Evolent Clinical Guideline 3083 for Imbruvica™ (ibrutinib)

Guideline Number: Evolent_CG_3083	**Applicable Codes**	
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STATEMENT

Purpose

To define and describe the accepted indications for Imbruvica (ibrutinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Chronic Graft-versus-Host Disease (cGVHD)

- Imbruvica (ibrutinib) may be used in adult and pediatric members age 1 year and older with chronic graft-versus-host disease after failure of one or more lines of systemic therapy.

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

- Imbruvica (ibrutinib) may be used as a single agent for initial or subsequent therapy for all prognostic categories of CLL/SLL.
- NOTE: The use of Imbruvica (ibrutinib) in combination with an anti-CD20 antibody [e.g., Rituxan (rituximab) or Gazyva (obinutuzumab)] is not supported by Evolent Policy. This policy position is based on Level 1 evidence from the trial by Burger et al, referenced below, which showed no added benefit of adding rituximab/obinutuzumab to single agent ibrutinib in first line therapy of CLL. Please refer to Evolent alternative agents/regimens recommended by Evolent, including but not limited to regimens available at **Evolent Pathways**.

Mantle Cell Lymphoma (MCL) and Marginal Zone Lymphoma (MZL)

- NOTE: Imbruvica (ibrutinib) is not supported by Evolent Policy for the treatment of patients with relapsed/refractory mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL). This policy position is based on the manufacturer's voluntary withdrawal of Imbruvica and FDA guidance following confirmatory study results (please see reference below). The results showed no overall survival and progression free survival advantage in MCL and MZL, respectively. Please refer to the Evolent recommended alternative agents/regimens, including but not limited to regimens available at **Evolent Pathways**.

Waldenstrom's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma

- The member has a diagnosis Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma AND
- Imbruvica (ibrutinib) will be used as a single agent or in combination with rituximab/rituximab biosimilar product as initial therapy or therapy for relapsed disease.

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Disease progression while receiving Imbruvica/Imbruvica (ibrutinib) containing regimen or another BTK inhibitor/BTK inhibitor containing regimen, e.g., Calquence (acalabrutinib) or Brukinsa (zanubrutinib).
- For the treatment of CLL: concurrent use with an anti-CD20 antibody including any rituximab products or Gazyva (obinutuzumab). Per Evolent Policy, single agent Imbruvica (ibrutinib) is as effective as Imbruvica (ibrutinib) + rituximab/obinutuzumab (Burger et al - see reference below).
- Dosing exceeds single dose limit of Imbruvica (ibrutinib) 420 mg (for CLL/SLL, WM, and cGVHD).
- Treatment exceeds the maximum limit of 120 (140 mg) or 140 (70 mg) capsules/month; 28 (140 mg), 28 (280 mg), or 28 (420 mg) tablets/month; or 2 (70 mg/mL) bottles of oral suspension/month.
- Investigational use of Imbruvica (ibrutinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

- Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
- Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
- Whether the experimental design, considering he drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - ibrutinib

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
May 2026	• Added oral suspension formulation details to exclusion criteria • Updated references
May 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1262 Imbruvica (ibrutinib) • Updated indication section • Updated maximum dosage form quantities in exclusion criteria • Updated exclusion criteria • Updated references
May 2024	• Added cGVHD indication to include use in adult and pediatric members ≥ 1 year • Added new reference • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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