PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Imbruvica Prior Authorization Policy
- Imbruvica® (ibrutinib tablets, capsules, and oral suspension – Pharmacyclics/Janssen)

REVIEW DATE: 06/12/2024

OVERVIEW

Imbruvica, a Bruton's tyrosine kinase inhibitor, is indicated for the following uses:[1]

- **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 ≥ 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.[2] 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 ± rituximab is recommended as second-line and subsequent therapy as "other recommended regimen" and Imbruvica + venetoclax as "useful in certain circumstances" (both category 2A).[2] 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).[3]
- **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).[4] 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).[4] Imbruvica is used with high-dose methotrexate and rituximab in some clinical scenarios (category 2A).[4] 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

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

- **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).[6]
- **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 ≥ 1 years of age (category 2A).[7] 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).[8] 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).[8]

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 ≥ 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 ≥ 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 ≥ 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 ≥ 18 years of age.

4. **Waldenström Macroglobulinemia.** Approve for 1 year if the patient is ≥ 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 ≥ 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 ≥ 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, thiotepa, 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 ≥ 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 ≥ 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 ≥ 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.