Policy Title:	**Rituxan (rituximab) and Biosimilar (Truxima, Riabni, Ruxience) Non-Oncology and Non-Hematology Policy** (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	09/25/2019, 12/20/2019, 1/29/2020, 8/3/2020, 9/9/2020, 1/28/2021, 3/18/2021, 7/15/2021, 9/23/2021, 1/06/2022, 3/17/2022		
Revision Date:	09/25/2019, 12/20/2019, 1/29/2020, 8/3/2020, 9/9/2020, 3/18/2021, 7/15/2021, 9/23/2021, 1/06/2022		

Purpose: To support safe, effective and appropriate use of Rituxan (rituximab), and biosimilars (Truxima, Riabni, Ruxience).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Rituxan (rituximab), and biosimilars (Truxima, Riabni, Ruxience) are covered under the Medical Benefit when used within the following guidelines for non-oncology and non-hematology indications. Use outside of these guidelines may result in non-payment unless approved under an exception process. **Refer to the Rituxan (rituximab), Truxima (rituximab-abbs), Riabni (rituximab-arrx) & Ruxience (rituximab-pvvr) Policy for oncology indications.**

Procedure:

Coverage of Rituxan (rituximab), and biosimilars (Truxima, Riabni, Ruxience) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria

- Patient must be screened for HBV infection (i.e., HBsAg and anti-HBc) prior to initiating therapy; AND
- For new start to therapy and requesting Rituxan or Riabni, patient must have failure or intolerable side effects to Ruxience or Truxima OR patients that are currently on treatment with Rituxan or Riabni can remain on treatment OR MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Non-Oncology Indications:

Rheumatoid arthritis (RA)

- Adult patient (18 years or older); **AND**
- Documented moderate to severe disease; **AND**
- Must be used in combination with methotrexate unless the patient has a contraindication or intolerance; **AND**
- Patient tried and failed at least a 3 month trial with ONE oral disease modifying antirheumatic drug (DMARD) (e.g., methotrexate, azathioprine, hydroxychloroquine, sulfasalazine, leflunomide, etc.); **AND**
- Previous trial (or lack of response) for a minimum of 3 months with one or more preferred TNF antagonist at least one of which should be a self-injectable; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Patient has not had treatment with Rituxan in the previous 4 months

Pemphigus vulgaris

- Patient has a diagnosis of pemphigus vulgaris as determined by the following:
    - One or more of the following clinical features:
        - Appearance of lesions, erosions and/or blisters
        - Nikolsky sign (induction of blistering via mechanical pressure at the edge of a blister or on normal skin)
        - Characteristic scarring and lesion distribution; **AND**
    - Histopathologic confirmation by skin/mucous membrane biopsy; **AND**
    - Positive direct immunofluorescence (DIF) microscopy result OR presence of autoantibodies as detected by indirect immunofluorescence (IIF) or enzyme-linked immunosorbent assay (ELISA); **AND**
- Patient has moderate to severe disease as assessed utilizing an objective measure/tool (i.e., PDAI, PSS, ABSIS, etc.); **AND**
- Other causes of blistering or erosive skin and mucous membrane diseases have been ruled out; **AND**
- Used in combination with glucocorticoids (e.g., prednisone, prednisolone, etc.)

Granulomatosis with Polyangiitis (GPA) (Wegener's granulomatosis) and Microscopic polyangiitis (MPA)

- Patient is at least 2 years of age; **AND**
- Used in combination with glucocorticoids (e.g., prednisone, methylprednisolone, etc.)

Autoimmune Hemolytic Anemia (AIHA)

- Patient has warm-reactive disease refractory to or dependent on glucocorticoids; **OR**

- Patient has cold agglutinin disease with symptomatic anemia, transfusion-dependence, and/or disabling circulatory symptoms

Lupus Nephritis

- Patient has disease that is non-responsive or refractory to standard first line therapy [e.g., mycophenolate mofetil, mycophenolic acid, cyclophosphamide, calcineurin inhibitors (e.g., tacrolimus)]; **AND**
- Used as a single agent or add-on therapy in combination with mycophenolate mofetil, mycophenolic acid, cyclophosphamide

Myasthenia Gravis (unrelated to immunotherapy-related toxicity)

- Patient has muscle-specific tyrosine kinase (MuSK)-antibody positive disease; **AND**
- Patient is refractory to standard first-line therapy (e.g., glucocorticoids, azathioprine, mycophenolate mofetil, etc.)

