Reference number(s)
1997-A

Specialty Guideline Management Imbruvica

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Imbruvica	ibrutinib

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

- Imbruvica is indicated for the treatment of adult patients with CLL/SLL.
- Imbruvica is indicated for the treatment of adult patients with CLL/SLL with 17p deletion.

Waldenström's Macroglobulinemia (WM)

Imbruvica is indicated for the treatment of adult patients with WM.

Chronic Graft versus Host Disease (cGVHD)

Imbruvica is indicated for the treatment of adult and pediatric patients age 1 year and older with cGVHD after failure of one or more lines of systemic therapy.

Compendial Uses[2]

- Mantle cell lymphoma
- Marginal zone lymphomas
    - Extranodal (gastric and nongastric MALT) marginal zone lymphoma
    - Nodal marginal zone lymphoma
    - Splenic marginal zone lymphoma
- Hairy cell leukemia
- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)
- Central nervous system cancers
- Diffuse large B-cell lymphoma
- High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
- HIV-related B-cell lymphoma
- Monomorphic post-transplant lymphoproliferative disorders (PTLD) (B-cell type)
- Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

All other indications are considered experimental/investigational and not medically necessary.

Coverage Criteria[1-6]

Mantle Cell Lymphoma (MCL)

Authorization of 12 months may be granted for treatment of MCL when any of the following criteria is met:

- The member has received at least one prior therapy when the requested medication is used as a single agent or in combination with rituximab or venetoclax.
- The requested medication will be used in combination with rituximab as pretreatment to induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen.
- The requested medication will be used as aggressive induction therapy as a component of TRIANGLE regimen: alternating RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) + covalent Bruton tyrosine kinase inhibitor (ibrutinib)/RDHA (rituximab, dexamethasone, and cytarabine) + carboplatin regimen.
- The requested medication will be used in combination with rituximab for members aged 65 years and older.

Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

- Authorization of 12 months may be granted for treatment of CLL/SLL as a single agent, in combination with rituximab with or without bendamustine, in combination with obinutuzumab, or as first line therapy in combination with venetoclax.
- Authorization of 12 months may be granted for treatment of Histologic (Richter) transformation to diffuse large B-cell lymphoma in combination with nivolumab or pembrolizumab.

Waldenström's Macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)/ Bing-Neel syndrome

Authorization of 12 months may be granted for treatment of WM/LPL and Bing-Neel syndrome when the requested medication is used as a single agent or in combination with rituximab.

Marginal Zone Lymphoma (MZL)

Authorization of 12 months may be granted for treatment of MZL, such as extranodal (gastric or non-gastric MALT lymphoma) marginal zone lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma, when the member has received at least one prior therapy.

Chronic Graft-Versus-Host Disease (cGVHD)

Authorization of 12 months may be granted for treatment of cGVHD when the member has failed one or more lines of therapy.

Hairy Cell Leukemia

Authorization of 12 months may be granted for treatment of relapsed/refractory hairy cell leukemia when the requested medication is used as a single agent for disease progression.

Central Nervous System Cancers

Authorization of 12 months may be granted for treatment of central nervous system cancers when any of the following criteria is met:

- The requested medication is used for relapsed or refractory disease as either a single agent, or in combination with high-dose methotrexate and rituximab for primary central nervous system lymphoma.

- The requested medication is used for induction therapy as a single agent for primary central nervous system lymphoma.
- The requested medication is used as a single agent for brain metastases in lymphoma.

Diffuse Large B-cell Lymphoma

Authorization of 12 months may be granted for single agent subsequent treatment of non-germinal diffuse large B-cell lymphoma.

High-Grade B-cell Lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)

Authorization of 12 months may be granted for single agent subsequent treatment of non-germinal high-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified).

HIV-Related B-cell Lymphomas

Authorization of 12 months may be granted for single agent subsequent treatment of non-germinal HIV-related B-cell lymphomas.

Monomorphic Post-Transplant Lymphoproliferative Disorders

Authorization of 12 months may be granted for single agent subsequent treatment of non-germinal monomorphic post-transplant lymphoproliferative disorders (B-cell type).

Continuation of Therapy

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

References

1. Imbruvica [package insert]. South San Francisco, CA: Pharmacyclics LLC; December 2024.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed June 17, 2025.

3. Clinical Consult. CVS Caremark Clinical Programs Review: Focus on Hematology-Oncology Clinical Programs. September 2021.
4. Jain P, Zhao S, Lee HJ, et al Ibrutinib with rituximab in first-line treatment of older patients with mantle cell lymphoma. J Clin Oncol. 2022;40(2):202-212.
5. Wang ML, Jurczak W, Jerkeman M, et al. Ibrutinib plus bendamustine and rituximab in untreated mantle-cell lymphoma. N Engl J Med. 2022;386:2482-2494.
6. Lexicomp [database online]. Hudson, OH: Lexi-Comp, Inc.; https://online.lexi.com/lco/action/home [available with subscription]. Accessed June 17, 2025.