

**POLICY:** Rituximab Intravenous Products

- Rituxan<sup>®</sup> (rituximab injection for intravenous use – Genentech)
- Ruxience<sup>™</sup> (rituximab-pvvr injection for intravenous use – Pfizer)
- Truxima<sup>®</sup> (rituximab-abbs injection for intravenous use – Celltrion/Teva)

**DATE REVIEWED:** 06/03/2020

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**OVERVIEW**

Rituximab products are CD20-directed cytolytic antibodies. All approved rituximab intravenous products are indicated for treatment of the following conditions:

1. **Non-Hodgkin lymphoma (NHL)**, for the following uses:
  - previously untreated follicular, CD20-positive disease, in combination with first-line chemotherapy, and in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as a single-agent maintenance therapy; AND
  - for relapsed or refractory, low-grade or follicular, CD20-positive, B-cell, disease; AND
  - for non-progressing (including stable disease) low-grade, CD20-positive, B-cell disease as a single agent after first-line cyclophosphamide/vincristine/prednisone (CVP) chemotherapy; AND
  - for previously untreated diffuse large B-cell, CD20-positive disease, in combination with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) or other anthracycline-based chemotherapy regimens; AND
2. **Chronic lymphocytic leukemia (CLL)**, in combination with fludarabine and cyclophosphamide (FC) for the treatment of patients with previously untreated and previously treated CD20-positive disease; AND
3. **Granulomatosis with polyangiitis (GPA)** [Wegener's granulomatosis {WG}] and **microscopic polyangiitis (MPA)** in adults, in combination with glucocorticoids.

In addition to the above indications, Rituxan IV and Truxima are also indicated for treatment of the following condition:

1. **Rheumatoid arthritis (RA)**, in adult patients with moderately to severely active disease, in combination with methotrexate (MTX) for patients who have had an inadequate response to one or more tumor necrosis factor inhibitors (TNFis).

In addition to the above indications, Rituxan IV is also indicated for treatment of the following conditions:

1. **Pemphigus vulgaris**, for adults with moderate to severe; AND
2. **Granulomatosis with polyangiitis (GPA)** [Wegener's granulomatosis {WG}] and **microscopic polyangiitis (MPA)** in patients  $\geq$  2 years of age, in combination with glucocorticoids.

Rituximab products are monoclonal antibody directed specifically against the CD20 antigen found on the surface of normal and malignant B lymphocytes.<sup>1-3</sup> The antigen CD20 is expressed on > 90% of B-cell non-Hodgkin's lymphomas (NHLs). B-cells are thought to play a role in the pathogenesis of rheumatoid arthritis (RA) and associated chronic synovitis.

Ruxience and Truxima are approved as biosimilar to Rituxan intravenous (IV), indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, dosage form, and strength as Rituxan IV. However, minor differences in clinically inactive

components are allowed. At this time, Ruxience and Truxima has only demonstrated biosimilarity, not interchangeability.

## Guidelines

The use of rituximab is supported in clinical guidelines in numerous situations, both as first-line therapy and in patients who are refractory or have relapsed following treatment with other therapies.<sup>4-21</sup>

