



Rituximab Products (Rituxan®, Rituximab-abbs [Truxima®], Rituximab-arxx [Riabni™] and Rituximab-pvvr [Ruxience®])

(Hematologic and Oncology Indications)

Some agents on this policy may require step therapy See “Step Therapy Requirements for Provider Administered Specialty Medications” Document at:

https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Rituxan is indicated for the treatment of pediatric patients aged 6 months and older with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy.

Rituxan, Ruxience, Truxima, and Riabni are indicated for:

1. Non-Hodgkin's lymphoma (NHL) in adult patients with:
 - a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
 - b. Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
 - c. Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
 - d. Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
2. Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.
3. Granulomatosis with polyangiitis (Wegener's Granulomatosis) and microscopic polyangiitis (MPA) in combination with glucocorticoids (Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)



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4. Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely active RA who have inadequate response to one or more TNF antagonist therapies. (Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)

Rituxan is also indicated for:

Rituxan is indicated for moderate to severe pemphigus vulgaris in adult patients

(Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)

B. Compendial Uses

1. Autoimmune hemolytic anemia
2. B-cell acute lymphoblastic leukemia (ALL)
3. B-cell lymphomas
 - a. Human immunodeficiency Virus (HIV) Related B-cell lymphomas
 - b. B-cell lymphoblastic lymphoma
 - c. Burkitt lymphoma
 - d. Castleman's disease
 - e. Diffuse Large B-Cell lymphoma
 - f. Follicular lymphoma
 - g. High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
 - h. Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma
 - i. Histological transformation of indolent lymphomas to high-grade B-cell lymphoma with MYC and BCL6 without BCL2 rearrangements
 - j. Mantle cell lymphoma
 - k. Marginal zone lymphomas
 - i. Nodal marginal zone lymphoma
 - ii. Extranodal marginal zone lymphoma (gastric and non-gastric mucosa associated lymphoid tissue {MALT} lymphoma)
 - iii. Splenic marginal zone lymphoma
 - l. Post-transplant lymphoproliferative disorder (PTLD)
 - m. Pediatric Aggressive Mature B-Cell Lymphomas
 - n. Primary Mediastinal Large B-Cell Lymphoma
4. Central nervous system (CNS) cancers
 - a. Leptomeningeal metastases from lymphomas
 - b. Primary CNS lymphomas
5. Chronic graft-versus-host disease (GVHD)
6. CLL/Small lymphocytic lymphoma (SLL)
7. Hairy cell leukemia
8. Rosai-Dorfman disease
9. Hodgkin's lymphoma, nodular lymphocyte-predominant
10. Immune checkpoint inhibitor-related toxicities
11. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
12. Primary cutaneous B-cell lymphoma
13. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
14. Thrombotic thrombocytopenic purpura
15. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL) / Bing-Neel Syndrome
16. Allogeneic transplant conditioning
17. For other compendial uses, refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM

All other indications are considered experimental/investigational and not medically necessary.



II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell (if applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Oncologic indications

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

1. B-cell acute lymphoblastic leukemia (ALL)
2. B-cell lymphomas:
 - i. HIV-related B-cell lymphomas
 - ii. B-cell lymphoblastic lymphoma
 - iii. Burkitt lymphoma
 - iv. Castleman's disease
 - v. Diffuse large B-cell lymphoma
 - vi. Follicular lymphoma
 - vii. High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
 - viii. Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma
 - ix. Histological transformation of indolent lymphomas to high-grade B-cell lymphoma with MYC and BCL6 without BCL2 rearrangements
 - x. Mantle cell lymphoma
 - xi. Marginal zone lymphomas
 - a. Nodal marginal zone lymphoma
 - b. Extranodal marginal zone lymphoma (gastric and non-gastric (MALT) lymphoma)
 - c. Splenic marginal zone lymphoma
 - xii. Post-transplant lymphoproliferative disorder (PTLD)
 - xiii. Pediatric Aggressive Mature B-Cell Lymphomas
 - xiv. Primary Mediastinal Large B-Cell Lymphoma
3. Central nervous system (CNS) cancers:
 - i. Leptomeningeal metastases from lymphomas
 - ii. Primary CNS lymphoma
4. CLL/Small lymphocytic lymphoma (SLL)
5. Hairy cell leukemia
6. Rosai-Dorfman disease
7. Hodgkin's Lymphoma, nodular lymphocyte-predominant
8. Primary cutaneous B-cell lymphoma
9. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL) / Bing-Neel Syndrome

B. Hematologic indications

Authorization of 12 months may be granted for treatment of any of the following indications:

1. Refractory immune or idiopathic thrombocytopenic purpura (ITP)
2. Autoimmune hemolytic anemia
3. Thrombotic thrombocytopenic purpura
4. Chronic graft-versus-host disease (GVHD)
5. Prevention of Epstein-Barr virus (EBV)-related PTLD
6. As part of a non-myeloablative conditioning regimen for allogeneic transplant



C. Immune checkpoint inhibitor-related toxicities

Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

IV. CONTINUATION OF THERAPY

For oncologic indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an oncologic indication listed in Section III A. when there is no evidence of unacceptable toxicity.

