Utilization Review Policy 164

POLICY: Oncology (Injectable – Programmed Death-Ligand 1) – Imfinzi
- Imfinzi® (durvalumab intravenous infusion – AstraZeneca)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 10/25/2023

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Imfinzi, a programmed cell death ligand 1 (PD-L1) blocking antibody, is indicated for the following uses:[1]
- **Biliary tract cancers**, in combination with gemcitabine and cisplatin for the treatment of locally advanced or metastatic disease in adults.
- **Hepatocellular carcinoma**, in combination with Imjudo® (tremelimumab-actl intravenous infusion) for the treatment of unresectable disease in adults.
- **Non-small cell lung cancer (NSCLC)**, in adults with unresectable Stage III disease that has not progressed following concurrent platinum-based chemotherapy and radiation therapy.
- **NSCLC**, in adults with metastatic disease with no sensitizing epidermal growth factor receptor (*EGFR*) mutations or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations, in combination with Imjudo and platinum-based chemotherapy.
- **Small cell lung cancer**, in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of extensive-stage disease in adults.

The recommended dose of Imfinzi is weight-based. For biliary tract cancer, if the patient's body weight is ≥ 30 kg, the dose is 1,500 mg administered as an intravenous (IV) infusion in combination with chemotherapy every 3 weeks (21 days) for up to 8 cycles, followed by 1,500 mg every 4 weeks as a single agent. For patients with body weight < 30 kg, the dose is 20 mg/kg in combination with chemotherapy every 3 weeks for up to 8 cycles, followed by 20 mg/kg every 4 weeks as a single agent. For hepatocellular carcinoma, if the patient's weight is ≥ 30 kg, the dose is 1,500 mg IV once every 4 weeks. If the patient's weight is < 30 kg, the dose is 20 mg/kg IV once every 4 weeks. For NSCLC, if the patient's body weight is ≥ 30 kg, the dose is 10 mg/kg administered IV every 2 weeks or 1,500 mg IV no more frequently than once every 3 weeks. For patients with a body weight of < 30 kg, the dose is 10 mg/kg administered IV once every 2 weeks or 20 mg/kg administered IV once every 3 weeks. Imfinzi is administered until disease progression or unacceptable toxicity for a maximum of 12 months. For small cell lung cancer, if the patient's body weight is ≥ 30 kg, the dose is 1,500 mg administered 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. For patients with body weight < 30 kg, the dose is 20 mg/kg in combination with chemotherapy every 3 weeks for 4 cycles, followed by 10 mg/kg every 2 weeks as a single agent. Management of adverse events may require that Imfinzi be withheld or discontinued, as determined by the prescribing physician. No dose reductions are recommended.

Guidelines

Imfinzi is addressed in National Comprehensive Cancer Network guidelines:
- **Ampullary Adenocarcinoma:** Guidelines (version 1.2023 – April 27, 2023) recommend Imfinzi for the first-line treatment of pancreatobiliary/mixed type disease in patients with unresectable localized disease or metastatic disease.[2,8]