- **Vasculitis:** EULAR/ERA-EDTA recommendations for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis mention rituximab in combination with low-dose corticosteroids as a potential treatment option for remission-maintenance therapy.<sup>4</sup> Remission-maintenance therapy is recommended for at least 24 months following induction of sustained remission. British guidelines for use of rituximab in ANCA-associated vasculitis recommend rituximab for maintenance of remission to reduce the risk of relapse and its consequences.<sup>5</sup>
- National Comprehensive Cancer Network (NCCN) guidelines:<sup>6</sup>
  - **CLL/SLL:** Rituximab features prominently in the guidelines (version 4.2020 – December 20, 2019) and is included in multiple treatment regimens across the spectrum of disease.<sup>7</sup>
  - **B-Cell Lymphomas:** In the guidelines (version 1.2020 – January 22, 2020), rituximab is included in multiple treatment regimens across the spectrum of disease.<sup>8</sup> Guidelines for pediatric aggressive mature B-cell lymphomas (version 2.2020 – April 10, 2020) include rituximab intravenous among treatment regimens for induction therapy/initial treatment and as subsequent therapy for relapsed or refractory disease.<sup>9</sup> For primary cutaneous lymphomas (version 2.2020 – April 10, 2020), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.<sup>10</sup>
  - **Acute Lymphoblastic Leukemia (ALL):** Guidelines (version 1.2020 – January 15, 2020) list rituximab in multiple induction regimens for Philadelphia chromosome (Ph)-negative disease.<sup>11</sup> In those with Ph-positive disease, rituximab should be considered in addition to chemotherapy for those with CD20-positive disease, especially in those < 60 years of age. Rituximab is also included in a regimen for relapsed/refractory disease for those with Ph-positive or –negative disease.
  - **Hairy Cell Leukemia:** Guidelines (version 1.2020 – August 23, 2019) recommend rituximab in multiple regimens for relapsed/refractory disease, including in patients with progressive disease after relapsed/refractory therapy.<sup>12</sup>
  - **Hodgkin Disease:** Guidelines (version 2.2020 – April 17, 2020) recommend rituximab ± chemotherapy (depending on the clinical presentation) in the first-line setting for nodular lymphocyte-predominant disease.<sup>13</sup> Rituximab is also used for relapsed/refractory disease and for maintenance.
  - **Waldenstrom Macroglobulinemia/lymphoplasmacytic lymphoma:** Guidelines (version 2.2020 – April 15, 2020) include rituximab in regimens across the spectrum of disease (primary therapy, previously treated disease, and maintenance).<sup>14</sup>
  - **Graft Versus Host Disease:** Guidelines (version 2.2020 – March 23, 2020) list rituximab among the agents used for steroid-refractory chronic GVHD.<sup>15</sup>
- **Rheumatoid Arthritis:** Guidelines from the American College of Rheumatology (ACR) [2015] have tumor inhibitors and non-TNF biologics (including rituximab), equally positioned following a trial of a conventional synthetic DMARD.<sup>16</sup>
- **Immune Thrombocytopenia (ITP):** Guidelines from the American Society of Hematology (ASH) for ITP (2011) mention rituximab as an appropriate agent for children and adolescents with ITP who have significant on-going bleeding despite treatment with intravenous immunoglobulin G (IVIG), anti-D, or corticosteroids.<sup>17</sup> Rituximab is also appropriate as an alternative to splenectomy in children/adolescents with chronic ITP or in patient who do not respond to splenectomy. In adults,

rituximab is recommended for patients with ITP who are at risk for bleeding and who have failed one other line of therapy (e.g., corticosteroids, IVIg, splenectomy).

- **Multiple Sclerosis (MS):** In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.<sup>18</sup> Rituximab is listed among various options, involving different mechanisms of action and modes of administration, which have shown benefits in patients with MS. The American Academy of Neurology has practice guidelines regarding disease-modifying therapies for adults with MS.<sup>19</sup> The guidelines mention rituximab for use in MS.
- **Neuromyelitis Optica Spectrum Disorders:** A review article lists rituximab as an effective treatment for neuromyelitis optica.<sup>20</sup>
- **Systemic Lupus Erythematosus (SLE):** EULAR recommendations for the management of systemic lupus erythematosus (2019) mention rituximab as a therapeutic option for patients who are refractory to standard immunosuppressive therapies.<sup>21</sup>

## Safety

Rituximab IV products have Boxed Warnings due to fatal infusion reactions, severe mucocutaneous reactions, hepatitis B virus (HBV) reactivation, and progressive multifocal leukoencephalopathy (PML). Deaths within 48 hours of rituximab infusions have been reported, primarily (80%) associated with the first infusion. Screen all patients for HBV infection and monitor during and after treatment with rituximab IV. Discontinue rituximab products in cases of HBV reactivation.

## POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of rituximab IV products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because of the specialized skills required for evaluation and diagnosis of patients treated with rituximab products as well as the monitoring required for adverse events (AEs) and long-term efficacy, initial approval requires rituximab to be prescribed by or in consultation with a physician who specializes in the condition being treated.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of rituximab IV products is recommended in those who meet the following:

### FDA-Approved Indications

- 1. Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
  - A) Induction Treatment.** Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):
    - i.** The patient has an ANCA-associated vasculotide; AND  
Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis (GPA) [Wegener's granulomatosis] or microscopic polyangiitis (MPA).
    - ii.** The requested agent is being administered in combination with glucocorticoids; AND
    - iii.** The agent is prescribed by or in consultation with a rheumatologist, nephrologist, or immunologist.

