VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 07/13/2022; selected revision 08/31/2022, 04/19/2023, and 05/24/2023

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**, in adults and pediatric patients ≥ 1 year old after failure of one or more lines of systemic therapy.
- **Waldenström macroglobulinemia,** in adults.

Guidelines

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

- **B-Cell Lymphomas:** NCCN guidelines (version 3.2023 – May 11, 2023) 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 is also recommended as second-line and subsequent therapy (category 2A).[2] For marginal zone lymphoma, Imbruvica is recommended 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 diffuse large B-cell lymphomas, AIDS-related B-Cell lymphomas, post-transplant lymphoproliferative disorders, double/triple hit lymphoma, and high-grade B-cell lymphoma (category 2A).[3]
- **Central Nervous System (CNS) Cancers**: NCCN guidelines (version 1.2022 – June 2, 2022) recommend Imbruvica as one of the options for patients with relapsed or refractory disease for primary CNS lymphoma (category 2A).[4] The guidelines also recommend Imbruvica (category 2A) for induction therapy as a single agent (useful in certain circumstances) if the patient is unsuitable for or intolerant to high-dose methotrexate.[4] Imbruvica is used with high-dose methotrexate and rituximab in some clinical scenarios.[4]
- **CLL/SLL:** NCCN guidelines (version 3.2022 – June 3, 2022) 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 subsequent therapy [category 1 recommendations for many scenarios]).[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 1.2022 – September 8, 2021) recommend Imbruvica as one of the options for treatment of relapsed or refractory disease after progression on another therapy (category 2A).[6]
- **Graft-Versus-Host Disease:** NCCN guidelines for hematopoietic stem cell transplantation (version 1.2022 – April 1, 2022) recommend Imbruvica as a systemic agent for steroid-refractory

chronic graft-versus-host disease after failure of one or more lines of systemic therapy (category 2A).[7]

- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphomas:** NCCN guidelines (version 1.2023 – July 6, 2022) 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 the following criteria (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 the following criteria (A and B):
   Note: Examples of B-cell lymphomas include: diffuse large B-cell lymphomas, Acquired Immune Deficiency Syndrome (AIDS)-related B-cell lymphomas, post-transplant lymphoproliferative disorders, double/triple hit lymphoma, 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 the following criteria (A and B):
   A) Patient ≥ 18 years of age; AND
   B) Patient meets one of the following criteria (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 the following criteria (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 the following criteria (A, B and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient is continuing therapy with Imbruvica; AND
   C) Patient meets one of the following criteria: (i or ii):
      i. Patient meets one of the following criteria (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.
      Note: Examples of induction therapy include: rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone.

9. **Marginal Zone Lymphoma.** Approve for 1 year if the patient meets the following criteria (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 2023.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 3.2023 – May 11, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 22, 2023.
3. The NCCN Drugs and Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 11, 2022. Search term: ibrutinib.
4. The NCCN Central Nervous System Cancers Guidelines in Oncology (version 1.2022 – June 2, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 11, 2022.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2022 – June 3, 2022). © 2022 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on July 11, 2022.
6. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 1.2022 – September 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 11, 2022.
7. The NCCN Hematopoietic Cell Transplantation (HCT): Pre-Transplantation Recipient Evaluation and Management of Graft-Versus-Host Disease (version 1.2022 – April 1, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 11, 2022.
8. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – July 6, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 11, 2022.

HISTORY

Type of Revision	Summary of Change	Review Date
Annual Revision	**Graft-Versus-Host Disease, Chronic**: A requirement was added that the patient is ≥ 18 years of age. **Marginal Zone Lymphoma:** A requirement was added that the patient is ≥ 18 years of age. A Note was added with the types of marginal zone lymphoma. A requirement was added that the patient has to try at least one systemic regimen. A Note was added with the examples of systemic regimens. **B-Cell Lymphoma**: A requirement was added that the patient is ≥ 18 years of age. The requirement that the " according to the prescribing physician, the patient is using the agent as second line or subsequent therapy" was changed to "patient has tried at least one systemic regimen." A Note was added with examples of systemic regimens. **Central Nervous System Lymphoma (Primary):** A requirement was added that the patient is ≥ 18 years of age. The requirement that the "according the prescribing physician, the patient has relapsed or refractory disease" was changed to "patient has tried at least one therapy," and a Note was added with examples of therapies. Also, the following qualifier was added, "according to the prescriber, the patient is not a candidate for or is intolerant to high-dose methotrexate." **Hairy Cell Leukemia:** A requirement was added that the patient is ≥ 18 years of age. The requirement that "according to the prescribing physician the patient has relapsed or refractory disease" was changed to "patient has tried at least two systemic regimens." A Note was added with examples of systemic regimens.	06/30/2021
Selected Revision	Automation was updated to include an age requirement that the patient is ≥ 18 years of age. Mantle cell lymphoma was removed from the automation. **Chronic Lymphocytic Leukemia:** A requirement was added that the patient is ≥ 18 years of age. **Mantle Cell Lymphoma:** A requirement was added that the patient is ≥ 18 years of age. A requirement was added that the patient has to try at least one systemic regimen or that Imbruvica is used in combination with rituximab prior to induction therapy . A Note was added with the examples of systemic regimens. A note was added with examples of induction therapy. **Small Lymphocytic Lymphoma:** A requirement was added that the patient is ≥ 18 years of age. **Waldenström Macroglobulinemia:** A requirement was added that the patient is ≥ 18 years of age.	07/28/2021

Selected Revision	**Chronic Lymphocytic Leukemia:** The duration of approval was changed from 3 years to 1 year. **Mantle Cell Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Marginal Zone Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Small Lymphocytic Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Waldenström Macroglobulinemia:** The duration of approval was changed from 3 years to 1 year. **B-Cell Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Central Nervous System Lymphoma (Primary):** The duration of approval was changed from 3 years to 1 year. **Hairy Cell Leukemia:** The duration of approval was changed from 3 years to 1 year.	06/22/2022
Annual Revision	**Waldenström Macroglobulinemia:** A note was included that states this includes lymphoplasmacytic lymphoma and Bing-Neel syndrome.	07/13/2022
Selected Revision	The oral suspension formulation was added to the policy with the same criteria previously in place for Imbruvica tablets and capsules. The overview section was updated to include "adults and pediatrics ≥ 1 year of age" for chronic graft-versus-host disease due to new FDA-approved indication. **Graft-Versus-Host Disease, Chronic:** The age requirement was changed from ≥ 18 years of age to ≥ 1 year of age due to new pediatric FDA labeling.	08/31/2022
Selected Revision	**Mantle Cell Lymphoma:** An alternative option of approval was added to the requirement for a trial of one systemic regimen that according to the prescriber, the patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail).	04/19/2023
Selected Revision	**Mantle Cell Lymphoma:** This indication was moved from the FDA-approved indication section to Other Uses with Supportive Evidence section due to FDA removal of this indication from labeling. Criteria now only applies to patients who are continuing therapy with Imbruvica. **Marginal Zone Lymphoma:** This indication was moved from the FDA-approved indication section to Other Uses with Supportive Evidence section due to FDA removal of this indication from labeling. Criteria now only applies to patients who are continuing therapy with Imbruvica.	05/24/2023