BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Rituximab for the Treatment of Rheumatoid Arthritis

File Name:	rituximab_for_the_treatment_of_rheumatoid_arthritis
Origination:	4/2008
Last CAP Review:	2/2020
Next CAP Review:	2/2021
Last Review:	1/2021

Description of Procedure or Service

Rituximab is a chimeric murine-human monoclonal antibody directed against the CD20 surface antigen, which is expressed on pre-B and mature B lymphocytes. Rituximab induces lysis of normal and malignant CD20-expressing B cells; possible mechanisms of cell lysis include complement-dependent cytotoxicity and antibody-dependent cell-mediated cytotoxicity. B cells are thought to play a role in the pathogenesis of rheumatoid arthritis and other autoimmune diseases by producing autoantibodies and proinflammatory cytokines and by activating T lymphocytes. Rituximab reduces the number of B cells in the peripheral blood and in lymphoid tissues, thereby interrupting pathogenic processes of autoimmune diseases. Rituximab is administered by intravenous infusion.

Tumor necrosis factor inhibiting drugs such as Remicade® (infliximab), Enbrel® (etanercept), or Humira® (adalimumab) are considered first line treatment before considering the use of Rituxan® (rituximab). Patients will sometimes become intolerant or unresponsive to TNF inhibiting therapy and for these; Rituxan® (rituximab) may be considered.

The following biosimilars for rituximab have been approved by the FDA for the same labeled indications as the originator drug, Rituxan® (rituximab):

- November 2018, Truxima® (rituximab-abbs; Teva)
- July 2019, Ruxience™ (rituximab-pvvr; Pfizer)
- December 2020, Riabni™ (rituximab-arrx; Amgen)

Note*This policy only applies to rituximab (Rituxan) and rituximab biosimilars (Truxima, Riabni, and Ruxience) when used for the treatment of Rheumatoid Arthritis.**

For oncologic uses of rituximab and rituximab biosimilars, please see BCBSNC Corporate Medical Policy, Monoclonal Antibodies for Non-Hodgkin Lymphoma and Acute Myeloid Leukemia In the Non-Hematopoietic Stem Cell Transplant Setting

Related Policies:
Abatacept (Orencia)
Golimumab (Simponi Aria)
Infliximab (Remicade)
Tocilizumab (Actemra)

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for rituximab (Rituxan®) and rituximab biosimilars (Truxima®, Riabni™, and Ruxience™) for the treatment of rheumatoid arthritis when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Rituximab and rituximab biosimilars (rituximab-abbs rituximab-arrx, and rituximab-pvvr) may be subject to prior review requirements.

When Rituximab for the Treatment of Rheumatoid Arthritis is covered

Rituximab (Rituxan®) and rituximab biosimilars (Truxima®, Riabni™, and Ruxience™) for the treatment of adults with rheumatoid arthritis may be considered medically necessary under the following conditions:

1. The patient has moderately to severely active rheumatoid arthritis; **AND**
2. Rituximab is administered in combination with methotrexate (unless contraindicated); **AND**
3. Either:
    a. Patient has had an inadequate response to one or more tumor necrosis factor (TNF) inhibitors or has a contraindication to treatment with TNF inhibitors; **OR**
    b. Patient has had an inadequate response to methotrexate or other conventional synthetic disease modifying anti-rheumatic drug (DMARD); **AND**
4. If the request is for rituximab (Rituxan) or non-preferred rituximab biosimilars [e.g., rituximab-arrx (Riabni)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred rituximab biosimilar products [rituximab-abbs (Truxima), rituximab-pvvr (Ruxience)] that is not anticipated with the requested product; **AND**
    b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form.

When Rituximab for the Treatment of Rheumatoid Arthritis is not covered

1. Rituximab (Rituxan®) and rituximab biosimilars (Truxima®, Riabni™, and Ruxience™) for the treatment of rheumatoid arthritis are considered not medically necessary when the criteria stated above are not met.

2. Rituximab (Rituxan®) and rituximab biosimilars (Truxima®, Riabni™, and Ruxience™) are considered not medically necessary when used in combination with TNF-inhibiting drugs.

Policy Guidelines

The U.S. Food and Drug Administration has approved rituximab for individuals who have moderately to severely active rheumatoid arthritis and inadequate response to one or more standard agent (e.g., tumor necrosis factor inhibitors, methotrexate or other conventional synthetic disease-modifying anti-rheumatic drugs), and who receive rituximab and methotrexate. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome. Rituximab should be administered by a healthcare professional with appropriate medical support to manage severe and potentially fatal infusion reactions.