- B) Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis** (Note: This includes patients who received induction treatment using a rituximab product or other standard of care immunosuppressants). Approve for 1 year if the patient meets BOTH of the following (i and ii):
- i. According to the prescriber, the patient achieved disease control with induction treatment; AND
  - ii. If the patient previously received a course of therapy, at least 16 weeks will elapse between courses.

**Dosing.** Approve the following (A or B):

- A) Initial Therapy: Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion not more frequently than once weekly; OR
- B) Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis: Up to two 500 mg administered as an intravenous infusion separated by at least 14 days, then up to 1,000 mg administered by intravenous infusion not more frequently than once every 6 months.

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- 2. Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL).** Approve for 1 year if prescribed by or in consultation with an oncologist.

**Dosing.** Approve up to 500 mg/m<sup>2</sup> administered as an intravenous infusion on 1 day of each cycle.

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- 3. B-Cell Lymphoma** (Note: Examples of B Cell Lymphomas include Follicular Lymphoma, Diffuse Large B-Cell Lymphoma [DLBCL], Acquired Immune Deficiency [AIDS]-Related B-Cell Lymphoma, Burkitt Lymphoma, Castleman's Disease, Marginal Zone Lymphoma [e.g., extranodal or MALT {gastric or nongastric}, nodal, or splenic marginal zone lymphoma], Primary Mediastinal Large B-Cell Lymphoma, Mantle Cell Lymphoma, Post-Transplant Lymphoproliferative Disorders, Gray Zone Lymphoma, Primary Cutaneous B-Cell Lymphoma, Pediatric Aggressive Mature B-cell Lymphomas). Approve for 1 year if prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following (A and B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND
- B) Doses are separated by at least 7 days.

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- 4. Pemphigus Vulgaris.** Approve for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Treatment. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets BOTH of the following (i and ii):
  - i. Therapy is initiated in combination with a corticosteroid unless contraindicated; AND  
Note: An example of a corticosteroid is prednisone.
  - ii. The agent is prescribed by or in consultation with a dermatologist.
- B) Patient is Being Treated of a Relapse or for Maintenance of Pemphigus Vulgaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):
  - i. Subsequent infusions of will be administered no sooner than 16 weeks following the previous infusion of a rituximab product; AND

- ii. The agent is prescribed by or in consultation with a dermatologist.

**Dosing.** Approve the following (A or B):

- A) Initial Treatment or Treatment of a Relapse: Approve one course of therapy, which consists of up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks; OR
- B) Maintenance Therapy: Approve up to 500 mg per dose administered intravenously.

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**5. Rheumatoid Arthritis (RA).** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets ALL of the following conditions (i, ii, and iii):

- i. The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND

Note: Examples of conventional synthetic disease-modifying antirheumatic drugs include methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. These patients who have already tried a biologic for RA are not required to “step back” and try a conventional synthetic DMARD.

- ii. The agent will not be used concurrently with another biologic or with a targeted synthetic DMARD; AND

Note: Examples of biologics include Cimzia, adalimumab products, etanercept products, infliximab products, Simponi [Aria or SC], Actemra [IV or SC], Kevzara, Kineret, and Orencia [IV or SC]). Examples of targeted synthetic DMARDs include Xeljanz/XR, Oluminat, and Rinvoq.

iii. The requested agent is prescribed by or in consultation with a rheumatologist.

B) Patient has already Received One or More Courses of a Rituximab Product for Rheumatoid Arthritis (RA). Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets BOTH of the following conditions (i and ii):

- i. 16 weeks or greater will elapse between treatment courses; AND

Note: For example, there will be a minimum of 16 weeks since the first dose of the previous course and the first dose of the next course of a rituximab product.

- ii. If the patient has already received two or more courses of therapy, the patient has responded to therapy as determined by the prescriber.

Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids).

**Dosing.** Approve one course of therapy, which consists of up to two 1,000-mg intravenous doses separated by at least 2 weeks.

