PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 07/12/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

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 4.2023 – June 2, 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 ± 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 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, 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 1.2023 – March 24, 2023) 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.[4] Imbruvica is also recommended as treatment for brain metastases in lymphoma (category 2A).
- **CLL/SLL:** NCCN guidelines (version 3.2023 – June 12, 2023) 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 1.2023 – August 30, 2022) recommend Imbruvica as one of the options for treatment of progressive disease after therapy for relapsed or refractory disease (category 2A).[6]
- **Graft-Versus-Host Disease:** NCCN guidelines for hematopoietic stem cell transplantation (version 1.2023 – March 31, 2023) 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] The guidelines note that Imbruvica should be used with caution in patients with history of heart arrhythmias or heightened risk of bleeding.
- **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.

Imbruvica® (ibrutinib tablets, capsules, and oral suspension (Pharmacyclics/Janssen)
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 (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 (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 the following (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 (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 (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets one of the following (i, iii, or iii):
      i. Patient is continuing therapy with Imbruvica and 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; 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.

9. **Marginal Zone Lymphoma.** Approve for 1 year if the patient meets 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 COVERED

**Imbruvica® (ibrutinib tablets, capsules, and oral suspension (Pharmacyclics/Janssen)
is(are) considered experimental, investigational or unproven for ANY other use(s).**

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 4.2023 – June 2, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 3, 2023.
3. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 3, 2023. Search term: ibrutinib.
4. The NCCN Central Nervous System Cancers Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 3, 2023.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2023 – June 12, 2023). © 2023 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on July 3, 2023.
6. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 1.2023 – August 30, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 3, 2023.
7. The NCCN Hematopoietic Cell Transplantation (HCT) Guidelines in Oncology (version 1.2023 – March 31, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 3, 2023.
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 3, 2023.

HISTORY

Type of Revision	Summary of Change	Review Date
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	05/24/2023

	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.	
Annual Revision	**Mantle Cell Lymphoma**: The requirement that the patient is continuing therapy now only applies to a patient that has tried at least one systemic regimen or according to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail); previously this criteria only approved for patients continuing therapy. An alternative option of approval was added when Imbruvica is used as induction or maintenance therapy in combination with chemotherapy.	07/12/2023