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P&T Date: 06/05/2025

Imfinzi™ (durvalumab)

HCPCS: J9173

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Treatment must follow the FDA approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1 or 2A recommendation
      i. Must be used with concomitant treatment according to FDA indication or NCCN category 1 or 2A recommendation
   b. Must be prescribed by or in consultation with an oncologist
   c. FDA approved age
   d. No prior use or failure with Imfinzi or another program death receptor 1 (PD-L1) inhibitor
   e. Patient is not receiving therapy for a chronic condition, such as autoimmune disease, that requires treatment with a systemic immunosuppressant
   f. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in WyoBlue Advantage's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria:
      i. Unresectable stage III non-small cell lung cancer: Treatment may be continued until disease progression or until unacceptable toxicity occurs, up to maximum of 12 months
      ii. Extensive stage small cell lung cancer: Treatment may be continued until disease progression or until unacceptable toxicity occurs
      iii. Locally advanced or metastatic biliary tract cancer: Treatment may be continued until disease progression or until unacceptable toxicity occurs
      iv. Unresectable hepatocellular carcinoma: Treatment may be continued until disease progression or unacceptable toxicity occurs
      v. Metastatic non-small cell lung cancer: Treatment until unacceptable toxicity or disease progression for up to a total of 24 months of therapy

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Imfinzi is indicated for
    - In combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by Imfinzi 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
    - The treatment of adult patients with unresectable stage III NSCLC who's disease has not progressed following concurrent platinum-based chemotherapy and radiation
    - In combination with 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 adult patients with extensive stage small cell lung cancer (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, for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC)
    - 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)
    - In combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single agent Imfinzi as adjuvant treatment following radical cystectomy, for the treatment of adult patients with muscle invasive bladder cancer (MIBC)
- Efficacy and safety for Imfinzi in non-small cell lung cancer was determined in the PACIFIC trial, a randomized, double-blind, placebo-controlled phase III study of 713 patients with unresectable stage III NSCLC who completed at least 2 prior cycles of concurrent platinum-based chemotherapy and radiation. Patients were randomized to Imfinzi or placebo for up to 12 months or unacceptable toxicity or progressive disease. Treatment was initiated 6 weeks following completion of chemoradiation. Patients must have had an ECOG performance status of 0 – 1 and were excluded if they required systemic immunosuppression. The primary endpoint was progression free survival which was shown to be statistically significant compared to placebo.
- Safety and efficacy for use in extensive disease small cell lung cancer was assessed in the CASPIAN trial, a phase III, randomized, active-control, open-label study of 537 patients with extensive disease small cell lung cancer. The

target population included those with histologically or cytologically documented extensive disease or those with 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. Eligible patients had an ECOG performance status of 0 – 1 and were suitable to receive platinum-based chemotherapy. Patients could not have received prior therapy and were excluded if they required systemic immunosuppression. The primary endpoint was overall survival of Imfinzi plus chemotherapy versus chemotherapy alone. The Imfinzi plus chemotherapy arm had a statistically significant overall survival rate compared to chemotherapy alone.

- Safety and efficacy for use in BTC was investigated in the TOPAZ-1 study, a randomized, double-blind, placebo-controlled, multicenter trial of 685 patients with histologically confirmed locally advanced unresectable or metastatic disease who have not previously received systemic therapy. Patients with recurrent disease greater than 6 months after surgery and/or completion of adjuvant therapy were eligible. Patients had an ECOG performance status of 0 and 1 and least one target lesion by RECIST 1.1. The primary endpoint was overall survival of Imfinzi plus chemotherapy versus chemotherapy alone. The Imfinzi plus chemotherapy arm had a statistically significant overall survival rate compared to chemotherapy alone.

