Rituxan (rituximab)
Truxima (rituximab-abbs)
Ruxience (rituximab-pvvr)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Rituxan (rituximab) and Truxima (rituximab-abbs) policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies.The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Rituxan, Ruxience, and Truxima 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)

Rituxan and Truxima are also indicated for:
Rheumatoid Arthritis (RA)

Rituxan or Truxima, in combination with methotrexate, is indicated for the treatment of adult patients with moderately- to severely- active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

Rituxan is also indicated for:
Pemphigus Vulgaris (PV)
Rituxan is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris.

Compendial Use

1. Sjögren's syndrome
2. Multiple sclerosis, relapsing remitting
3. Neuromyelitis optica (Devic disease)
4. Autoimmune blistering disease
5. Cryoglobulinemia
6. Solid organ transplant
7. Opsoclonus-myoclonus ataxia
8. Systemic lupus erythematosus
9. B-cell acute lymphoblastic leukemia (ALL)
10. Non-Hodgkin's lymphoma
    a. Small lymphocytic lymphoma (SLL)
    b. Mantle cell lymphoma
    c. Marginal zone lymphomas (nodal, splenic, gastric MALT, nongastric MALT)
    d. Burkitt lymphoma
    e. Primary cutaneous B-cell lymphoma
    f. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
    g. High-grade B-cell lymphoma, not otherwise specified
    h. Castleman's disease
    i. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
    j. Hairy cell leukemia
    k. Post-transplant lymphoproliferative disorder (PTLD)
    l. B-cell lymphoblastic lymphoma
11. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
12. Autoimmune hemolytic anemia
13. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
14. Thrombotic thrombocytopenic purpura
15. Myasthenia gravis, refractory
16. Hodgkin's lymphoma, nodular lymphocyte-predominant
17. Chronic graft-versus-host disease (GVHD)
18. Central nervous system (CNS) cancers
    a) Leptomeningeal metastases from lymphomas
    b) Primary CNS lymphoma
19. B-cell acute lymphoblastic leukemia (ALL)
20. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
21. Immune checkpoint inhibitor-related toxicities

POLICY

Required 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)

Exclusions

A. Coverage will not be provided for requests for the treatment of rheumatoid arthritis (RA) when planned date of administration is less than 16 weeks since date of last dose received.
B. Member will not receive Rituxan, Ruxience, or Truxima with other biologics for RA.
C. Member will not receive Rituxan, Ruxience, or Truxima with other multiple sclerosis (MS) drugs excluding Ampyra

Criteria for Initial Approval

A. 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

B. 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. Non-Hodgkin's lymphoma (NHL) with any of the following subtypes:
   a) Diffuse large B-cell lymphoma
   b) High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
   c) High-grade B-cell lymphoma, not otherwise specified
   d) Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   e) Follicular lymphoma
   f) Mantle cell lymphoma
   g) Marginal zone lymphomas (nodal, splenic, gastric/nongastric MALT)
   h) Burkitt lymphoma
   i) Primary cutaneous B-cell lymphoma
   j) Castleman's disease
   k) AIDS-related B-cell lymphoma
   l) Hairy cell leukemia
   m) Post-transplant lymphoproliferative disorder (PTLD)
   n) B-cell lymphoblastic lymphoma
2. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
3. Hodgkin's lymphoma, nodular lymphocyte-predominant
4. Central nervous system (CNS) cancers with either of the following:
   a) Leptomeningeal metastases from lymphomas
   b) Primary CNS lymphoma
5. B-cell acute lymphoblastic leukemia (ALL)

C. Myasthenia gravis

Authorization of 12 months may be granted for treatment of refractory myasthenia gravis.

D. Immune checkpoint inhibitor-related toxicities

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

E. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for the treatment of moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate (MTX) unless the member has a contraindication (see Appendix A) or intolerance to MTX and either of the following criteria are met:

a) The members previously received any biologic disease-modifying antirheumatic drug (DMARD) or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis; or
b) The member has received at least two full doses of Rituxan, Ruxience, or Truxima for the treatment of RA, where the most recent dose was given within 6 months of the request.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA in combination with MTX when either of the following criteria are met:
   a) The member has experienced an inadequate response to at least a 3-month trial of MTX despite adequate dosing (i.e., titrated to 20 mg/week); or
   b) The member has an intolerable adverse effect or contraindication to MTX (see Appendix A), and an inadequate response to another conventional DMARD (e.g., hydroxychloroquine, leflunomide, sulfasalazine).

F. Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA) and Churg-Strauss and pauciimune glomerulonephritis
Authorization of 12 months may be granted for treatment of GPA, MPA or and Churg-Strauss and pauciimune glomerulonephritis.

G. Autoimmune blistering disease
Authorization of 12 months may be granted for treatment of corticosteroid refractory autoimmune blistering disease (e.g., pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa acquista and paraneoplastic pemphigus).

H. Sjögren's syndrome
Authorization of 12 months may be granted for treatment of Sjögren's syndrome when corticosteroids and other immunosuppressicve agents were ineffective.

