Drug Policy:

Imbruvica™ (ibrutinib)

POLICY NUMBER UM ONC_1262	SUBJECT Imbruvica™ (ibrutinib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 11/12/14, 12/18/15, 04/13/16, 02/08/17, 02/14/18, 02/13/19, 10/09/19, 12/11/19, 05/13/20, 08/12/20, 08/11/21, 09/09/21, 11/10/21, 02/09/22, 03/09/22, 05/11/22, 10/12/22, 11/09/22, 03/08/23, 05/10/23, 05/08/24	**APPROVAL DATE** May 08, 2024	**EFFECTIVE DATE** May 31, 2024	**COMMITTEE APPROVAL DATES** 11/12/14, 12/18/15, 04/13/16, 02/08/17, 02/14/18, 02/13/19, 10/09/19, 12/11/19, 05/13/20, 08/12/20, 08/11/21, 09/09/21, 11/10/21, 02/09/22, 03/09/22, 05/11/22, 10/12/22 11/09/22, 03/08/23, 05/10/23, 05/08/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

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

1. Imbruvica (ibrutinib) may be used as a single agent for initial or subsequent therapy for all prognostic categories of CLL/SLL.

2. NOTE: The use 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 http://pathways.newcenturyhealth.com.

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

1. 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 http://pathways.newcenturyhealth.com.

D. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma

1. The member has a diagnosis Waldenstrom's macroglobulinemia/Lymphoplasmacytic Lymphoma AND
2. 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.

E. Chronic Graft-versus-Host Disease (cGVHD)

1. 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.

III. EXCLUSION CRITERIA

A. Disease progression while receiving Imbruvica/Imbruvica (ibrutinib) containing regimen or another BTK inhibitor/BTK inhibitor containing regimen, e.g., Calquence (acalabrutinib) or Brukinsa (zanubrutinib).

B. 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).

C. Dosing exceeds single dose limit of Imbruvica (ibrutinib) 420 mg (for CLL/SLL, and WM).

D. Treatment exceeds the maximum limit of 120 (140 mg) or 240 (70 mg) capsules a month; 120 (140 mg), 60 (280 mg), 30 (420 mg), 30 (560 mg) tablets a month.

E. 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:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. 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.

4. 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).
5. 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.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Update on IMBRUVICA® (ibrutinib) U.S. Accelerated Approvals for Mantle Cell Lymphoma and Marginal Zone Lymphoma Indications. Accessed on 4/23/2023: https://www.jnj.com/update-on-imbruvica-ibrutinib-u-s-accelerated-approvals-for-mantle-cell-lymphoma-and-marginal-zone-lymphoma-indications#:~:text=HORSHAM%2C%20Pa.%2C%20April%206%2C%202023%20%E2%80%93%20The%20Janssen,have%20received%20at%20least%20one%20prior%20anti-CD20-based%20therapy.

B. Jain N, et al. CAPTIVATE Clinical Trial. Ibrutinib and Venetoclax for First-Line Treatment of CLL. N Engl J Med. 2019 May 30;380(22):2095-2103.

C. Byrd JC, et al. Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial. J Clin Oncol. 2021 Nov 1;39(31):3441-3452.

D. Carpenter PA, et al. Ibrutinib Treatment of Pediatric Chronic Graft-versus-Host Disease: Primary Results from the Phase 1/2 iMAGINE Study. Transplant Cell Ther. 2022 Nov;28(11):771.e1-771.e10. doi: 10.1016/j.jtct.2022.08.021.

E. Burger JA, et al. Randomized trial of ibrutinib vs ibrutinib plus rituximab in patients with chronic lymphocytic leukemia. Blood. 2019 Mar 7;133(10):1011-1019.

F. Imbruvica prescribing information. Pharmacyclics, Inc. Sunnyvale, CA 2024.

G. Clinical Pharmacology Elsevier Gold Standard 2023.

H. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

I. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

J. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

K. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

L. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.