# Drug Policy:

# Imbruvica™ (ibrutinib)

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| **POLICY NUMBER**<br>UM ONC_1262 | **SUBJECT**<br>Imbruvica™ (ibrutinib) | | **DEPT/PROGRAM**<br>UM Dept | **PAGE 1 OF 4** |
| **DATES COMMITTEE REVIEWED**<br>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 | **APPROVAL DATE**<br>March 9, 2022 | **EFFECTIVE DATE**<br>March 25, 2022 | **COMMITTEE APPROVAL DATES**<br>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 | |
| **PRIMARY BUSINESS OWNER:** UM | | **COMMITTEE/BOARD APPROVAL**<br>Utilization Management Committee | | |
| **URAC STANDARDS**<br>HUM 1 | **NCQA STANDARDS**<br>UM 2 | | **ADDITIONAL AREAS OF IMPACT** | |
| **CMS REQUIREMENTS** | **STATE/FEDERAL REQUIREMENTS** | | **APPLICABLE LINES OF BUSINESS**<br>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.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH 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. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs.

### B. Mantle Cell Lymphoma (MCL)

1. Imbrivica (ibrutinib) may be used in a member with relapsed or refractory MCL that has failed or has progressed on first line chemotherapy/chemo-immunotherapy AND
2. Imbruvica (ibrutinib) will be used as a single agent or in combination with rituximab/rituximab biosimilar product.
3. NOTE: Per NCH Pathway & NCH Policy, [Ibrutinib + Lenalidomide + Rituximab] and [Ibrutinib + Venetoclax] are both Non-Preferred regimens for the treatment of MCL. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with the above regimens compared to NCH Preferred regimens. When clinically appropriate, please refer to NCH Pathway for the preferred treatments.

### C. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

1. Imbruvica (ibrutinib) use as a single agent is supported for initial and subsequent therapy for all prognostic categories of CLL/SLL.
2. Imbruvica (ibrutinib) in combination with Venclexta (venetoclax) is supported if the member has CLL with any one of the following additional risk factors: age 65 years or older, del(17p), mutated TP53, del (11q), unmutated IGHV (Immunoglobulin Heavy Chain).
3. NOTE: Imbruvica (ibrutinib) use in combination with an anti-CD20 antibody [e.g., Rituxan (rituximab) or Gazyva (obinutuzumab)] is not supported per NCH policy/NCH Pathway. This is based on the lack of benefit from the addition of rituximab/obinutuzumab to ibrutinib compared to ibrutinib alone.

### 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. Nodal & Extra-Nodal Marginal Zone Lymphoma & Splenic Marginal Zone Lymphoma

1. The member has relapsed or refractory nodal/extra-nodal/splenic marginal zone lymphoma AND
2. Imbruvica (ibrutinib) will be used as a single agent as second-line or subsequent therapy in members who have received an anti-CD20 based therapy [e.g., rituximab, ofatumumab, or obinutuzumab).

## 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 NCH Policy and NCH Pathway single agent Imbruvica

(ibrutinib) is as effective as Imbruvica (ibrutinib) + any anti-CD20 antibody, e.g., Gazyva (obinutuzumab) & Rituxan (rituximab).

C. Dosing exceeds single dose limit of Imbruvica (ibrutinib) 560 mg (for MCL and MZL) or 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), 30 (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 definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of the 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. Jain et al. CAPTIVATE trial. N Engl J Med 2019;380:2095-2013

B. 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.

C. 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.

D. Imbruvica prescribing information. Pharmacyclics, Inc. Sunnyvale, CA 2021.

E. Clinical Pharmacology Elsevier Gold Standard 2022.

F. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2022.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2022.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2022.

I. 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.

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