

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Imbruvica Prior Authorization Policy

- Imbruvica® (ibrutinib tablets, capsules, and oral suspension – Pharmacyclics/Janssen)

**REVIEW DATE:** 06/12/2024

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### OVERVIEW

Imbruvica, a Bruton’s tyrosine kinase inhibitor, is indicated for the following uses:<sup>1</sup>

- **Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)**, in adults.
- **CLL or SLL**, with 17p deletion, in adults.
- **Graft-versus-host disease, chronic**, after failure of one or more lines of systemic therapy in adults and pediatric patients  $\geq$  1 year old.
- **Waldenström macroglobulinemia**, in adults.

### Guidelines

Imbruvica is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **B-Cell Lymphomas:** NCCN guidelines (version 2.2024 – April 30, 2024) address mantle cell lymphoma, marginal zone lymphoma, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, non-gastric MALT lymphoma, diffuse large B-cell lymphomas, Acquired Immune Deficiency Syndrome (AIDS)-related B-Cell lymphomas, and post-transplant lymphoproliferative disorders.<sup>2</sup> For mantle cell lymphoma, Imbruvica + rituximab can be used as pretreatment in order to limit the number of cycles of aggressive induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen (category 2A); Imbruvica  $\pm$  rituximab is recommended as second-line and subsequent therapy as “other recommended regimen” and Imbruvica + venetoclax as “useful in certain circumstances” (both category 2A).<sup>2</sup> Imbruvica is recommended as a preferred aggressive induction therapy as a component of TRIANGLE regimen: alternating RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) + covalent Bruton tyrosine kinase inhibitor (Imbruvica)/RDHAP (rituximab, dexamethasone, and cytarabine) + carboplatin regimen (category 2A). Imbruvica can also be used in combination with rituximab as maintenance therapy (category 2A). For marginal zone lymphoma, Imbruvica is recommended as second-line and subsequent therapy as “other recommended regimens” (category 2A). For mantle cell and marginal zone lymphoma, there is a footnote that states head-to-head clinical trials in other B-cell malignancies have demonstrated a more favorable toxicity profile for Calquence and Brukinsa compared to Imbruvica without compromising efficacy. The NCCN compendium recommends Imbruvica as a second-line and subsequent therapy for diffuse large B-cell lymphomas, human immunodeficiency virus (HIV)-related B-Cell lymphomas, post-transplant lymphoproliferative disorders, and high-grade B-cell lymphoma (category 2A).<sup>3</sup>
- **Central Nervous System (CNS) Cancers:** NCCN guidelines (version 1.2024 – May 31, 2024) recommend Imbruvica as one of the options for patients with relapsed or refractory disease for primary CNS lymphoma as “other recommended regimens” (category 2A).<sup>4</sup> The guidelines also recommend Imbruvica for induction therapy as a single agent as “useful in certain circumstances” if the patient is unsuitable for or intolerant to high-dose methotrexate (category 2A).<sup>4</sup> Imbruvica is used with high-dose methotrexate and rituximab in some clinical scenarios (category 2A).<sup>4</sup> Imbruvica is also recommended as treatment for brain metastases in lymphoma (category 2A).
- **CLL/SLL:** NCCN guidelines (version 3.2024 – March 26, 2024) recommend Imbruvica as a treatment option in various scenarios (e.g., first-line therapy for patients with or without 17p

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deletion/TP53 mutation and as second-line and third therapy [category 1 recommendations for many scenarios]) as “other recommended regimens”.<sup>5</sup> Imbruvica plays a vital role in the management of CLL/SLL and many trials describe its efficacy.<sup>5</sup>

- **Hairy Cell Leukemia:** NCCN guidelines (version 2.2024 – April 22, 2024) recommend Imbruvica as one of the options for treatment of progressive disease after therapy for relapsed or refractory disease as “other recommended regimens” (category 2A).<sup>6</sup>
- **Graft-Versus-Host Disease:** NCCN guidelines for hematopoietic stem cell transplantation (version 1.2024 – April 26, 2024) recommend Imbruvica as a systemic agent for steroid-refractory chronic graft-versus-host disease after failure of one or more lines of systemic therapy in patients  $\geq 1$  years of age (category 2A).<sup>7</sup> The guidelines note that Imbruvica should be used with caution in patients with of heart arrhythmias or heightened risk of bleeding.
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphomas:** NCCN guidelines (version 2.2024 – December 5, 2023) recommend Imbruvica, with or without rituximab, as a primary therapy option as one of several “preferred” regimens (category 1).<sup>8</sup> For previously treated patients, Imbruvica, with or without rituximab, is also cited as a “preferred” regimen (category 1). Imbruvica is also a “preferred” regimen for symptomatic management of Bing Neel Syndrome (category 2A).<sup>8</sup>

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Imbruvica. All approvals are provided for the duration noted below.

