Clinical Policy: Durvalumab (Imfinzi)

Reference Number: LA.PHAR.339
Effective Date: 07.23.22
Last Review Date: 06.02.23
Line of Business: Medicaid

Coding Implications
Revision Log

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

****Please note: This policy is for medical benefit****

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®) for the 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 Louisiana HealthCare Connections® 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 recurrent, advanced, or metastatic with neither sensitizing EGFR mutations, ALK genomic tumor aberrations, or negative for other actionable molecular biomarkers (e.g., KRAS, ROS1, BRAF, NTRK1/2/3, MET, RET, ERBB2 (HER2)) and is prescribed in combination with Imjudo (tremelimumab-actl) and platinum-based chemotherapy as first-line therapy (*Appendix E)*;
c. Continuation maintenance therapy for recurrent, advanced, or metastatic disease that is negative for actionable molecular biomarkers 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);

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. Prescribed as first-line treatment with etoposide and either carboplatin or cisplatin, followed by maintenance with Imfinzi as a single agent;
4. 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. 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;
5. 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

F. 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 LA.PMN.255
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 LA.PMN.53

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 stage II – III 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 -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 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-NSCLC (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, 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 LA.PMN.255
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 2 above does not apply, refer to the off-label use policy LA.PMN.53

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 policy LA.PMN.53

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

NECC: neuroendocrine carcinoma of the cervix
PD-L1: programmed death-ligand
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 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 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
- Actionable molecular biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, 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, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

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

Indication	Dosing Regimen	Maximum Dose
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 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.]*

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 January 5, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 24, 2023.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 24, 2023.
4. National Comprehensive Cancer Network. Small Cell Lung Cancer Version 3.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 24, 2023.

5. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 5.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed January 24, 2023.
6. National Comprehensive Cancer Network. Cervical Cancer Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed January 24, 2023.

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	LDH Approval Date
Converted corporate to local policy	04.22	07.23.22
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. Added criteria for newly FDA-approved indications for metastatic NSCLC and HCC; HCC converted from off-label to FDA approved status. 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.	06.02.23	

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.

LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.