body weight < 30 kg: Dose does not exceed 20 mg/kg every 4 weeks as a single agent for up to 12 cycles after surgery;
      2) For body weight ≥ 30 kg: Dose does not exceed 1,500 mg every 4 weeks as a single agent for up to 12 cycles after surgery;
d. For LS-SCLC (i or ii):
   i. For body weight < 30 kg: New dose does not exceed 20 mg/kg every 4 weeks;
   ii. For body weight ≥ 30 kg: New dose does not exceed 1,500 mg every 4 weeks;
e. 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;
f. 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;
g. For HCC (i or ii):
   i. For body weight < 30 kg: New dose does not exceed 20 mg/kg in combination with Imjudo, then 20 mg/kg every 4 weeks;
   ii. For body weight ≥ 30 kg: New dose does not exceed 1,500 mg in combination with Imjudo, then 1,500 mg every 4 weeks;
h. For endometrial cancer (i or ii):
   i. For body weight < 30 kg: New dose does not exceed 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles, then 20 mg/kg every 4 weeks as a single agent;

ii. For body weight ≥ 30 kg: New dose does not exceed 1,120 mg every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles, then 1,500 mg every 4 weeks as a single agent;

i. 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:
Medicaid/HIM – 12 months (*up to a total duration of 12 months for unresectable, Stage II-II NSCLC; up to a total of 12 cycles for resectable NSCLC; up to a total duration of 24 months for LS-SCLC*)
Commercial – 6 months or to the member's renewal date, whichever is longer (*up to a total duration of 12 months for unresectable, Stage II-II NSCLC; up to a total of 12 cycles for resectable NSCLC; up to a total duration of 24 months for LS-SCLC*)

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
dMMR: mismatch repair deficient
ES-SCLC: extensive-stage small cell lung cancer
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
LS-SCLC: limited-stage small cell lung cancer
NECC: neuroendocrine carcinoma of the cervix

NSCLC: non-small cell lung cancer
PD-L1: programmed death-ligand
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		
LS-SCLC (regimen examples as included in the NCCN SCLC guidelines)		
cisplatin and etoposide	Varies	Varies
carboplatin and etoposide	Varies	Varies

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.
- For NSCLC, actionable molecular biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, and ERBB2 (HER2). If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.
- Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R mutation; ALK, RET, or ROS1 rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.
- SCLC stage definitions per NCCN:
  - Limited stage: Stage I-III (T any, N any, M0) that can be safely treated with definitive radiation doses. Excludes T3-4 due to multiple lung nodules that are too extensive or

have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan
- Extensive stage: Stage IV (T any, N any, M 1a/b/c), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan

Appendix E: Recommended Combination Regimens for Metastatic NSCLC

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	Unresectable stage 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 Imjudo 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 Imjudo 75 mg in combination with Imfinzi dose 6 at week 16* • Weight < 30 kg: 20 mg/kg every 3 weeks in combination with Imjudo 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 Imjudo 1 mg/kg in combination with Imfinzi dose 6 at week 16* Resectable: • Neoadjuvant therapy:	Stage III: See regimen; maximum duration of 12 months Metastatic: See regimen Resectable: See regimen;

Indication	Dosing Regimen	Maximum Dose
	○ Weight < 30 kg: 20 mg/kg every 3 weeks in combination with platinum-based chemotherapy for up to 4 cycles prior to surgery ○ Weight ≥ 30 kg: 1,500 mg every 3 weeks in combination with platinum-based chemotherapy for up to 4 cycles prior to surgery • Adjuvant therapy: ○ Weight < 30 kg: 20 mg/kg every 4 weeks as a single agent for up to 12 cycles after surgery ○ Weight ≥ 30 kg: 1,500 mg every 4 weeks as a single agent for up to 12 cycles after surgery	maximum duration of 12 cycles after surgery
LS-SCLC	Following concurrent platinum-based chemotherapy and radiation therapy: • Weight ≥ 30 kg: 1,500 mg IV every 4 weeks • Weight < 30 kg: 20 mg/kg IV every 4 weeks	See regimen; maximum duration of 24 months
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 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 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
Endometrial cancer	• Weight < 30 kg: 15 mg/kg IV every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles, then 20 mg/kg every 4 weeks as a single agent • Weight ≥ 30 kg: 1,120 mg IV every 3 weeks in combination with carboplatin and paclitaxel for 6	See regimen

Indication	Dosing Regimen	Maximum Dose
	cycles, then 1,500 mg every 4 weeks as a single agent	

* 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.

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; February 2025. Available at: https://www.imfinzi.com. Accessed March 6, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 5, 2025.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 5, 2025.
4. National Comprehensive Cancer Network. Small Cell Lung Cancer Version 4.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed February 5, 2025.
5. National Comprehensive Cancer Network. Hepatocellular Carcinoma Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed February 5, 2025.
6. National Comprehensive Cancer Network. Biliary Tract Cancers Version 6.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed February 5, 2025.

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 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	01.15.21	05.21

Reviews, Revisions, and Approvals	Date	P& T Approval Date
per updated FDA label; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.		
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	
2Q 2023 annual review: for NSCLC per NCCN Compendium added recurrent or advanced disease and additional actionable molecular biomarkers that could be negative for use in combination with Imjudo and platinum therapy, added off-label continuation maintenance therapy; added off-label use for cervical cancer; clarified maximum 12 month continued approval duration applies only to stage II-III NSCLC; references reviewed and updated.	01.05.23	05.23
2Q 2024 annual review: per NCCN – for NSCLC, added recommended uses when actionable molecular biomarkers are present; for BTC, added resected gross residual (R2) disease; added off-label uses for gastric, esophageal, esophagogastric junction, and ampullary adenocarcinoma; for all indications, added redirection to generic if available; references reviewed and updated.	02.06.24	05.24
RT4: added criteria for newly FDA-approved indication of dMMR endometrial cancer.	06.20.24	
RT4: added criteria for newly FDA-approved indication for use as neoadjuvant/adjuvant therapy in resectable NSCLC; revised Commercial continued approval duration from 12 months to standard duration for injectables, 6 months or to the member's renewal date, whichever is longer.	08.22.24	
RT4: added criteria for newly FDA-approved indication of LS-SCLC.	12.11.24	
2Q 2025 annual review: per NCCN – for NSCLC, added that Imfinzi must be prescribed as a single agent and that disease does not have EGFR exon 19 deletion or exon 21 L858R mutation if stage II-III; added use as first-line therapy for NRG1 gene fusion positive tumors; removed use as subsequent therapy for EGFR exon	03.06.25	05.25

Reviews, Revisions, and Approvals	Date	P& T Approval Date
19 deletion, exon 21 deletion, exon 21 L858R tumors, ALK1 rearrangement, and ROS1 rearrangement positive tumors; for HCC; added additional qualifier of extrahepatic; for endometrial cancer, added additional qualifiers of metastatic, stage III, and stage IV; for cervical cancer, added that Imfinzi can be used as a single agent for maintenance therapy following combination use; for ampullary adenocarcinoma, removed qualifiers of unresectable localized and stage IV resected; for BTC, added "with curative intent" for recurrent definition to align with NCCN compendium wording; RT4: updated FDA approved indication for dMMR endometrial cancer to include FDA approved testing language; references reviewed and updated.		

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.