Rituximab carries the following black box warnings:

- Fatal infusion reactions within 24 hours of rituximab infusion; approximately 80% of fatal reactions occurred with first infusion.
- Severe mucocutaneous reactions, some with fatal outcomes.
- Hepatitis B virus reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death.
- Progressive multifocal leukoencephalopathy resulting in death.

Labeled warnings and precautions include:

- Tumor lysis syndrome (for patients with hematologic malignancies)
- Infections
- Cardiac arrhythmias and angina
- Bowel obstruction and perforation
- Live virus vaccines: Do not administer live virus vaccines before or during rituximab therapy
- Cytopenias

Rituximab is pregnancy category C: There are no adequate and well-controlled studies for rituximab during pregnancy. Individuals of childbearing potential should use effective contraception while receiving rituximab and for 12 months after treatment. Rituximab may be used during pregnancy only if potential benefit justifies potential risks to the fetus.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *C9399, J3490, J3590, J9312, Q5115, Q5119*

Diagnoses that are subject to medical necessity review: M05.00, M05.011, M05.012, M05.019, M05.021, M05.022, M05.029, M05.031 M05.032, M05.039, M05.041, M05.042, M05.049, M05.051, M05.052, M05.059, M05.061, M05.062, M05.10, M05.111, M05.112, M05.119, M05.319, M05.069, M05.071, M05.072, M05.079, M05.09, M05.30, M05.311, M05.312, M05.321, M05.322, M05.329, M05.331, M05.332, M05.339, M05.341, M05.342, M05.349, M05.351, M05.352, M05.359, M05.361,

M05.362, M05.369, M05.371, M05.372, M05.379, M05.39, M05.60, M05.611, M05.612, M05.619, M05.621, M05.622, M05.629, M05.631, M05.632, M05.639, M05.641, M05.642, M05.649, M05.651, M05.652, M05.659, M05.661, M05.662, M05.669, M05.671, M05.672, M05.679, M05.69, M06.9, M06.80, M06.811, M06.812, M06.819, M06.821, M06.822, M06.829, M06.831, M06.832, M06.839, M06.841, M06.842, M06.849, M06.851, M06.852, M06.859, M06.861, M06.862, M06.869, M06.871, M06.872, M06.879, M06.88, M06.89,M08.00, M08.09, M08.29, M08.011, M08.012, M08.019, M08.021, M08.022, M08.029, M08.031, M08.032, M08.039, M08.041, M08.042, M08.049, M08.051, M08.052, M08.059, M08.061, M08.062, M08.069, M08.071, M08.072, M08.079, M08.08, M08.20, M08.211, M08.212, M08.219, M08.221, M08.222, M08.229, M08.231, M08.232, M08.239, M08.241, M08.242, M08.249, M08.251, M08.252, M08.259, M08.261, M08.262, M08.269, M08.271, M08.272, M08.279, M08.28, M08.29, M08.00, M08.011, M08.012, M08.019, M08.021, M08.022, M08.029, M08.031, M08.032, M08.039, M08.041, M08.042, M08.049, M08.051, M08.052, M08.059, M08.061, M08.062, M08.069, M08.071, M08.072, M08.079, M08.09, M08.40, M08.411, M08.412, M08.419, M08.421, M08.422, M08.429, M08.431, M08.432, M08.439, M08.441, M08.442, M08.449, M08.451, M08.452, M08.459, M08.461, M08.462, M08.469, M08.471, M08.472, M08.479, M08.48, M12.00, M12.011, M12.012, M12.019, M12.021, M12.022, M12.029, M12.031, M12.032, M12.039, M12.041, M12.042, M12.049, M12.051, M12.052, M12.059, M12.061, M12.062, M12.069, M12.071, M12.072, M12.079, M12.08, M12.09, M06.4, M45.0, M45.1, M45.2, M45.3, M45.4, M45.5, M45.6, M45.7, M45.8, M45.9

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Genetech Inc. Rituxan® (rituximab) targeted B-cell therapy, product information. Retrieved 3/12/08 from http://www.rituxan.com/

Senior Medical Director review, 3/20/2008.