- **Biliary Tract Cancers:** Guidelines (version 2.2023 – May 10, 2023) recommend Imfinzi for the primary and subsequent treatment of unresectable or metastatic biliary tract cancers and for the neoadjuvant treatment of resectable locally advanced gallbladder disease, in combination with cisplatin and gemcitabine.[2,7]
- **Cervical Cancer:** Guidelines (version 1.2023 – January 6, 2023) recommend Imfinzi, in combination with etoposide and either cisplatin or carboplatin for the treatment of persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix.[2,5]
- **Esophageal and Esophagogastric Junction Cancers:** The guidelines (version 3.2023 – August 29, 2023) recommend Imfinzi in combination with Imjudo for the neoadjuvant treatment of microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) adenocarcinoma in patients who are medically fit for surgery.[2,10]
- **Gastric Cancer:** The guidelines (version 2.2023 – August 29, 2023) recommend Imfinzi in combination with Imjudo for the neoadjuvant treatment of microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) locoregional disease in patients who are medically fit for surgery.[2,11]
- **Hepatocellular Carcinoma:** Guidelines (version 1.2023 – March 10, 2023) recommend Imfinzi, as monotherapy or in combination with Imjudo, as first-line treatment of hepatocellular carcinoma in patients with unresectable disease who are not transplant candidates, in patients with inoperable disease due to performance status or comorbidities, and in those with metastatic disease.[2,5] Imfinzi is also recommended for the primary and subsequent treatment of unresectable or metastatic biliary tract cancers in combination with cisplatin and gemcitabine.
- **Non-Small Cell Lung Cancer:** Guidelines (version 3.2023 – April 13, 2023) recommend Imfinzi as consolidation therapy for patients with unresectable stage II (category 2A) or stage III (category 1) disease with a performance status of 0 or 1 and no disease progression following definitive chemoradiation.[2,3] The guidelines recommend Imfinzi for the first-line treatment of recurrent, advanced, or metastatic disease with PD-L1 expression ≥ 1% and negative for actionable molecular markers. The guidelines also recommend Imfinzi for disease with PD-L1 expression < 1%, and for disease that is positive for a variety of molecular markers.
- **Small Cell Lung Cancer:** Guidelines (version 3.2023 – December 21, 2022) recommend Imfinzi in combination with etoposide and carboplatin/cisplatin as a "Preferred" primary treatment, followed by Imfinzi as single-agent maintenance therapy (category 1) for patients with extensive stage disease.[2,4]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Imfinzi. Approval is recommended for those who meet the conditions of coverage in the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Imfinzi, as well as the monitoring required for adverse events and long-term efficacy, approval requires Imfinzi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Imfinzi is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Biliary Tract Cancer.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Patient has resectable locally advanced disease: Approve for 6 months (total) if the patient meets ALL of the following (i, ii, iii, iv, and v):
     a. Patient is ≥ 18 years of age; AND
     b. Patient has gallbladder cancer; AND
     c. The medication is used as neoadjuvant therapy; AND
     d. The medication is used in combination with cisplatin and gemcitabine; AND
     e. The medication is prescribed by or in consultation with an oncologist; OR
   - **B)** Patient has unresectable, recurrent, or metastatic disease: Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v):
     a. Patient is ≥ 18 years of age; AND
     b. If the patient has recurrent disease, recurrence occurred at least 6 months after surgery and at least 6 months after adjuvant therapy; AND
     c. Patient has ONE of the following (a b, or c):
        - **i.** Gallbladder cancer; OR
        - **ii.** Intrahepatic cholangiocarcinoma; OR
        - **iii.** Extrahepatic cholangiocarcinoma; AND
     d. The medication will be used in combination with cisplatin and gemcitabine; AND
     e. The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following doses (A or B):
   - **A)** For a patient with a body weight ≥ 30 kg: Approve 1,500 mg administered as an intravenous infusion not more frequently than once every 3 weeks; OR
   - **B)** For a patient with a body weight < 30 kg: Approve 20 mg/kg administered as an intravenous infusion not more frequently than once every 3 weeks.

2. **Hepatocellular Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has unresectable or metastatic disease; OR
     - **ii.** According to the prescriber, the patient is not a surgical candidate; AND
   - **C)** The medication will be used first-line; AND
   - **D)** Patient meets ONE of the following (i or ii):
     - **i.** The medication is used as monotherapy; OR
     - **ii.** The medication is used in combination with Imjudo (tremelimumab-actl intravenous infusion); AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following doses (A or B):

A) For a patient weighing ≥ 30 kg: 1,500 mg administered as an intravenous infusion not more frequently than once every 4 weeks; OR
B) For a patient weighing < 30 kg: 20 mg/kg administered as an intravenous infusion not more frequently than once every 4 weeks.

---

3. Non-Small Cell Lung Cancer. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Patient has unresectable Stage II or III disease: Approve for 1 year (total) of therapy if the patient meets ALL of the following (i, ii, and iii):
a. Patient is ≥ 18 years of age; AND
b. Patient has not had disease progression following treatment with concurrent platinum-based chemotherapy and radiation therapy; AND
c. The medication is prescribed by or in consultation with an oncologist; OR