**Automation:** When available, the ICD-9/ICD-10 codes for patients  $\geq 18$  years of age with chronic lymphocytic leukemia (ICD-9: 204.1\* [lymphoid leukemia chronic] and ICD-10: C91.1\* [chronic lymphocytic leukemia of B-cell type]), small lymphocytic lymphoma (ICD-10: C83.0\* [small cell B-cell lymphoma]) and Waldenström macroglobulinemia (ICD-9: 273.3\* [macroglobulinemia] and ICD-10: C88.0\* [Waldenström macroglobulinemia]) will be used as part of automation to allow approval of the requested medication.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Imbruvica is recommended in those who meet one of the following criteria:

### FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia.** Approve for 1 year if the patient is  $\geq 18$  years of age.
2. **Graft-Versus-Host Disease, Chronic:** Approve for 1 year if the patient meets BOTH of the following (A and B):
  - A) Patient is  $\geq 1$  year of age; AND
  - B) Patient has tried at least one conventional systemic treatment for graft-versus-host disease.  
Note: Examples of conventional systemic treatments include: corticosteroids (methylprednisolone, prednisone), imatinib, low-dose methotrexate, sirolimus, mycophenolate mofetil, and Jakafi (ruxolitinib tablets).
3. **Small Lymphocytic Lymphoma.** Approve for 1 year if the patient is  $\geq 18$  years of age.
4. **Waldenström Macroglobulinemia.** Approve for 1 year if the patient is  $\geq 18$  years of age.  
Note: This includes lymphoplasmacytic lymphoma and Bing-Neel syndrome.

### Other Uses with Supportive Evidence

- 5. B-Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):  
Note: Examples of B-cell lymphomas include: diffuse large B-cell lymphomas, Human immunodeficiency virus (HIV)-related B-cell lymphomas, post-transplant lymphoproliferative disorders, and high-grade B-cell lymphoma.  
A) Patient is  $\geq 18$  years of age; AND  
B) Patient has tried at least one systemic regimen.  
Note: Examples of a systemic regimen include one or more of the following products: cisplatin, cytarabine, rituximab, oxaliplatin, gemcitabine, ifosfamide, carboplatin, etoposide, or rituximab.
- 6. Central Nervous System Lymphoma (Primary).** Approve for 1 year if the patient meets BOTH of the following (A and B):  
A) Patient  $\geq 18$  years of age; AND  
B) Patient meets ONE of the following (i or ii):  
i. According to the prescriber, the patient is not a candidate for or is intolerant to high-dose methotrexate; OR  
ii. Patient has tried at least one therapy.  
Note: Examples of therapies include methotrexate, rituximab, vincristine, procarbazine, cytarabine, thiotepea, carmustine, intrathecal methotrexate, cytarabine, or rituximab.
- 7. Hairy Cell Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):  
A) Patient is  $\geq 18$  years of age; AND  
B) Patient has tried at least two systemic regimens.  
Note: Examples of a systemic regimen include one or more of the following products: cladribine, Nipent (pentostatin injection), rituximab, or Pegasys (peginterferon alfa-2a subcutaneous injection).
- 8. Mantle Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):  
A) Patient is  $\geq 18$  years of age; AND  
B) Patient meets ONE of the following (i, ii, or iii):  
i. Patient is continuing therapy with Imbruvica and meets ONE of the following (a or b):  
a) Patient has tried at least one systemic regimen; OR  
Note: Examples of a systemic regimen include one or more of the following products: bendamustine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, cytarabine, carboplatin, cisplatin, oxaliplatin, or lenalidomide.  
b) According to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail); OR  
ii. Imbruvica is used in combination with rituximab prior to induction therapy; OR  
Note: Examples of induction therapy include: rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone.  
iii. Imbruvica is used as induction or maintenance therapy in combination with chemotherapy.

**Marginal Zone Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B and C):

Note: Marginal zone lymphoma includes gastric mucosa-associated lymphoid tissue (MALT) lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma.

A) Patient is  $\geq 18$  years of age; AND

B) Patient is continuing therapy with Imbruvica; AND

C) Patient has tried at least one systemic regimen.

Note: Examples of a systemic regimen include one or more of the following products: bendamustine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, or lenalidomide.

### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Imbruvica is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

1. Imbruvica® tablets, capsules, and oral solution [prescribing information]. Sunnyvale, CA and Horsham, PA: Pharmacyclics/Janssen; May 2024.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 4, 2024.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed June 4, 2024. Search term: ibrutinib.
4. The NCCN Central Nervous System Cancers Guidelines in Oncology (version 1.2024 – May 31, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 4, 2024.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2024 – March 26, 2024). © 2024 National Comprehensive Cancer Network. Available at <http://www.nccn.org>. Accessed on June 4, 2024.
6. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 2.2024 – April 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 4, 2024.
7. The NCCN Hematopoietic Cell Transplantation (HCT) Guidelines in Oncology (version 1.2024 – April 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 4, 2024.
8. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 4, 2024.