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: 10/2023
Next Review: 10/2024

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 in adults for:

1. **Non-Small Cell Lung Cancer**
    - 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.
    - IMFINZI, in combination with tremelimumab-actl and platinum-based chemotherapy, is indicated 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.
2. **Small cell lung cancer, extensive stage**
    - IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)
3. **Biliary tract carcinoma, locally advanced or metastatic**
    - IMFINZI, in combination with gemcitabine and cisplatin, is indicated for the treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC).
4. **Hepatocellular carcinoma, unresectable**
    - IMFINZI in combination with tremelimumab-actl, is indicated for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC).

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.

NCDs
https://www.cms.gov/medicare-coverage-database/search-results.aspx?keyword=&keywordType=starts&areaId=s29&docType=NCD&contractOption=all

LCDs
https://www.cms.gov/medicare-coverage-database/search-results.aspx?keyword=&keywordType=starts&areaId=s29&docType=F,P&contractOption=all

Description of Procedure or Service

Durvalumab is a human immunoglobulin G1 kappa monoclonal antibody which blocks programmed cell death ligand 1 (PD-L1) binding to PD-1 and CD80 (B7.1); PD-L1 blockade leads to increased T-cell activation, allowing T-cells to kill tumor cells (Massard 2016). PD-L1 is an immune check point protein expressed on tumor cells and tumor infiltrating cells and down regulates anti-tumor t-cell function by binding to PD-1 and B7.1; blocking PD-1 and B7.1 interactions restores antitumor t-cell function.

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, Thyroid Disorders (Thyroiditis, Hyperthyroidism, and Hypothyroidism), 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.
- Immune-Mediated Dermatology Reactions: Exfoliative dermatitis (Stevens-Johnson Syndrome, Drug Rash with Eosinophilia and Systemic Symptoms, and Toxic Epidermal Necrolysis).
- 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.
- Complications of Allogeneic HSCT: Consider the benefit versus risks of treatment with PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.
- Lactation: Advise women not to breastfeed during treatment and for 3 months after the last dose.

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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Government Agency, Medical Society, and Other Authoritative Publications:

1. American Cancer Society (ACS). Key Statistics for Bladder Cancer. Revised on January 5, 2017. Available at: https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html. Accessed on March 20, 2017.

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

1. American Cancer Society. Immune checkpoint inhibitors to treat cancer. Last revised February 3, 2017. Available at: https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html. Accessed on March 7, 2017.

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.

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Billing Coding/Physician Documentation Information

IMFINZI is considered a medical benefit; specialty infusion sourcing	
J9173	Injection, durvalumab, 10 mg

Additional Policy Key Words

5.02.542

Policy Implementation/Update Information

09/2017	New policy titled IMFINZI (durvalumab)
07/2018	Add NSCLC indication
10/2018	No changes made
10/2019	Annual review – no changes made
10/2020	Updated to include indication for small cell lung cancer, extensive stage
10/2021	Annual review – no changes made
10/2022	Annual review – added new FDA approved indication #4
07/2023	Updated to include hepatocellular carcinoma, unresectable and warnings and precautions
10/2023	Annual review – no changes made