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

<table>
<thead>
<tr>
<th>Indications</th>
<th>Rituxan</th>
<th>Truxima</th>
<th>Ruxience</th>
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<tbody>
<tr>
<td>Oncology indications (adults)</td>
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<tr>
<td>Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>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</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide,</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
## Indications

| Chronic Lymphocytic Leukemia (CLL) | Previously untreated and treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC) | X | X | X |

### Non-oncology indications (adults)

| Rheumatoid Arthritis (RA) | Moderately to severely active RA in combination with methotrexate in patients who have inadequate response to one or more TNF antagonist therapies | X |

| Granulomatosi with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) | Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA) in combination with glucocorticoids | X | X |

| Pemphigus Vulgaris (PV) | Moderate to severe PV | X |

### Compendial Use

1. Sjögren’s syndrome
2. Multiple sclerosis, relapsing remitting
3. B-cell acute lymphoblastic leukemia (ALL)
4. 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
   m) High-grade B-cell lymphoma
5. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
6. Autoimmune hemolytic anemia
7. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
8. Thrombotic thrombocytopenic purpura
9. Myasthenia gravis, refractory
10. Hodgkin’s lymphoma, nodular lymphocyte-predominant
11. Chronic graft-versus-host disease (GVHD)
12. Central nervous system (CNS) cancers
   a) Leptomeningeal metastases from lymphomas
   b) Primary CNS lymphoma
13. B-cell acute lymphoblastic leukemia (ALL)
14. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
15. Refractory idiopathic inflammatory myopathy
16. Neuromyelitis optica
17. Immune checkpoint inhibitor-related toxicities
18. Antibody-mediated rejection (AMR)
Required Documentation

Submission of testing or analysis confirming CD20 protein on the surface of the B cell (if applicable)

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
      o) High-grade B-cell 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. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted to members who have previously received any biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis OR have received at least two full doses of Rituxan for the treatment of RA, where the most recent dose was given within 6 months of the
request. Rituxan must be prescribed in combination with methotrexate (MTX) unless the member has a contraindication or intolerance to MTX (see Appendix A).

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   a) Member is prescribed Rituxan in combination with MTX or has a contraindication or intolerance to MTX.
   b) Member meets any of the following criteria:
      i). 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)
      ii). Member has an intolerance or contraindication to MTX (see Appendix A).

E. Moderate to severe pemphigus vulgaris (PV)
   Authorization of 24 months may be granted for treatment of PV

F. Anti-neutrophil cytoplasmic antibody-associated (ANCA-associated) vasculitis - Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomotosis) and Microscopic Polyangiitis (MPA)
   Authorization of 24 months may be granted for treatment of GPA or MPA.

G. Sjögren’s syndrome
   Authorization of 24 months may be granted for treatment of Sjögren’s syndrome.

H. Multiple sclerosis
   Authorization of 24 months may be granted for treatment of multiple sclerosis (MS) when both of the following criteria are met:
   1. Member has a diagnosis of relapsing remitting MS
   2. Member has had an inadequate response to two or more disease-modifying drugs indicated for MS despite adequate duration of treatment (see Appendix B)

I. Refractory idiopathic inflammatory myopathy
   Authorization of 24 months may be granted for treatment of refractory polymyositis or dermatomyositis

J. Neuromyelitis optica
   Authorization of 24 months may be granted for treatment of neuromyelitis optica

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

L. Antibody-mediated rejection (AMR)
   Authorization of 6 months may be granted for treatment of antibody-mediated rejection following solid organ transplant

Continuation of Therapy
A. Rheumatoid arthritis
   Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least two doses of therapy with Rituximab as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. 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.

C. **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.

D. **Other indications**

Authorization may be granted for all members (including new members) who meet all initial authorization criteria.

**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., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

**Appendix B: Disease-modifying drugs indicated for multiple sclerosis**

1. Aubagio (teriflunomide)
2. Avonex (interferon beta-1a)
3. Betaseron (interferon beta-1a)
4. Copaxone/Glatopa (glatiramer acetate)
5. Extavia (interferon beta-1a)
6. Gilenya (fingolimod)
7. Tecfidera (dimethyl fumarate)
8. Pledridy (peginterferon beta-1a)
9. Rebif (interferon beta-1a)
10. Tysabri (natalizumab)
11. Ocrevus (ocrelizumab)
12. Mavenclad (cladribine)
13. Mayzent (siponimod)
14. Lemtrada (alemtuzumab)

**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)
• C9399 unclassified drugs or biologicals
• J3490 Unclassified drugs
• J3590 Unclassified biologics

REFERENCES

• Truxima [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; November 2018.
• Ruxience [prescribing information]. Cork, Ireland: Pfizer Ireland Pharmaceuticals; July 2019.

POLICY HISTORY

Policy #: 05.01.10
Reviewed: October 2019
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Current Effective Date: February 7, 2020

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