Drug Policy:

Rituximab Products

POLICY NUMBER UM ONC_1132	**SUBJECT** Rituximab Products (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni)	**DEPT/PROGRAM** UM Dept	**PAGE 1 of 5**
DATES COMMITTEE REVIEWED 07/22/11, 01/02/13, 03/13/13, 07/24/14, 12/16/15, 12/21/16, 12/03/17, 11/08/18, 01/09/19, 08/14/19, 12/11/19, 02/12/20, 03/11/20, 04/08/20, 10/14/20, 02/10/21, 11/15/21, 01/12/22, 03/09/22, 05/11/22, 06/08/22	**APPROVAL DATE** June 8, 2022	**EFFECTIVE DATE** June 24, 2022	**COMMITTEE APPROVAL DATES** 07/22/11, 01/02/13, 03/13/13, 07/24/14, 12/16/15, 12/21/16, 12/03/17, 11/08/18, 01/09/19, 08/14/19, 12/11/19, 02/12/20, 03/11/20, 04/08/20, 10/14/20, 02/10/21, 11/15/21, 01/12/22, 03/09/22, 05/11/22, 06/08/22
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee	
URAC STANDARDS HUM v8: UM1-2; UM 2-1	**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 Rituximab Products (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni) 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 (http://pathways.newcenturyhealth.com/) 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 AND
6. When there is a documented drug shortage, disease progression, contraindication, or confirmed intolerance to a Preferred drug/regimen, per NCH Policy and Pathway, the available alternative product may be used if deemed medically appropriate and the indication is listed in a standard reference compendia or accepted peer review literature. For a list of current drug shortages, please refer to FDA drug shortage website in the reference section.

B. CD-20 positive B-Cell Non-Hodgkin's Lymphomas (NHL) or Acute Lymphoblastic Leukemia (B-ALL)

1. The member is an adult or pediatric member ≥6 months of age who has CD20 positive B-cell NHL (e.g., follicular, diffuse large B-cell, Mantle Cell Lymphoma, pediatric aggressive mature B-Cell Lymphomas) or B-ALL and Rituximab/ritixumab biosimilar is being used as a single agent or in combination with chemotherapy for ANY of the following:
    a. Initial therapy (for use in combination with chemotherapy only) OR
    b. Treatment of relapsed or refractory disease OR
    c. Maintenance therapy:
        i. For up to two years for Indolent B-Cell Lymphomas (Follicular B Cell Lymphoma and all subtypes of Marginal Zone Lymphoma).
        ii. For up to disease progression or intolerable toxicity for Mantle Cell Lymphoma.
2. NOTE 1: Per NCH Pathway and NCH Policy, the following regimens are Non-Preferred due to lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes/lower toxicity compared to the NCH Preferred regimens. Please refer to NCH L1 pathway for the preferred treatments in these settings:
    a. In relapsed/refractory DLBCL: Gemcitabine + vinorelbine +/- rituximab; lenalidomide +/- rituximab (non-GCB DLBCL)
    b. As primary therapy for Follicular Lymphoma: lenalidomide + rituximab
    c. As initial therapy for Marginal Zone Lymphoma: lenalidomide + rituximab
    d. As second line or subsequent therapy for Mantle Cell Lymphoma: Ibrutinib + lenalidomide + rituximab; venetoclax + rituximab.
3. NOTE 2: Per NCH Pathway & NCH Policy, Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase), and Riabni (rituximab-arrx) are non-Preferred drugs. Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) are the Preferred products for the treatment of CD-20 positive NHL and B-ALL. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superiority of one rituximab product over another.

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

1. Rituximab/rituximab biosimilar is being used for first or subsequent line of therapy:
    a. In combination with chemotherapy OR

b. As maintenance therapy for up to 2 years.

