

5.21.041

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	1 of 7

---

**Last Review Date:** December 2, 2022

---

## Imbruvica

### Description

#### Imbruvica (ibrutinib)

#### 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 indication: Imbruvica is a kinase inhibitor indicated for the treatment of patients with: (1)

1. Adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
2. Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
3. Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion
4. Adult patients with Waldenström's macroglobulinemia (WM)/lymphoplasmacytic lymphoma
5. Adult patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
6. 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

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	2 of 7

---

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 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, 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).

**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.*

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	3 of 7

---

Imbruvica may be considered **medically necessary** in patients with mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), Waldenström's macroglobulinemia (WM)/lymphoplasmacytic lymphoma, follicular lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), 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** 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 (WM)/lymphoplasmacytic lymphoma
4. Follicular lymphoma (FL)
5. Diffuse large B-cell lymphoma (DLBCL)
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

**AND ALL** of the following:

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

**Age** 1 year of age and older

### Diagnosis

Patient must have the following:

1. Chronic graft versus host disease (cGVHD)

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	4 of 7

---

- 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 (WM)/ lymphoplasmacytic lymphoma
4. Follicular lymphoma (FL)
5. Diffuse large B-cell lymphoma (DLBCL)
6. Small lymphocytic lymphoma (SLL)
7. Marginal zone lymphoma (MZL)

**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

**Age** 1 year of age and older

### Diagnosis

Patient must have the following:

1. 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

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	5 of 7

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

#### Quantity

Strength	Daily Dosing Limits
70 mg	560 mg per day
140 mg	
140 mg	
280 mg	
420 mg	
560 mg	
70 mg/mL oral suspension	

**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)/small lymphocytic lymphoma (SLL), Waldenstrom’s macroglobulinemia (WM), marginal zone lymphoma (MZL), 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.

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	6 of 7

## References

1. Imbruvica [package insert]. Horsham, PA: Janssen Biotech, Inc; August 2022.
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<sup>®</sup> Ibrutinib 2022. National Comprehensive Cancer Network, Inc. Accessed on October 7, 2022.
4. NCCN Clinical Practice Guidelines in Oncology<sup>®</sup> B-Cell Lymphomas (Version 5.2022). National Comprehensive Cancer Network, Inc. July 2022. Accessed on October 7, 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

# 5.21.041

---

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	January 1, 2023
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	March 7, 2014
<b>Subject:</b>	Imbruvica	<b>Page:</b>	7 of 7

---

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
September 2022	Per PI update, revised age for cGVHD to 1 year and older from 18 and older. Added oral suspension to quantity chart and also revised chart to remove quantities and set all dosage forms and strengths at 560 mg per day
December 2022	Annual review and reference update

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2022 and is effective on January 1, 2023.**