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5.21.41

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 7, 2014
Subject:	Imbruvica	**Page:**	1 of 6

Last Review Date: June 16, 2022

Imbruvica

Description

Imbruvica (ibrutinib)

Background
Imbruvica is a kinase inhibitor that is used to treat B-cell malignancies. Lymphoma is the most common blood cancer and occurs when lymphocytes, a form of white blood cell, grow and multiply uncontrollably. Imbruvica inhibits the enzyme needed by the cancer to multiply and spread (1).

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

1. Mantle cell lymphoma (MCL) who have received at least one prior therapy
2. Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
3. Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion
4. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
5. Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
6. Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy

Off-Label Uses: (2-4)

1. Follicular lymphoma
2. Diffuse large B-cell lymphoma

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, mantle-cell lymphoma, and B-cell chronic lymphocytic leukemia (CLL). Bruton 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 with MCL and CLL 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, myelosuppression, renal toxicity, hepatic toxicity and primary malignancies including skin cancers. 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 has not been established (1).

Related policies
Aliqopa, Arzerra, Bendeka, Brukinsa, Calquence, Copiktra, Gazyva, Revlimid, Rituxan, Treanda, Zydelig

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Imbruvica may be considered **medically necessary** in patients who are 18 years of age or older with a confirmed diagnosis of mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma, follicular lymphoma, diffuse large B-cell lymphoma,small lymphocytic lymphoma (SLL), marginal zone lymphoma (MZL), or chronic graft versus host disease (cGVHD) and if the conditions indicated below are met.

Imbruvica may be considered **investigational** in patients who are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
    a. The patient has received at least one prior therapy
2. Chronic lymphocytic leukemia (CLL)
3. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
4. Follicular lymphoma
5. Diffuse large B-cell lymphoma
6. Small lymphocytic lymphoma (SLL)
7. Marginal zone lymphoma (MZL) who require systemic therapy
    a. The patient has received at least one prior anti-CD20-based therapy
8. Chronic graft versus host disease (cGVHD)
    a. The patient has received at least one prior systemic therapy

AND ALL of the following:

1. Prescriber agrees to monitor for bleeding and malignancies
2. Prescriber agrees to monitor CBC for cytopenias

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
2. Chronic lymphocytic leukemia (CLL)
3. Waldenström's macroglobulinemia/ lymphoplasmacytic lymphoma
4. Follicular lymphoma
5. Diffuse large B-cell lymphoma
6. Small lymphocytic lymphoma (SLL)

7. Marginal zone lymphoma (MZL)
8. Chronic graft versus host disease (cGVHD)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for bleeding and malignancies
3. Prescriber agrees to monitor CBC for cytopenias

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity
70 mg	84 capsules per 84 days **OR**
140 mg	90 capsules per 90 days **OR**
140 mg	84 tablets per 84 days **OR**
280 mg	84 tablets per 84 days **OR**
420 mg	84 tablets per 84 days **OR**
560 mg	84 tablets per 84 days

Maximum daily limit of any combination: 560 mg

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Imbruvica is an orally administered kinase inhibitor indicated for the treatment of patients with mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL) who have received at least one prior therapy or in patients with CLL and SLL. Imbruvica has also shown effectiveness in diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, marginal zone lymphoma (MZL) and chronic graft versus host disease (cGVHD). Current warnings include the possibility for

hemorrhage, myelosuppression, renal toxicity, hepatic toxicity and primary malignancies including skin cancers. The safety and effectiveness of Imbruvica in pediatric patients 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.

References

1. Imbruvica [package insert]. Horsham, PA: Janssen Biotech, Inc; December 2020.
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 2022. National Comprehensive Cancer Network, Inc. Accessed on April 18, 2022.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2022). National Comprehensive Cancer Network, Inc. March 2022. Accessed on April 18, 2022.

Policy History

Date	Action
March 2014	New addition to PA
September 2014	Addition that the FDA indication of chronic lymphocytic leukemia (CLL) with 17p deletion does not require failure on prior therapy for CLL. Removal of the following criteria requirements: no baseline hepatic impairment, Physician agrees to monitor for: Hemorrhage, Myelosuppression with complete blood counts monthly, Renal toxicity by checking creatinine levels periodically, Second primary malignancies including skin cancers.
December 2014	Annual editorial review and reference update
February 2015	Addition of Waldenström's macroglobulinemia, follicular lymphoma and diffuse large B-cell lymphoma
June 2015	Annual editorial review and reference update
March 2016	Addition of Small lymphocytic lymphoma (SLL) and removal of who have received at least one prior therapy or in patients with chronic lymphocytic leukemia with 17p deletion Policy number change from 5.04.41 to 5.21.41
June 2016	Annual review
September 2016	Annual review

February 2017	Addition of marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
June 2017	Annual editorial review Addition of age requirements to renewal criteria
August 2017	Addition of chronic graft versus host disease (cGVHD)
September 2017	Annual review
March 2018	Annual editorial review Addition of quantity limits
March 2019	Annual review and reference update
September 2019	Addition of “maximum daily limit of any combination: 560 mg”
December 2019	Annual review and reference update
March 2020	Annual review and reference update. Removed systemic therapy requirement from MZL diagnosis for renewal. Added requirements to monitor for bleeding and malignancies and monitor CBC for cytopenias. Also added renewal requirement of no disease progression or unacceptable toxicity per SME
June 2021	Annual review and reference update
December 2021	Annual review and reference update
June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.