Utilization Review Policy 164

POLICY: Oncology (Injectable – Programmed Death-Ligand 1) – Imfinzi Utilization Management Medical Policy

- Imfinzi® (durvalumab intravenous infusion – AstraZeneca)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All Aspirus Medicare 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.
- **Endometrial cancer**, in combination with carboplatin and paclitaxel, followed by single-agent Imfinzi for the treatment of adults with mismatch repair deficient (dMMR), primary advanced or recurrent disease.
- **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.

Guidelines

Imfinzi is addressed in National Comprehensive Cancer Network guidelines:

- **Ampullary Adenocarcinoma:** Guidelines (version 1.2024 – December 13, 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 3.2024 – July 2, 2024) recommend Imfinzi for the primary and subsequent treatment of unresectable, resected gross residual, or metastatic biliary tract cancers; for recurrent disease > 6 months after surgery with curative intent and > 6 months after completion of adjuvant therapy; and for the neoadjuvant treatment of resectable locoregionally advanced gallbladder disease, in combination with cisplatin and gemcitabine.[2,7]

- **Cervical Cancer:** Guidelines (version 2.2024 – February 23, 2024) 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 3.2024 – April 26, 2024) 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 2.2024 – May 29, 2024) 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 2.2024 – July 2, 2024) recommend Imfinzi, as monotherapy or in combination with Imjudo, as first-line treatment of hepatocellular carcinoma in patients with liver-confined, unresectable disease who are not transplant candidates; and in patients with extrahepatic or metastatic disease who are deemed ineligible for resection, transplant, or locoregional therapy.[2,5]
- **Non-Small Cell Lung Cancer:** Guidelines (version 7.2024 – June 26, 2024) 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 3.2024 – June 11, 2024) 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

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1. **Biliary Tract Cancer.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Patient has resectable locoregionally 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, resected gross residual, 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.

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2. **Endometrial 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 primary advanced or recurrent disease; AND
   - **C)** Disease is mismatch repair deficient (dMMR); AND
   - **D)** Patient meets ONE of the following (i or ii):

i. The medication is used in combination with carboplatin and paclitaxel; OR
ii. The medication is used as a single agent; 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 approve BOTH of the following (i and ii):
a. 1,120 mg administered as an intravenous infusion not more frequently than once every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles; AND
b. 1,500 mg administered by intravenous infusion no more frequently than once every 4 weeks as a single agent; OR
B) For a patient weighing < 30 kg approve BOTH of the following (i and ii):
a. 15 mg/kg administered as an intravenous infusion not more frequently than once every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles; AND
b. 20 mg/kg administered by intravenous infusion not more frequently than once every 4 weeks as a single agent.

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3. 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 meets BOTH of the following (a and b):
a) Patient has liver-confined, unresectable disease; AND
b) According to the prescriber, the patient is not eligible for transplant; OR
ii. Patient meets BOTH of the following (a and b):
a) Patient has metastatic disease; AND
b) According to the prescriber, the patient is not eligible for resection, transplant, or locoregional therapy; 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.

4. 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, *ROS1*, *BRAF*, *NTRK1/2/3*, *MET*, *RET*, and *ERBB2* (*HER2*). *KRAS G12C* is not considered an actionable mutation (the tumor may be *KRAS G12C* mutation positive).
  - 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) or (2)]:
    1. Epidermal growth factor receptor (*EGFR*) exon 20 mutation positive; OR
    2. *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.

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5. 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

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6. 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.

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7. 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) Patient meets ONE of the following (i or ii):

a. The medication is used in combination with etoposide and platinum chemotherapy; OR

Note: Examples of platinum chemotherapy agents include cisplatin and carboplatin

b. The medication is used as a single agent for maintenance therapy; 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, 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.

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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.

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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

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HISTORY

Type of Revision	Summary of Changes	Review Date
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
Annual Revision	**Biliary Tract Cancer:** Revised locally to locoregionally in "patient has resectable locoregionally advanced disease". Removed recurrent and added resected gross residual in "patient has unresectable, resected gross residual, or metastatic disease". **Endometrial Cancer:** Added new condition of approval. **Hepatocellular Carcinoma:** Removed "metastatic" and added "liver-confined" to criterion patient has "liver-confined, unresectable disease"; and added "according to the prescriber, the patient is not eligible for transplant", as a new option for approval. Added "patient has metastatic disease" and "according to the prescriber, the patient is not eligible for resection, transplant, or locoregional therapy" as a new option for approval. Removed criterion that the patient is not a surgical candidate. **Non-Small Cell Lung Cancer:** Added "*KRAS G12C* is not considered an actionable mutation (the tumor may be *KRAS G12C* mutation positive)" to the Note for criterion the tumor is negative for actionable molecular markers. Removed *KRAS G12C* mutation positive as an option for approval for first-line use of Imfinzi. **Cervical Cancer:** Added medication is used as a single-agent for maintenance therapy as a new option for approval.	07/24/2024
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024