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**Other Uses with Supportive Evidence**

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**6. Acute Lymphoblastic Leukemia (ALL).** Approve for 1 year if the patient meets ALL of the following (A and B):

- A) The patient has CD20-positive disease; AND
- B) The agent is prescribed by or in consultation with an oncologist.

**Dosing:** Approve the following (A and B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND
- B) The patient receives a maximum of two doses per 28-day cycle.

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**7. Graft Versus Host Disease (GVHD).** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) The patient has tried at least one conventional systemic treatment for graft versus host disease; AND

**Note:** Examples include systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica<sup>®</sup> (ibrutinib capsules and tablets), imatinib, antithymocyte globulin, Nipent<sup>®</sup> (pentostatin infusion), or an infliximab product.

- B) The agent is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center.

**Dosing.** Approve the following dosing (A and B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND
- B) Doses are separated by at least 7 days.

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**8. Hairy Cell Leukemia.** Approve for 1 year if the patient meets BOTH of the following conditions (A and B):

- A) The patient has relapsed/refractory hairy cell leukemia; AND
- B) The agent is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following (A and B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND
- B) The patient receives a maximum of four doses per 28-day treatment cycle.

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**9. Hodgkin Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) The patient has nodular lymphocyte-predominant disease; AND
- B) The agent is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following (A and B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND
- B) The patient receives a maximum of four doses per 28-day treatment cycle.

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**10. Immune Thrombocytopenia (ITP).** Approve if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 1 month if the patient meets BOTH of the following (i and ii):

- i. The patient has tried one other therapy; AND

**Note:** Examples of therapies for ITP include intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, and splenectomy.

- ii. The agent is prescribed by or in consultation with a hematologist.

- B) Patient has Already Received a Course of a Rituximab Product for ITP. Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):

- i. At least 6 months will elapse between treatment courses; AND  
Note: For example, there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of a rituximab product.
- ii. The patient responded to therapy as determined by the prescriber; AND  
Note: Examples of a response include a platelet count increase from baseline following treatment with a rituximab product.
- iii. The prescriber has determined that the patient has relapsed.  
Note: Examples of a relapse include the patient experiences thrombocytopenia after achievement of a remission.

**Dosing.** Approve up to 375 mg/m<sup>2</sup> administered intravenously with doses separated by at least 7 days.

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**11. Multiple Sclerosis.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A) The patient has had an inadequate response or was unable to tolerate at least ONE other disease-modifying agent for MS; AND
- B) The agent will not be used concurrently with another disease-modifying agent used for multiple sclerosis; AND  
Note: Examples of disease-modifying agents for MS include Ocrevus (ocrelizumab IV infusion), Avonex (interferon beta-1a for intramuscular injection), Rebif (interferon beta-1a SC injection), Betaseron (interferon beta-1b SC injection), Extavia (interferon beta-1b SC injection), Copaxone (glatiramer acetate SC injection), Glatopa (glatiramer acetate SC injection), Plegridy (peginterferon beta-1a SC injection), Gilenya (fingolimod capsules), Aubagio (teriflunomide tablets), Tecfidera (dimethyl fumarate delayed-release capsules), or Lemtrada (alemtuzumab IV injection), mitoxantrone IV (Novantrone, generics), Tysabri (natalizumab IV injection), and Mavenclad (cladribine tablets).
- C) The requested agent is prescribed by or in consultation with a physician who specializes in the treatment of MS and/or a neurologist; AND
- D) At least 6 months will elapse between treatment courses.  
Note: For example, if the patient has already received a course of therapy there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of therapy.

**Dosing.** Approve the following (A and B):

- A) Each course is up to 2,000 mg (total); AND
- B) Each course is administered as one or two intravenous infusions administered over 1 month.

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**12. Neuromyelitis Optica (NMO) Spectrum Disorder.** Approve for 1 month if prescribed by or in consultation with a neurologist.

**Dosing.** Approve ONE of the following (A or B):

- A) Each single dose must not exceed 375 mg/m<sup>2</sup> IV administered as an intravenous infusion not more frequently than once weekly; OR
- B) Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

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**13. Systemic Lupus Erythematosus (SLE) [Lupus].** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month (adequate duration to receive one course) if the patient meets BOTH of the following (i and ii):

i. The patient has tried at least ONE standard immunomodulating or immunosuppressant agent; AND

Note: Examples of standard immunomodulating or immunosuppressant agents include hydroxychloroquine, corticosteroids (e.g., prednisone, methylprednisolone), methotrexate, azathioprine, mycophenolate, and cyclophosphamide.

ii. The agent is prescribed by or in consultation with a rheumatologist, nephrologist, or neurologist.