Genetech Inc. Rituxan® (rituximab) targeted B-cell therapy, full prescribing information. Retrieved 10/29/09 from http://www.gene.com/gene/products/information/pdf/rituxan-prescribing.pdf

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Genetech Inc. Rituxan® (rituximab) targeted B-cell therapy, product information. Retrieved 3/30/10 from http://www.rituxan.com/

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Genetech Inc. Rituxan® (rituximab) targeted B-cell therapy, product information. Retrieved 1/21/11 from http://www.rituxan.com/

Specialty Matched Consultant Review Panel- 2/2012

Genetech Inc. Rituxan® (rituximab) targeted B-cell therapy, product information. Retrieved 2/4/13 from http://www.rituxan.com/

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Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). May 2012;64(5):625-639. PMID 22473917

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.24, 12/10/15

Specialty Matched Consultant Advisory Panel review- 2/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.24, 10/13/16

Singh JA, Saag KG, Bridges SL, Jr., et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. Jan 2016;68(1):1-26. PMID 26545940

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.24, 10/12/2017

Specialty Matched Consultant Advisory Panel review- 2/2018

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BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.24, 10/10/2018

Specialty Matched Consultant Advisory Panel review- 2/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.24, 10/17/2019

Specialty Matched Consultant Advisory Panel review- 2/2020

Teva Pharmaceuticals USA, Inc. Truxima (rituximab-abbs) injection, for intravenous use. Highlights of prescribing information. May 2019. Available at: https://www.truxima.com/globalassets/truxima-dtc/pdfs/truxima-prescribing-information.pdf. Last accessed July 2020.

Pfizer Inc. Ruxience (rituximab-pvvr) injection, for intravenous use. Highlights of prescribing information. May 2020. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=12090. Last accessed July 2020.

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Amgen, Inc. Riabni (rituximab-arrx) injection, for intravenous use. Highlights of prescribing information. December 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761140s000lbl.pdf. Last accessed January 2021.

Medical Director review 1/2021

Policy Implementation/Update Information

4/1/08 New policy developed. Under the "When Covered" section; "Rituxan® (rituximab) may be medically necessary for the treatment of rheumatoid arthritis when the medical criteria and guidelines shown below are met: 1. The patient has moderate to severe rheumatoid arthritis; and 2. The patient has failed to respond adequately to at least one Tumor Necrosis Factor (TNF) inhibiting drug or is intolerant to all TNF-inhibiting drugs (i.e., Remicade (infliximab), Enbrel (etanercept), or Humira (adalimumab); and 3. Rituxan® (rituximab) is to be used in combination with methotrexate; and 4. The patient is 18 years old or older. 5. Continued use of Rituxan® (rituximab) can only be renewed after 6 months have passed from the last course of treatment and retreatment is necessary to control symptoms." Under the "When Not Covered" section; " 1. When the criteria stated above are not met. 2. Rituxan® should not be used in combination with TNF-inhibiting drugs." Senior Medical Director review, 3/20/2008. References added. Notification given April 1, 2008. Policy effective 7/1/2008. References added.

11/3/08 Added "Note" at the end of the "Description" section indicating; "NOTE: This policy only applies to Rituximab (Rituxan®) when used for the treatment of Rheumatoid Arthritis." (btw)

3/2/10 Specialty Matched Consultant Advisory Panel review 1/5/2010. Updated "Description" section. No change to policy statement. Added wording to clarify #3 in the "When Covered" section to indicate; "Rituxan (rituximab) is to be used **preferably** in combination with methotrexate **unless contraindicated**". References added. (btw)

5/11/10 Under the "When Covered" section, updated guideline #5 to indicate "Subsequent courses of Rituxan (rituximab)should be administered every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks." Update due to a change in Rituxan's FDA-approved labeling. References added. (LR)

10/26/10 Added diagnoses codes to the "Billing/Coding" section. (lpr)

3/15/11 Specialty Matched Consultant Advisory Panel review 2/2011. Under "When Covered" section, moved #5 "Subsequent courses of Rituxan (rituximab) should be administered every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks" to Policy Guidelines section since this refers to continuation of treatment and not initial approval. Under "When Not Covered" section, added phrase "not medically necessary" to statement #1 "Rituximab for the treatment of rheumatoid arthritis is considered not medically necessary when the criteria stated above are not met. (lpr)

8/16/11 In the description section, added a cross reference to the Corporate Medical Policy, Monoclonal Antibodies for Non-Hodgkin Lymphoma, including Chronic Lymphocytic, &Acute Myeloid Leukemia in the Non-Hematopoietic Stem Cell Transplant Setting. (lpr)

11/22/11 Removed the x from the ICD-9 codes 714.0, 714.4, 714.8, 720.0 in the Billing/Coding section since there are no 5th digits for these codes. (lpr)

