BlueCross BlueShield
Federal Employee Program.

IMBRUVICA
(ibrutinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Imbruvica is a kinase inhibitor that is used to treat different types of cancer and chronic graft versus host disease. Imbruvica is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. Studies show that Imbruvica inhibits B-cell proliferation and survival (1).

Regulatory Status

FDA-approved indications: Imbruvica is a kinase inhibitor indicated for the treatment of patients with: (1)

1. Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
2. Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion
3. Adult patients with Waldenström's macroglobulinemia (WM)/lymphoplasmacytic lymphoma
4. Adult and pediatric patients 1 year and older with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy

Off-Label Uses: (2-4)

1. Follicular lymphoma (FL)
2. Diffuse large B-cell lymphoma (DLBCL)

The B-cell antigen receptor (BCR) pathway is implicated in the pathogenesis of several B-cell malignancies, including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-cell lymphoma (MCL), and B-cell chronic lymphocytic leukemia (CLL). Bruton's tyrosine kinase (BTK) is a critical signaling kinase in this pathway. Imbruvica is an irreversible inhibitor of the BTK in patients with B-cell malignancies (2).

Patients treated with Imbruvica have a chance of Grade 3 or higher bleeding events (subdural hematoma, gastrointestinal bleeding, and hematuria). Imbruvica may increase the risk of

hemorrhage in patients receiving antiplatelet or anticoagulant therapies. Consider the benefit-risk of withholding Imbruvica for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding (1).

Significant adverse reactions may occur with Imbruvica therapy including fatal and non-fatal infections, hemorrhage, cardiac arrhythmias and cardiac failure, hypertension, cytopenias, second primary malignancies, and tumor lysis syndrome. Patients should have the following monitored while on Imbruvica therapy: fever, infections, complete blood counts, creatinine levels, and hydration (1).

Advise women to avoid becoming pregnant while taking Imbruvica. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus (1).

The safety and effectiveness of Imbruvica in pediatric patients less than 1 years of age with cGVHD has not been established. The safety and effectiveness of Imbruvica in pediatric patients less than 18 years of age for all other indications has not been established (1).

Summary

Imbruvica is an orally administered kinase inhibitor indicated for the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), Waldenstrom's macroglobulinemia (WM), and chronic graft versus host disease (cGVHD). Warnings include infections, hemorrhage, cardiac arrhythmias and cardiac failure, hypertension, cytopenias, second primary malignancies, and tumor lysis syndrome. The safety and effectiveness of Imbruvica in pediatric patients less than 1 years of age with cGVHD has not been established. The safety and effectiveness of Imbruvica in pediatric patients less than 18 years of age for all other indications has not been established (1-4).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Imbruvica while maintaining optimal therapeutic outcomes.

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References

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2. Advani, RH, Buggy JJ, et al. Bruton tyrosine kinase inhibitor ibrutinib (PCI-32765) has significant activity in patients with relapsed/refractory B-cell malignancies. J Clin Oncol. 2013 Jan 1; 31(1):88-94.
3. NCCN Drugs & Biologics Compendium® Ibrutinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 14, 2025.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 1.2025). National Comprehensive Cancer Network, Inc. December 2024. Accessed on January 14, 2025.