Continuation of Therapy Criteria:

- Patient continues to meet initial criteria; **AND**
- Patient is tolerating treatment with absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe infusion reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions, progressive multifocal leukoencephalopathy (PML), viral hepatitis, serious bacterial, fungal, or viral infections, cardiac arrhythmias, renal toxicity, bowel obstruction or perforation; **AND**

Non-Oncology Indications:
Rheumatoid arthritis (RA)

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts, reduction of C-reactive protein, improvement of patient global assessment, and/or an improvement on a disease activity scoring tool [e.g., an improvement on a composite scoring index such as Disease Activity Score-28 (DAS28) of 1.2 points or more or a ≥20% improvement on the American College of Rheumatology-20 (ACR20) criteria]; **AND**
- Dose escalation (up to the maximum dose and frequency specified below) may occur upon clinical review on a case by case basis provided that the patient has:
    - Shown an initial response to therapy; **AND**
    - Received a minimum of one maintenance dose at the dose and interval specified below; **AND**
    - Responded to therapy with subsequent loss of response

Granulomatosis with Polyangiitis (GPA) (Wegener's granulomatosis) and Microscopic polyangiitis (MPA)

- Disease response as indicated by disease control and improvement in signs and symptoms of condition compared to baseline; **AND**

- A decreased frequency in the occurrence of major relapses (defined by the reappearance of clinical and/or laboratory signs of vasculitis activity that could lead to organ failure or damage, or could be life threatening)

Pemphigus vulgaris

- Patient is currently receiving tapering doses of corticosteroids or has discontinued use of corticosteroids; **AND**
    - Disease response as indicated by complete epithelialization of lesions and improvement in signs and symptoms of condition compared to baseline; **OR**
    - Patient has not experienced continued development of new lesions, continued extension of old lesions, or failure of established lesions to begin to heal despite therapy; **OR**
        - For Relapses ONLY: Patient has previously had active disease control; **AND**
        - Patient has the appearance of 3 or more new lesions a month that do not heal spontaneously within 1 week, or by the extension of established lesions

Autoimmune Hemolytic Anemia (AIHA)

- Disease response as indicated by improvement in anemia signs and symptoms (e.g., dyspnea, fatigue, etc.) as well as: improvement in laboratory values (Hb/Hct), reduced transfusion needs, and/or reduced glucocorticoid use

Lupus Nephritis

- Coverage may only be renewed in patients experiencing a disease relapse (e.g., increased serum creatinine, increase in protein urine excretion, decrease in eGFR, etc.)

Myasthenia Gravis (unrelated to immunotherapy-related toxicity)

- Disease response as indicated by a decrease in the daily dose of corticosteroids and/or an improvement in signs and symptoms compared to baseline.

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months, unless otherwise stated in continuation of therapy criteria

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable. ***

Dosage/Administration:

Indication	Dose
RA	1,000 mg on days 1 and 15, repeated up to every 16 weeks
Pemphigus	Initiation: 1,000 mg on days 1 and 15; OR 375 mg/m² IV weekly for 4 doses Maintenance: 500 mg at month 12 and repeat every 6 months thereafter or based on clinical evaluation. <u>Relapse</u> – 1,000 mg IV upon relapse, resumption of glucocorticoids may be considered **Subsequent infusions (maintenance and relapse) should be no sooner than 16 weeks after the previous infusion.*
GPA(WG)/MPA	Induction (Pediatric and Adult): • 375 mg/m² weekly x 4 doses; OR • Adults: 1,000 mg IV on days 1 and 15; **OR** • Pediatric (up to a maximum of 1,000 mg per dose): o 575 mg/m² IV on days 1 and 15 (BSA ≤1.5m²) o 750 mg/m² IV on days 1 and 15 (BSA >1.5m²) Maintenance: • Pediatric: 250 mg/m² on days 1 and 15, then 250 mg/m² every 6 months thereafter based on clinical evaluation • Adult: 500 mg on days 1 and 15, then 500 mg every 6 months thereafter based on clinical evaluation
AIHA	375 mg/m² weekly x 4 doses in a 6 month period
Lupus Nephritis	1,000 mg IV on days 1 and 15 **-OR-** 375 mg/m² IV once weekly for 4 doses
Myasthenia Gravis (unrelated to immunotherapy-related toxicity)	1,000 mg IV on days 1 and 15, may repeat a full or partial course every 6 months **-OR-** 375 mg/m² IV once weekly for 4 doses, may repeat a full or partial course every 6 months

Dosing Limits:

Indication	Maximum dose (1 billable unit = 10 mg)