3/20/12 Specialty Matched Consultant Advisory Panel review meeting 2/29/2012. Under "When Not Covered" statement 2. changed to not medically necessary. No change to policy statement. (lpr)

9/4/12 Added ICD-9 code 714.89 to the Billing/Coding section for 2012 code update. (lpr)

12/1/12 "When Covered" section modified to revise statement "The patient has failed to respond adequately to at least one Tumor Necrosis Factor (TNF) inhibiting drug or is

intolerant to all TNF-inhibiting drugs (i.e., Remicade® (infliximab), Enbrel® (etanercept), or Humira® (adalimumab);" to "The patient has failed to respond adequately or is intolerant to Remicade ® (infliximab)." Notice 12/1/12 effective 2/1/13.

3/12/13 Specialty Matched Consultant Advisory Panel review meeting 2/20/2013. No change to policy statement. Reference added. (lpr)

7/1/13 Added ICD-10 codes to the "Billing/Coding" section. (lpr)

10/15/13 Added trial of Simponi Aria (golimumab) to statement #2 under When Covered section. Added ICD-10 diagnosis code M05.319 to Billing/Coding section. Medical director review 10/2013. (lpr)

12/31/13 Added ICD-10 diagnosis code M08.029 to Billing/Coding section and changed M05.11 to M05.111 for 2014 code update. (lpr)

4/1/14 Specialty Matched Consultant Advisory Panel review meeting 2/25/2014. Under Description section, changed DC20 to CD20 in description of the drug; changed "bad" cells to "targeted" cells to describe B cells. Medical director review. No change to policy statement. (lpr)

7/1/14 Removed ICD-10 effective date from Billing/Coding section. (lpr)

3/10/15 Specialty matched consultant advisory panel review meeting 2/25/2015. No change to policy statement. (lpr)

4/1/16 Description section and coverage guidelines updated for clarity. No change to policy intent. References added. Specialty Matched Consultant Advisory Panel review 2/24/16. (an)

12/30/16 Minor changes to Description section. Reference updated. No change to policy statement. (an)

4/28/17 Description section and Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 2/22/2017. No change to policy statement. (an)

9/29/17 Item 2 in the When Rituximab is Covered section revised to read: "Rituximab is administered in combination with methotrexate **(unless contraindicated**)… (an)

4/13/18 Under "When Covered" section: added phrase "active" to statement #1 and removed "(eg, > 8 swollen and > 8 tender joints)", added "or has a contraindication to treatment with TNF inhibitors" to statement #3a, and removed "and is not suitable for treatment with TNF inhibitors due to a recent (within 5 years) history of: a. a lymphoma or other malignancy, b. latent tuberculosis and contraindications to chemoprophylaxis, or c. previous demyelinating disease" from statement #3b. Minor changes made to Policy Guidelines section for clarity. Removed ICD-9 codes from Billing/Coding section. Minor typographical errors corrected. References added. Specialty Matched Consultant Advisory Panel review 2/28/2018. Medical Director review. No change to policy intent. (krc)

12/31/18 Added HCPCS code J9312 to Billing/Coding section and deleted code J9310 effective 1/1/19. (krc)

3/12/19 Reference added. Specialty Matched Consultant Advisory Panel review 2/20/2019. No change to policy statement. (krc)

3/10/20 Reference added. Specialty Matched Consultant Advisory Panel review 2/19/2020. No change to policy statements. (krc)

9/22/20 Under "When Covered" for Rituxan (rituximab), added Truxima (rituximab-abbs) and Ruxience (rituximab-pvvr) biosimilars with same indications as Rituxan (rituximab). Added HCPCS codes C9399, J3490, J3590, Q5115, and Q5119 to Billing/Coding section. References added. Medical Director review 7/2020. Policy notification given 9/22/2020 for effective date 11/24/2020. (krc)

10/27/20 Added the following requirements to "When Covered" section: "If the request is for rituximab (Rituxan) or non-preferred rituximab biosimilars, then both of the following criteria are met: patient has a documented serious adverse event that required medical intervention to both preferred rituximab biosimilar products [rituximab-abbs (Truxima), rituximab-pvvr (Ruxience)] that is not anticipated with the requested product AND prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form." Medical Director review 10/2020. **Policy remains on notice for effective date 1/1/2021**. (krc)

1/12/21 Under "When Covered" for Rituxan (rituximab), added additional biosimilar, Riabni (rituximab-arrx), with same indications and coverage criteria as Rituxan (rituximab). Reference added. Medical Director review 1/2021. (krc)