Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

# IMFINZI (durvalumab)

**Policy Number:** 5.02.542
**Origination:** 09/2017
**Last Review:** 10/2018
**Next Review:** 10/2019

## Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for IMFINZI when it is determined to be medically necessary because the following criteria have been met.

## When Policy Topic is covered

The use of IMFINZI is considered medically necessary for:

1) The treatment of locally advanced or metastatic **urothelial carcinoma** when **all** of the following criteria are met:

   A. Inoperable or metastatic transitional-cell urothelial carcinoma histologically or cytologically confirmed; **and**

   B. One of the following:

      1. Disease has progressed during or following platinum-containing therapy; **or**

      2. Disease has progressed within 12 months of neoadjuvant or adjuvant treatment with platinum-containing therapy; **and**

   C. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **and**

   D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **and**

   E. Individual does not have *any* of the following:

      1. History of immunodeficiency; **or**

      2. History of severe autoimmune disease; **or**

      3. Require systemic immunosuppression; **or**

      4. Active immune-mediated disease; **or**

      5. Severe or life-threatening infection; **or**

      6. Untreated central nervous system (CNS) metastases.

2) Patients with **unresectable, stage III non-small cell lung cancer (NSCLC)** whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy when ALL of the following criteria are met:

   A. Member is 18 years of age or older, **AND**

B. Member has an ECOG performance status of 0-1, **AND**

C. Member has received at least 2 cycles of platinum-based chemotherapy concurrent with radiation therapy, **AND**

D. Member has not been previously treated with an anti-PD-1 or anti-PD-L1 antibody (i.e., nivolumab, pembrolizumab, atezolizumab, avelumab) , **AND**

E. Member does not have any of the following:

i. Active or prior autoimmune disease or history of immunodeficiency.

ii. Evidence of severe or uncontrolled systemic diseases, including active bleeding diatheses or active infections including hepatitis B, C and HIV.

iii. Evidence of uncontrolled illness such as symptomatic congestive heart failure, uncontrolled hypertension or unstable angina pectoris.

iv. Any unresolved toxicity more than Grade 2 from the prior chemoradiation therapy.

v. Active or prior documented inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis).

**Imfinzi must be provided by a specialty infusion provider.**

## When Policy Topic is not covered

The use of IMFINZI is considered investigational when the above criteria are not met and for all other uses.

## Considerations

IMFINZI requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

## Description of Procedure or Service

Urothelial carcinoma is the most common type of bladder cancer. The American Cancer Society (ACS) estimates that in 2017 there will be approximately 79,030 new cases of bladder cancer (about 60,490 in men and 18,540 in women) and 16,870 deaths from bladder cancer (about 12,240 in men and 4630 in women) in the United States.

IMFINZI is indicated for the treatment of patients with locally advanced or metastatic urothelial cancer. IMFINZI is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that blocks the interaction of programmed cell death ligand 1 (PD-L1) with the PD-1 and CD80 (B7.1) molecules. PD-L1 blockade with IMFINZI led to increased T-cell activation in vitro and decreased tumor size in co-engrafted human tumor and immune cell xenograft mouse models

IMFINZI (IMFINZI) 2017 FDA Product Information label includes the following warnings and precautions:

- Immune-Mediated Pneumonitis: Withhold for moderate and permanently discontinue for severe or life-threatening pneumonitis.

- Immune-Mediated Hepatitis: Monitor for changes in liver function. Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation.
- Immune-Mediated Colitis: Withhold for moderate and permanently discontinue for severe or life-threatening colitis.
- Immune-Mediated Endocrinopathies:
- Adrenal Insufficiency, Hypophysitis, or Type 1 Diabetes Mellitus: Withhold for moderate, severe or life-threatening.
- Immune-Mediated Nephritis: Monitor for changes in renal function. Withhold for moderate and permanently discontinue for severe or life-threatening nephritis.
- Infection: Withhold for severe or life-threatening infection.
- Infusion-Related Reactions: Interrupt infusion or slow the rate of infusion for mild or moderate and permanently discontinue for severe or life-threatening infusion-related reactions.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception.

## Rationale

On May 1, 2017, the U.S. Food and Drug Administration (FDA) approved IMFINZI for the treatment of individuals with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication was approved under an accelerated process and is based on tumor response rate and duration of response. The FDA also included a contingency that continued approval may be based upon verification and description of clinical benefit in confirmatory trials. The FDA approval was based upon an unpublished single arm, open-label study of 182 individuals with locally advanced or metastatic urothelial carcinoma.