2. NOTE 1: Per NCH Pathway and NCH Policy, the following regimens are Non-Preferred due to the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes compared to the NCH Preferred regimens. Please refer to NCH L1 pathway for the preferred treatments in these settings:
   a. Initial therapy: single agent rituximab, High-dose methylprednisolone (HDMP) + rituximab, ibrutinib + rituximab, fludarabine + rituximab (FR), alemtuzumab + ritixumab
   b. Subsequent therapy: idelalisib + rituximab, lenalidomide + rituximab, HDMP + rituximab, dose-dense rituximab, alemtuzumab + rituximab, bendamustine + rituximab + ibrutinib.
3. NOTE 2: Per NCH Pathway & NCH Policy, Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase), and Riabni (rituximab-arrx) are non-Preferred drugs. Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) are the Preferred products for the treatment of CLL/SLL. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superiority of one rituximab product over another.

D. Hodgkin's Lymphoma

1. The member has nodular lymphocyte predominant Hodgkin's Lymphoma and Rituximab/rituximab biosimilar is being used as a single agent or in combination with chemotherapy for initial or subsequent therapy OR
2. For maintenance therapy for up to 2 years.
3. NOTE 1: Per NCH Pathway & NCH Policy, the following regimens are Non-Preferred based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes compared to NCH preferred regimens. Please refer to NCH pathway for the preferred treatments in the treatment of CLL/SLL.
   a. First Line therapy: single agent rituximab; rituximab + ibrutinib; rituximab + fludarabine; rituximab + high-dose methylprednisolone (HDMP)
   b. Second line or subsequent therapy: as a single agent in dose-dense regimen; rituximab + high-dose methylprednisolone (HDMP); rituximab + alemtuzumab.
4. NOTE 2: Per NCH Pathway & NCH Policy, Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase), and Riabni (rituximab-arrx) are non-Preferred drugs. Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) are the Preferred products for the treatment of Hodgkin's Lymphoma. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superiority of one rituximab product over another.

E. Idiopathic Thrombocytopenic Purpura (ITP)

1. The member has acute ITP and Rituximab/rituximab biosimilar is being used as a single agent AND the following:
   a. The member has ITP that is refractory to corticosteroids and IVIG AND
   b. The platelet count is $< 30 \times 10^9$/L OR
   c. There are other clinical indications for therapy.
2. NOTE: Per NCH Pathway & NCH Policy, Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase), and Riabni (rituximab-arrx) are non-Preferred drugs. Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) are the Preferred products for the treatment of ITP. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superiority of one rituximab product over another.

F. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma

1. The member has Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma and Rituximab/rituximab biosimilar will be used in combination with chemotherapy and/or a BTK inhibitor (e.g., ibrutinib + rituximab) as primary therapy or as therapy for relapsed/refractory disease.
2. NOTE: Per NCH Pathway & NCH Policy, Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase), and Riabni (rituximab-arrx) are non-Preferred drugs. Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) are the Preferred products for the treatment of Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma. This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superiority of one rituximab product over another.

III. EXCLUSION CRITERIA

A. Use of Rituximab products (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni) as maintenance therapy after primary treatment of Diffuse Large B-Cell Lymphoma (DLBCL).

B. Treatment exceeds the maximum months duration limit of 2 years when used in combination with Venclexta (venetoclax) for the treatment of CLL.

C. Dosing exceeds single dose limit of rituximab products 500 mg/m^2 (CLL) and 375 mg/m^2 (NHL); Rituxan Hycela 1600 mg (CLL) and 1400 mg (NHL).

D. Investigational use of Rituximab Products (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni) 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. Leonard JP, et al. AUGMENT Clinical Trial. A Phase III Study of Lenalidomide Plus Rituximab Versus Placebo Plus Rituximab in Relapsed or Refractory Indolent Lymphoma. J Clin Oncol. 2019 May 10;37(14):1188-1199.

B. Riabni prescribing information. Amgen. Thousand Oaks, CA 2020.

C. Rituxan Hycela prescribing information. Genetech, Inc. San Francisco, CA 2019.

D. Truxima (rituximab-abbs) prescribing information. Teva Pharmaceuticals USA, Inc. North Wales, PA 2021.

E. Rituxan prescribing information. Genetech, Inc. San Francisco, CA 2022.

F. Ruxience (rtuximab-pvvr) prescribing information. Pfizer Inc. NY, NY 2021.

G. Clinical Pharmacology Elsevier Gold Standard 2022.

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

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

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

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.

M. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.