B) Patient has recurrent, advanced, or metastatic disease: Approve for 1 year if the patient meets ONE of the following (i, ii, iii, or iv):
a. Patient meets ALL of the following (a, b, c, and d):
i. Patient is ≥ 18 years of age; AND
ii. The tumor is negative for actionable molecular markers; AND
Note: Examples of actionable molecular markers include epidermal growth factor receptor (*EGFR*) mutations, anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations, *KRAS*, *ROS1*, *BRAF*, *NTRK1/2/3*, *MET*, *RET*, and *ERBB2* (*HER2*).
iii. Patient meets ONE of the following [(1) or (2)]:
1. Imfinzi is used as first-line therapy; OR
2. Imfinzi is used as continuation maintenance therapy; AND
iv. The medication is prescribed by or in consultation with an oncologist; OR
b. Patient meets ALL of the following (a, b, c, and d):
i. Patient is ≥ 18 years of age; AND
ii. The tumor is positive for ONE of the following [(1), (2), or (3)]:
1. Epidermal growth factor receptor (*EGFR*) exon 20 mutation positive; OR
2. *KRAS G12C* mutation positive; OR
3. *ERBB2* (*HER2*) mutation positive; AND
iii. Imfinzi is used as first-line therapy; AND
iv. The medication is prescribed by or in consultation with an oncologist; OR
c. Patient meets ALL of the following (a, b, c, and d):
i. Patient is ≥ 18 years of age; AND
b) The tumor is positive for ONE of the following [(1), (2), (3), or (4)]:
(1) *BRAF V600E* mutation positive; OR
(2) *NTRK1/2/3* gene fusion positive; OR
(3) *MET* exon 14 skipping mutation positive; OR
(4) *RET* rearrangement positive; AND
c) Imfinzi is used as first-line or subsequent therapy; AND
d) The medication is prescribed by or in consultation with an oncologist; OR
d. Patient meets ALL of the following (a, b, c, d, and e):
i. Patient is ≥ 18 years of age; AND
ii. The tumor is positive for ONE of the following [(1), (2), (3), or (4)]:
1. *EGFR* exon 19 deletion or exon 21 *L858R* mutation positive; OR
2. *EGFR S768I*, *L861Q*, and/or *G719X* mutation positive; OR

3. *ALK* rearrangement positive; OR
4. *ROS1* rearrangement; AND

iii. The patient has received targeted drug therapy for the specific mutation; AND
Note: Examples of targeted drug therapy include Gilotrif (afatinib tablets), Tagrisso (osimertinib tablets), erlotinib, Iressa (gefitinib tablets), Xalkori (crizotinib capsules), Zykadia (ceritinib capsules), Alecensa (alectinib capsules), Alunbrig (brigatinib tablets), Lorbrena (lorlatinib tablets), Rozlytrek (entrectinib capsules), or Vizimpro (dacomitinib tablets).

iv. Imfinzi is used as subsequent therapy; AND

v. Imfinzi is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following doses (A or B):

A) For a patient with a body weight ≥ 30 kg, approve ONE of the following (i or ii):
- **i.** Approve 10 mg/kg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
- **ii.** Approve 1,500 mg administered as an intravenous infusion not more frequently than once every 3 weeks; OR

B) For a patient with a body weight < 30 kg, approve ONE of the following (i or ii):
- a. Approve 10 mg/kg administered as an intravenous infusion not more frequently than once every 2 weeks; OR
- b. Approve 20 mg/kg administered as an intravenous infusion not more frequently than once every 3 weeks.

---

4. Small Cell Lung Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient has extensive stage disease; AND

C) Patient meets ONE of the following (i or ii):
- **i.** The medication is used in combination with etoposide and platinum chemotherapy; OR
  Note: Examples of platinum chemotherapy agents include cisplatin and carboplatin.
- **ii.** The medication is used as a single-agent for maintenance after chemotherapy; AND

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following doses (A or B):

A) For a patient with a body weight ≥ 30 kg: Approve 1,500 mg administered as an intravenous infusion not more frequently than once every 3 weeks; OR

B) For a patient with a body weight < 30 kg approve ONE of the following (i or ii):
- **i.** Approve 20 mg/kg administered as an intravenous infusion, in combination with chemotherapy, not more frequently than once every 3 weeks; OR
- **ii.** Approve 10 mg/kg administered as an intravenous infusion not more frequently than once every 2 weeks.

Other Uses with Supportive Evidence

5. Ampullary Adenocarcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has pancreatobiliary/mixed type disease; AND
- **C)** Patient has unresectable localized disease or metastatic disease; AND
- **D)** The medication is used as first-line therapy; AND
- **E)** The medication is used in combination with gemcitabine and cisplatin; AND
- **F)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following doses (A or B):
- **A)** For a patient with a body weight ≥ 30 kg: Approve 1,500 mg administered as an intravenous infusion, in combination with chemotherapy, not more frequently than once every 3 weeks; OR
- **B)** For a patient with a body weight < 30 kg: Approve 20 mg/kg administered as an intravenous infusion, in combination with chemotherapy, not more frequently than once every 3 weeks.

6. Cervical Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has small cell neuroendocrine carcinoma of the cervix; AND
- **C)** Patient has persistent, recurrent, or metastatic disease; AND
- **D)** The medication is used in combination with etoposide and platinum chemotherapy; AND
  Note: Examples of platinum chemotherapy agents include cisplatin and carboplatin
- **E)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following doses (A or B):
- **A)** For a patient with a body weight ≥ 30 kg: Approve 1,500 mg administered as an intravenous infusion, in combination with chemotherapy, not more frequently than once every 3 weeks; OR
- **B)** For a patient with a body weight < 30 kg: Approve 20 mg/kg administered as an intravenous infusion, in combination with chemotherapy, not more frequently than once every 3 weeks.