In February 2018, Imfinzi was approved for the indication of unresectable, stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy. The FDA approval was based on a multicenter, randomized, double-blind placebo-controlled study (PACIFIC trial) in 713 patients with unresectable stage III NSCLC who completed at least two cycles of concurrent platinum-based chemotherapy and definitive radiation within 42 days prior to initiation of the study. Patients were randomized 2:1 to receive Imfinzi 10mg/kg or placebo intravenously every 2 weeks for up to 12 months or until unacceptable toxicity or confirmed RECIST 1.1-defined progression. Assessment of tumor status was performed every 8 weeks. The median progression-free survival was 16.8 months for Imfinzi (95% CI, 13.0-18.1) vs 5.6 months for placebo (95% CI, 4.6-7.8). The response rate was significantly higher with Imfinzi than with placebo (28.4% vs 16.0%, P<0.001) and 16.5% of those who received Imfinzi vs 27.7% placebo had disease progression. The most frequent adverse events of any grade related to Imfinzi were diarrhea, pneumonitis, rash and pruritus. Grade 3 or 4 adverse events occurred at similar rates in both groups, pneumonia being the most common.

### Urothelial Carcinoma

In an open-label, phase 1/2 study by Massard and colleagues (2016), the safety and efficacy of IMFINZI was investigated. A total of 61 participants with inoperable or metastatic solid tumors were treated with IMFINZI every 2 weeks for up to 12 months. The majority of participants (93.4%) had received one or more prior systemic therapies and 31.1% had received three or more prior systemic therapies. The primary endpoint was safety and the secondary endpoint was objective response rate. Median duration of follow-up was 4.3 months. A total of 63.9% (39/61) individuals reported a treatment

related adverse event (AE). The most common AEs were low grade and included fatigue, diarrhea, and decreased appetite. There were 3 participants who experienced grade 3 AEs and there were no reported grade 4 or 5 events. In 42 participants, the objective response rate was 31.0% (95% confidence interval [CI], 17.6 to 47.1) and 46.4% (95% CI, 27.5 to 66.1) in the PD-L1-positive subgroup, and 0% (95% CI, 0.0 to 23.2) in the PD-L1-negative subgroup.

The National Comprehensive Cancer Network (NCCN) Bladder Cancer Guidelines (V2. 2017) indicate that IMFINZI is a PD-L1 inhibitor which is in clinical trials to evaluate its activity in the treatment of bladder cancer. There are no recommendations regarding treatment at this time.

**Other Potential Uses**

Clinical trials are in progress to study the use of IMFINZI as monotherapy and in combination with other medications as first-line therapy for metastatic urothelial cancer. There are several ongoing phase 3 trials involving the use of IMFINZI as a monotherapy or in combination with other treatments for non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck, hairy cell leukemia and multiple myeloma (Jelinek, 2016; Kumar, 2016).

**References**

**Peer Reviewed Publications:**


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3. Kumar R, Collins D, Dolly S, et al. Targeting the PD-1/PD-L1 axis in non-small cell lung cancer. Curr Probl Cancer. 2016. pii: S0147-0272(16)30188-X.
4. Levy A, Massard C, Soria JC, Deutsch E. Concurrent irradiation with the anti-programmed cell death ligand-1 immune checkpoint blocker IMFINZI: Single centre subset analysis from a phase 1/2 trial. Eur J Cancer. 2016; 68:156-162.
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**Government Agency, Medical Society, and Other Authoritative Publications:**


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2. NCCN Clinical Practice Guidelines in Oncology™. © 2017 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on March 7, 2017.

- Bladder Cancer. V2.2017. Revised February 15, 2017.
- Non-Small Cell Lung Cancer. V4.2017. Revised January 18, 2017.

3. IMFINZI™ (IMFINZI) [Product Information]. Wilmington, DE. AstraZeneca. February 2018.


**Websites for Additional Information**


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2. National Cancer Institute (NCI). NCI Drug Dictionary. IMFINZI. Available at: https://www.cancer.gov/publications/dictionaries/cancer-drug?cdrid=740856. Accessed on March 3, 2017.


## Billing Coding/Physician Documentation Information

IMFINZI is considered a medical benefit; specialty infusion sourcing

## Additional Policy Key Words

5.02.542

## Policy Implementation/Update Information

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| 09/2017 | New policy titled IMFINZI (durvalumab) |
| 07/2018 | Add NSCLC indication |
| 10/2018 | No changes made |
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