For immune checkpoint inhibitor-related toxicities: Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for treatment of immune checkpoint inhibitor-related toxicities who are experiencing benefit from therapy.

For all other indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III B. who are experiencing benefit from therapy.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Allogeneic Transplant Conditioning	Route of Administration: Intravenous 375mg/m ² on the day before transplant and 1,000 mg/m ² on days 1, 8, and 15 after transplant
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Autoimmune Hemolytic Anemia, B-Cell Acute Lymphoblastic Leukemia (B-ALL), B-Cell Lymphomas: Castleman's Disease, B-Cell Lymphomas: Diffuse Large B-Cell Lymphoma, HIV-related Diffuse Large B-cell Lymphoma, High-Grade B-Cell Lymphomas, Primary Mediastinal Large B-Cell Lymphoma, B-Cell Lymphomas: Follicular Lymphoma, B-Cell Lymphomas: Mantle Cell Lymphoma, B-Cell Lymphomas: Marginal Zone Lymphomas [Nodal Marginal Zone Lymphoma, Gastric Mucosa Associated Lymphoid Tissue (GMALT) Lymphoma, Nongastric MALT Lymphoma, Splenic Marginal Zone Lymphoma], B-Cell Lymphomas: Post-Transplant Lymphoproliferative Disorders, Chronic Graft Versus Host Disease (GVHD), Hairy Cell Leukemia, Immune or Idiopathic Thrombocytopenic Purpura	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)



	(ITP), Thrombotic Thrombocytopenic Purpura, Prevention of Epstein-Barr Virus (EBV)-related PTLID in high-risk patients, Rosai-Dorfman Disease, Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma (LPL)	
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Acute Lymphoblastic Leukemia (B-ALL)	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Burkitt Lymphoma and HIV-related Burkitt Lymphoma	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than every 14 days or on Days 1 and 5 of a 21-day cycle)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Castleman's Disease	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Diffuse Large B-Cell Lymphoma, HIV-related Diffuse Large B-cell Lymphoma, High-Grade B-Cell Lymphomas, Primary Mediastinal Large B-Cell Lymphoma	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Follicular Lymphoma	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Histological Transformation of Indolent Lymphomas to Diffuse Large B-cell Lymphoma B-Cell Lymphomas: Histological Transformation of Indolent Lymphomas to Diffuse Large B-cell Lymphoma or Histological Transformation of Indolent Lymphomas to High-grade B-cell Lymphoma with MYC and BCL6 without BCL2 rearrangements	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than every 14 days)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr),	B-Cell Lymphomas: Mantle Cell Lymphoma	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)



Truxima (Rituximab-abbs)		
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Marginal Zone Lymphomas [Nodal Marginal Zone Lymphoma, Gastric Mucosa Associated Lymphoid Tissue (GMALT) Lymphoma, Nongastric MALT Lymphoma, Splenic Marginal Zone Lymphoma]	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	B-Cell Lymphomas: Post-Transplant Lymphoproliferative Disorders	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Chronic Graft-Versus- Host Disease (GVHD)	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)	Route of Administration: Intravenous 500mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	CNS Cancers: Primary CNS Lymphoma	Route of Administration: Intravenous 750mg/m ² every week
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	CNS Cancers: Primary CNS Lymphoma or Leptomeningeal Metastases	Route of Administration: Intrathecal, Intraventricular 25mg (frequency and cycle length varies by regimen; should not be more frequent than twice a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Hairy Cell Leukemia	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab-pvvr), Truxima (Rituximab-abbs)	Hodgkin Lymphoma: Nodular Lymphocyte-Predominant	Route of Administration: Intravenous ≥18 Years 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)



Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Immune Checkpoint Inhibitor-Related Toxicities	Route of Administration: Intravenous 375mg/m ² every week OR 500 mg/m ² every 2 weeks OR 1000 mg every 2 weeks
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Immune or Idiopathic Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura,	Route of Administration: Intravenous 375mg/m ² every week for 4 doses (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Pediatric Aggressive Mature B-Cell Lymphomas: Diffuse Large B-cell Lymphoma, Burkitt Lymphoma, Burkitt- Like Lymphoma (BLL)] or Mature B-cell Acute Leukemia (B-AL)	Route of Administration: Intravenous ≥6 month(s) to <18 year(s) 375mg/m² (frequency and cycle length varies by regimen; should not be more frequent than 2 doses in one week) ≤17 Years 375mg/m² (frequency and cycle length varies by regimen; should not be more frequent than 2 doses in one week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Prevention of Epstein-Barr Virus (EBV)- related PTLD in high risk patients	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Primary Cutaneous B-cell Lymphoma	Route of Administration: Intravenous 375mg/m ² on Days 1, 8, 15, and 22 of a 28-day cycle for 1 cycle
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Rosai-Dorfman Disease	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Riabni (Rituximab-arrx), Rituxan (Rituximab), Ruxience (Rituximab- pvvr), Truxima (Rituximab- abbs)	Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma (LPL)/ Bing-Neel Syndrome	Route of Administration: Intravenous 375mg/m ² (frequency and cycle length varies by regimen; should not be more frequent than once a week)

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-

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label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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EFFECTIVE DATE

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