PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 06/12/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

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 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 history 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.

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 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.

9. **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 COVERED

Imbruvica® (ibrutinib tablets, capsules, and oral suspension (Pharmacyclics/Janssen)
is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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.

HISTORY

Type of Revision	Summary of Change	Review Date
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
Annual Revision	No criteria changes.	06/12/2024