7. Esophageal and Esophagogastric Junction Cancers. Approve for 3 months if the patient meets ALL of the following (A, B, C, D, E, F, and G):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has adenocarcinoma tumor; AND
- **C)** Patient has microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) disease; AND
- **D)** Imfinzi is as neoadjuvant therapy; AND
- **E)** Imfinzi is used in combination with Imjudo (tremelimumab intravenous infusion); AND
- **F)** According to the physician, the patient is medically fit for surgery; AND
- **G)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 1,500 mg administered by intravenous infusion, not more frequently than three times in a single 12 week cycle.

8. Gastric Cancer. Approve for 3 months if the patient meets ALL of the following (A, B, C, D, E, F, and G):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has locoregional disease; AND
- **C)** Patient has microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) disease; AND
- **D)** Imfinzi is as neoadjuvant therapy; AND
- **E)** Imfinzi is used in combination with Imjudo (tremelimumab intravenous infusion); AND
- **F)** According to the physician, the patient is medically fit for surgery; AND
- **G)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 1,500 mg administered by intravenous infusion, not more frequently than three times in a single 12 week cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Imfinzi is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Imfinzi® intravenous infusion [prescribing information]. Wilmington, DE: AstraZeneca; June 2023.
2. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 23, 2023. Search term: durvalumab.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2023 – April 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2023.
4. The NCCN Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2023 – December 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 10, 2023.
5. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2023.
6. The NCCN Cervical Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – January 6, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2023.
7. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2023 – May 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2023.
8. The NCCN Ampullary Adenocarcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – April 27, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2023.
9. Oh D-Y, Ruth HE A, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. *NEJM Evid*. 2022;1:EVIDoa2200015.
10. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 3.2023 – August 29, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed October 23, 2023.
11. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – August 29, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed October 23, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Small Cell Lung Cancer:** Added requirement that the patient has extensive stage disease. **Biliary Tract Cancer:** Added requirement that the patient has either unresectable or metastatic disease, OR recurrent disease > 6 months after surgery and > 6 months after adjuvant therapy.	07/20/2022
Selected Revision	**Biliary Tract Cancer:** This indication was moved from the Other Uses with Supportive Evidence section into the FDA-Approved Indications section of the policy. Revised 1,500 mg dose to be used for patient ≥ 30 kg. Added dosing for patients < 30 kg.	09/21/2022
Selected Revision	**Hepatocellular carcinoma:** This indication was moved to the FDA-Approved Indications section. Added requirement that Imfinzi is used either as monotherapy, or in combination with Imjudo (tremelimumab-actl intravenous infusion). Revised to dosing section to reflect weight-based dose for this indication.	11/02/2022
Selected Revision	**Non-small cell lung cancer:** Criteria were added for patients with metastatic disease. Dosing interval was revised for patients ≥ 30 kg and receiving 1,500 mg dose from not more frequently than once every 4 weeks, to not more frequently than once every 2 weeks. For patients < 30 kg, 20 mg/kg dose was added.	11/30/2022
Selected Revision	**Hepatocellular Carcinoma:** According to the prescriber was added to the requirement that the patient is not a surgical candidate. **Non-Small Cell Lung Cancer:** The descriptors "recurrent" and "advanced" added to Patient has recurrent, advanced, or metastatic disease. Added options for approval for patients without actionable molecular markers and for patients positive for epidermal growth factor receptor (*EGFR*) exon 20 mutation; *KRAS G12C* mutation; *ERBB2* (*HER2*) mutation; *BRAF V600E* mutation; *NTRK1/2/3* gene fusion; *MET* exon 14 skipping mutation; *RET* rearrangement; *EGFR* exon 19 deletion or *L858R* mutation; *EGFR S768I*, *L861Q* and/or *G719X* mutation; *ALK* rearrangement; or *ROS1* rearrangement.	12/21/2022
Annual Revision	**Biliary Tract Cancers:** Patient has resectable locally advanced disease added as new option of approval with a total duration of approval of 6 months. **Non-Small Cell Lung Cancer:** Exon 21 was added as a descriptor for exon 21 *L858R* mutation positive disease. **Ampullary Adenocarcinoma:** Added new condition of approval. **Cervical Cancer:** Added new condition of approval.	07/19/2023
Selected Revision	**Esophageal and Esophagogastric Junction Cancer:** Added new condition of approval. **Gastric Cancer:** Added new condition of approval.	10/25/2023