RA	100 units per dose every 14 days x 2 doses in a 16 week period
GPA(WG)/MPA	Induction: 100 units per dose weekly x 4 doses in a 4 month period Initial Maintenance: 50 units x 2 doses in a 6 month period Subsequent Maintenance: 50 units every 6 months
Pemphigus	Initiation: 100 units weekly x 4 doses in a 12 month period Maintenance: 50 units every 16 weeks
Lupus Nephritis & Myasthenia Gravis (unrelated to immunotherapy-related toxicity):	100 billable units per dose every 14 days x 2 doses in a 6 month period; **OR** 100 billable units per dose weekly x 4 doses in a 6 month period
All other non-oncology indications	100 units per dose weekly x 4 doses in a 6 month period

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT code is:

HCPCS/CPT Code	Description
J9312	Injection, rituximab, 10mg
Q5119	Injection, rituximab-pvvr, biosimilar, (Ruxience), 10mg
Q5115	Injection, rituximab-abbs, biosimilar, (Truxima), 10mg
Q5123	Injection, rituximab-arrx, biosimilar, (Riabni), 10mg

References:

1. Rituxan [package insert]. South San Francisco, CA; Genentech, Inc; June 2021. Accessed November 2021.
2. Truxima [package insert]. Incheon, Korea; Celltrion, Inc; June 2020. Accessed November 2021.
3. Ruxience [package insert]. New York, NY; Pfizer, Inc; May 2020. Accessed November 2021.
4. Riabni [package insert]. Thousand Oaks, CA;Amgen, Onc; December 2020. Accessed November 2021.

5. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 117(16):4190-4207.
6. Joly P, Mouquet H, Roujeau JC, et al. A single cycle of rituximab for the treatment of severe pemphigus. N Engl J Med 2007; 357:545-52.
7. Ahmed AR, Spigelman Z, Cavacini LA et al. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. N Engl J Med 2006; 355:1772-9.
8. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2015 Nov 6. doi: 10.1002/acr.22783.
9. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Mar 6. pii: annrheumdis-2016-210715.
10. González-Barca E, Domingo-Domenech E, Capote FJ, et al. Prospective phase II trial of extended treatment with rituximab in patients with B-cell post-transplant lymphoproliferative disease. Haematologica. 2007 Nov; 92(11):1489-94.
11. Chamberlain MC, Johnston SK, Van Horn A, et al. Recurrent lymphomatous meningitis treated with intra-CSF rituximab and liposomal ara-C. J Neurooncol. 2009 Feb;91(3):271-7.
12. Fakhouri F, Vernant JP, Veyradier A, et al. Efficiency of curative and prophylactic treatment with rituximab in ADAMTS13-deficient thrombotic thrombocytopenic purpura: a study of 11 cases. Blood. 2005;106:1932-37.
13. van Dorp S, Resemann H, te Boome L, et al. The immunological phenotype of rituximabsensitive chronic graft-versus-host disease: a phase II study. Haematologica 2011;96(9):1380- 1384.
14. Kim SJ, Lee JW, Jung CW, et al. Weekly rituximab followed by monthly rituximab treatment for steroid-refractory chronic graft-versus-host disease: results from a prospective, multicenter, phase II study. Haematologica 2010;95(11):1935-1942.
15. Cutler C, Miklos D, Kim HT, et al, "Rituximab for Steroid-Refractory Chronic Graft-VersusHost Disease," Blood, 2006, 108(2):756-62.
16. Wolff D, Schleuning M, von Harsdorf S, et al. Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2011 Jan;17(1):1-17. doi: 10.1016/j.bbmt.2010.05.011.
17. Gobert D, Bussel JB, Cunningham-Rundles C, et al. Efficacy and safety of rituximab in common variable immunodeficiency-associated immune cytopenias: a retrospective multicentre study on 33 patients. Br J Haematol. 2011;155(4):498-508.
18. YW Shin, ST Lee, KI Park, et al. Treatment strategies for autoimmune encephalitis. Ther Adv Neurol Disord. 2017 Aug 16;11:1756285617722347. doi: 10.1177/1756285617722347. eCollection 2018. Review.
19. First Coast Service Options, Inc. Local Coverage Determination (LCD): Rituximab (Rituxan®) (L33746). Centers for Medicare & Medicaid Services, Inc. Updated on 9/22/2017 with effective date 10/1/2017. Accessed March 2018.
20. National Government Services, Inc. Local Coverage Article: Rituximab (Rituxan®) (effective 2010) - Related to LCD L33394 (A52452). Centers for Medicare & Medicaid Services, Inc. Updated on 9/22/2017 with effective date of 10/1/2017. Accessed March 2018.

21. Palmetto GBA. Local Coverage Determination: Rituximab (Rituxan®) (L35026). Centers for Medicare & Medicaid Services, Inc. Updated on 03/02/2018 with effective date of 03/30/2018. Accessed March 2018.