- Safety and efficacy for use in HCC was established in the HIMALAYA trial, a randomized, open-label, multicenter, phase III study of 1,324 patients with unresectable, advanced HCC who had not been treated with prior systemic therapy and were not eligible for locoregional therapy. Patients were randomized to either Imfinzi alone, a single priming dose of Imjudo 300 mg added to Imfinzi 1500 mg followed by Imfinzi monotherapy every four weeks, or sorafenib 400 mg twice daily. The study excluded patients with co-infection of viral hepatitis B and hepatitis C; active or prior documented gastrointestinal (GI) bleeding within 12 months; ascites requiring non-pharmacologic intervention within 6 months; hepatic encephalopathy within 12 months before the start of treatment; and active or prior documented autoimmune or inflammatory disorders. All subjects had a Child-Pugh Score class A and an ECOG performance score of 0 – 1. The primary endpoint was overall survival (OS) between the Imjudo plus Imfinzi arm versus the sorafenib arm. OS improved from a median 13.8 months with sorafenib to 16.4 months with the dual immunotherapy representing a 22% reduction in the risk for death during the study period (HR 0.78; 95% CI: 0.66 - 0.92; p-value = 0.0035). At 3 years, OS rates were an estimated 31% with Imjudo in combination with Imfinzi versus 20% with sorafenib.

- The POSEIDON trial was a randomized, multicenter, active-controlled, open-label, phase III study of 1,013 previously untreated patients with EGFR/ALK wild-type mNSCLC. Patients were randomized to either Imjudo plus Imfinzi and platinum-based chemotherapy for up to four 21-day cycles, followed by Imfinzi once every 4 weeks until progression and one additional Imjudo dose; Imfinzi plus chemotherapy for up to four 21-day cycles, followed by Imfinzi once every 4 weeks until progression; or chemotherapy for up to six 21-day cycles. Chemotherapy options for all arms included carboplatin plus nab-paclitaxel regardless of histology, cisplatin or carboplatin plus gemcitabine for patients with squamous histology, and cisplatin or carboplatin plus pemetrexed for patients with non-squamous histology. Patients with non-squamous histology who received pemetrexed-platinum doublet could receive pemetrexed maintenance therapy if eligible. The study excluded patients with active infection, another primary malignancy, a medical contraindication to platinum-based doublet therapy, and active or prior documented autoimmune or inflammatory disorders. All subjects had an ECOG performance score of 0 – 1. The primary endpoints were progression-free survival (PFS) and OS for Imfinzi + chemotherapy versus chemotherapy. Key alpha-controlled secondary end points were PFS and OS for Imjudo plus Imfinzi and chemotherapy versus chemotherapy. PFS was significantly improved with Imfinzi plus chemotherapy versus chemotherapy (HR = 0.74; 95% CI: 0.62, 0.89; p-value = 0.0009; median 5.5 v 4.8 months); a trend for improved OS did not reach statistical significance (HR = 0.86; 95% CI: 0.72, 1.02; p-value = 0.0758; median 13.3 v 11.7 months; 24-month OS 29.6% v 22.1%). PFS (HR = 0.72; 95% CI: 0.60, 0.86; p-value = 0.0003; median 6.2 v 4.8 months) and OS (HR = 0.77; 95% CI: 0.65, 0.92; p-value = 0.0030; median 14.0 v 11.7 months; 24-month OS 32.9% v 22.1%) were significantly improved with Imjudo plus Imfinzi and chemotherapy versus chemotherapy alone.

- Safety and efficacy for use in combination with neoadjuvant chemotherapy, followed by surgery and continued adjuvant treatment with Imfinzi as a single agent was investigated in the AEGEAN trial, a randomized, double-blind, placebo-controlled, multicenter study of 802 patients with previously untreated and resectable squamous or non-squamous NSCLC. Patients were enrolled regardless of tumor PD-L1 expression. Eligible patients had no prior exposure to immune-mediated therapy, a ECOG performance status of 0 or 1, and at least one target lesion. Patients with active or prior documented autoimmune disease or use of any immunosuppressive medication within 14 days of the first dose of Imfinzi were ineligible. The primary endpoints were pathological complete response (pCR) and event-free survival. The trial demonstrated statistically significant improvements in EFS and pCR rate in the Imfinzi in combination with chemotherapy arm compared to the placebo in combination with chemotherapy arm.