I. Multiple sclerosis
Authorization of 12 months may be granted for treatment of relapsing remitting multiple sclerosis.

J. Neuromyelitis optica
Authorization of 12 months may be granted for treatment of neuromyelitis optica when at least one other immunotherapy was ineffective.

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

L. Solid organ transplant
Authorization of 3 months may be granted for treatment of solid organ transplant and prevention of antibody-mediated rejection in solid organ transplant.

M. Opsoclonus-myoclonus-ataxia
Authorization of 12 months may be granted for treatment of opsoclonus-myoclonus-ataxia associated with neuroblastoma when the member is refractory to steroids and chemotherapy.

N. Systemic Lupus Erythematosus
Authorization of 12 months may be granted for the treatment of systemic lupus erythematosus that is refractory to immunosuppressive therapy.

Continuation of Therapy

A. Rheumatoid arthritis

Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting authorization who meet all initial authorization criteria and achieve or maintain positive clinical response after at least two doses of therapy with Rituxan, Ruxience, or Truxima as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Multiple Sclerosis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for relapsing remitting multiple sclerosis (MS) who are experiencing disease stability or improvement while receiving Rituxan, Ruxience, or Truxima.

C. Oncologic indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an oncologic indication listed in Section B who have not experienced an unacceptable toxicity.

D. Immune checkoint 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.

E. Other indications

Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting authorization who meet all initial authorization criteria and are receiving benefit from therapy.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Appendices

Appendix A: Examples of contraindications to methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., bone marrow hypoplasia, thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. Hypersensitivity
6. Interstitial pneumonitis or clinically significant pulmonary fibrosis
7. Myelodysplasia
8. Pregnancy or planning pregnancy (male or female)
9. Renal impairment
10. Significant drug interaction

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J9310 Injection, rituximab, 100 mg (cancelled 1/1/2019)
- J9312 Rituxan, Injection, rituximab, 10 mg (effective 1/1/2019)
- Q5115 Injection, rituximab-abbs, biosimilar, 10 mg (effective 7/1/2019)
- Q5119 Injection, rituximab-pvvr, biosimilar, (ruxience), 10 mg
- C9399 unclassified drugs or biologicals

- J3490 Unclassified drugs
- J3590 Unclassified biologics

REFERENCES

- Rituxan [prescribing information]. South San Francisco, CA: Genentech, Inc.; September 2019.
- Truxima [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2019.
- Ruxience [prescribing information]. Cork, Ireland: Pfizer Ireland Pharmaceuticals; July 2019.
- Methotrexate [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; April 2018.
- Arber D, Orazi A, Vardiman J, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. May 19, 2016;127(20):2391-2405.
- Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 2009; 15(10):1143-1238.
- Dass S, Bowman SJ, Vital EM, et al. Reduction of fatigue in Sjögren syndrome with rituximab: results of a double blind, placebo-controlled study. Ann Rheum Dis. 2008;67:1541-1544.
- Meijer JM, Meiners PM, Vissink A, et al. Effectiveness of rituximab treatment in primary Sjögren's syndrome: a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2010;62(4):960-8.
- Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014;73:492-509.
- Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016;68(1)1-26.
- Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum. 2008;59(6):762-784.
- Hauser SL, Waubant E, Arnold DL, et al. B-cell depletion with rituximab in relapsing-remitting multiple sclerosis. N Engl J Med. 2008;358:676-688.
- Scott, T.F., Frohman, E.M., DeSeze, J., (2011). Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. American Academy of Neurology. 77: 2128-2134.
- Trebst, C., Jarius, S., et al. (2014). Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 261: 1-16.
- De Vita S, Quartuccio L, Isola M, et al. A randomized controlled trial of rituximab for the treatment of severe cryoglobulinemic vasculitis. Arthritis Rheum. 2012;64(3):843-53.
- Sneller MC, Hu Z, Langford CA. A randomized controlled trial of rituximab following failure of antiviral therapy for hepatitis C virus-associated cryoglobulinemic vasculitis. Arthritis Rheum. 2012 Mar; 64(3):835-42.
- Terrier B, Krastinova E, Marie I, et al. Management of noninfectious mixed cryoglobulinemia vasculitis: data from 242 cases included in the CryoVas survey. Blood. 2012 Jun 21; 119(25):5996-6004.
- Trappe R, Oertel S, Leblond V, et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet Oncol 2012.
- The American Society of Transplantation Infectious Diseases Guidelines. Am J Transplant 2009; 9 (Suppl 4):S92.
- Bell J, Moran C, Blatt J. Response to rituximab in a child with neuroblastoma and opsoclonus-myoclonus. Pediatr Blood Cancer 2008; 50:370.
- Hertl M, Geller S. Initial management of pemphigus vulgaris and pemphigus foliaceus. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed October 2019.

POLICY HISTORY

Policy #: 05.01.10
Reviewed: April 2020
Revised: April 2020
Current Effective Date: July 1, 2020