- Safety and efficacy were evaluated in the ADRIATIC study, a randomized, doubleblind, placebo-controlled, multicenter study in 730 patients with histologically or cytologically confirmed LS-SCLC whose disease had not progressed following concurrent chemoradiation therapy (cCRT). Eligible patients completed cCRT consisting of 4 cycles of platinum-based chemotherapy and either 60 - 66 Gy once daily over 6 weeks or 45 Gy twice daily over 3 weeks of radiation therapy within 42 days prior to the first dose of Imfinzi or placebo. Patients with active or prior documented autoimmune disease within 5 years of initiation into the study; a history of active primary immunodeficiency; a history of grade ≥ 2 pneumonitis or active tuberculosis or hepatitis B or C or HIV infection; or active interstitial lung disease were ineligible. Patients with mixed SCLC and NSCLC histology were also ineligible. The primary endpoints were overall survival (OS) and progression free survival (PFS). Imfinzi led to significantly longer OS than placebo (median: 55.9 months [95% CI: 37.3, NR] vs. 33.4 months [95% CI: 25.5, 39.9]; hazard ratio for death: 0.73; 98.321% CI: 0.54, 0.98; p-value = 0.01), as well as to significantly longer PFS (median 16.6 months [95% CI: 10.2, 28.2] vs. 9.2 months [95% CI: 7.4, 12.9]; hazard ratio for progression or death: 0.76; 97.195% CI: 0.59, 0.98; p-value = 0.02).

- Safety and efficacy for use in endometrial cancer were evaluated in the DUO-E trial, a randomized, multicenter, double-blind, placebo-controlled study in patients with advanced or recurrent endometrial cancer. The trial enrolled patients with newly diagnosed stage III disease or newly diagnosed stage IV disease. The trial also enrolled patients with recurrent disease with a low potential for cure by radiation therapy or surgery. For patients with recurrent disease, prior chemotherapy was allowed only if it was administered in the adjuvant setting and at least 12 months had elapsed from the date of last dose of chemotherapy to the date of relapse. Patients with endometrial sarcoma were excluded, and patients who had active autoimmune disease or a medical condition that required immunosuppression were ineligible. The primary endpoint was progression free survival (PFS). Statistically significant PFS benefit was observed in the Imfinzi arm (hazard ratio [HR]: 0.71 [95% CI: 0.57, 0.89]; p-value = 0.003) and the Imfinzi + olaparib arm (HR: 0.55 [95% CI: 0.43, 0.69]; p-value < 0.0001) versus the control arm.

- Safety and efficacy for use in muscle invasive bladder cancer (MIBC) were evaluated in the NIAGRA trial, a randomized, open-label, multicenter study of 1,063 patients who were candidates for radical cystectomy and who had not received prior systemic chemotherapy or immune-mediated therapy for the treatment of NMIBC MIBC. Patients who had active autoimmune disease or a medical condition that required immunosuppression were ineligible. The primary endpoint was event-free survival (EFS) with overall survival (OS) being an additional endpoint. At a pre-specified interim analysis, the trial demonstrated a statistically significant improvement in EFS and OS. Median EFS was not reached (NR) (95% CI: NR, NR) in the Imfinzi with chemotherapy arm and 46.1 months (95% CI: 32.2, NR) in the chemotherapy arm (hazard ratio 0.68 [95% CI: 0.56, 0.82]; two-sided p-value < 0.0001). Median OS was not reached in either arm (hazard ratio 0.75 [95% CI: 0.59, 0.93]; two-sided p-value = 0.0106).

- Imfinzi has not been studied as combination therapy when used to treat non-small cell lung cancer.

- There are no studies to support use of a different PD-L1 when treatment failure has occurred with another. The National Comprehensive Cancer Network guidelines also do not support use of a PD-L1 inhibitor following use of one in a prior line of therapy.

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Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*