B) Patient has Already Received a Course of a Rituximab Product for SLE. Approve for 1 month (adequate duration to receive one course) if 6 months or greater will elapse between treatment courses (i.e., there will be a minimum of 6 months separating the first dose of the previous rituximab course and the first dose of the requested course of rituximab).

**Dosing.** Approve the requested dose.

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**14. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following (A and B):

A) Each single dose must not exceed 375 mg/m<sup>2</sup> administered as an intravenous infusion; AND

B) The patient receives a maximum of four doses per 28-day treatment cycle.

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### Conditions Not Recommended for Approval.

Rituximab IV products have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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## HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Early annual revision	<p><b>ANCA-Associated Vasculitis:</b> Add criteria for follow-up treatment for patients who have achieved disease control with induction therapy (e.g., using rituximab infusion or a standard immunosuppressant). A minimum of 16 weeks are required to elapse between courses of rituximab. Add 500 mg on Days 1 and 15, then 500 mg every 6 months as an approvable dose.</p> <p><b>B-Cell Lymphoma:</b> Add primary mediastinal large B-cell lymphoma as an example of a B-cell lymphoma.</p> <p><b>Pemphigus Vulgaris:</b> Add this FDA-approved indication to the policy. Criteria require rituximab to be prescribed by or in consultation with a dermatologist. For initial therapy, approval is for 1 month, if initiated in combination with a corticosteroid, unless contraindicated. For relapse or maintenance, approve for 1 year if at least 16 weeks will elapse between courses. Dosing is per the approved labeling.</p> <p><b>RA:</b> Change approvals to 1 month, which is adequate to administer two infusions given 2 weeks apart (previously this dose was allowed over 4 months).</p> <p><b>GVHD:</b> Change approval duration to 1 year (previously was 1 month for initial therapy and 6 months for extended approvals). Because a specific response was not defined or required for extended approvals, remove criteria that generally required a response as determined by the prescriber.</p> <p><b>Multiple Sclerosis:</b> Change criteria to require an inadequate response or intolerance to a disease-modifying agent for MS; previously criteria required a trial of at least one of these agents. Remove Zinbryta (no longer available) from the list of examples of a therapy the patient may have tried prior to rituximab.</p> <p><b>SLE:</b> Because a specific response was not defined or required for extended approvals, remove criteria that generally required a response as determined by the prescriber.</p> <p><b>Patient has been Established on Rituxan:</b> Remove this approval condition from the policy. For each approvable condition, criteria and dosing must be met for each indication.</p> <p><b>ANCA-Associated Vasculitis:</b> Update terminology (Antineutrophil Cytoplasmic Antibody) to align with terminology in EULAR guidelines.</p>	10/31/2018
Selected revision	Add Truxima to the policy (use same criteria as Rituxan IV). Update policy name to be Rituximab Intravenous Products. Throughout the policy, reword references to Rituxan as rituximab products.	12/05/2018
Annual revision	<p><b>Ruxience</b> was added to the policy using the same criteria as other rituximab IV products.</p> <p><b>Dosing:</b> Throughout the policy, dosing was modified to allow for approval up to the maximum dose listed.</p> <p><b>B-Cell Lymphoma:</b> Primary Cutaneous B-Cell Lymphoma was added as an example of a B-cell lymphoma. To align with other policies that approve for this condition, remove hematologist from the specialists who are required to prescribe or be consulted prior to approval.</p> <p><b>Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL):</b> To align with other policies that approve for this condition, remove hematologist from the specialists who are required to prescribe or be consulted prior to approval.</p> <p><b>Rheumatoid Arthritis (RA):</b> A criterion that excludes concomitant use with another biologic or with a targeted synthetic DMARD was added. Previously, this was addressed in the Conditions Not Recommended for Coverage and applied to all indications.</p> <p><b>Acute Lymphoblastic Leukemia (ALL):</b> This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve if the patient has CD20-positive disease. If disease is Philadelphia chromosome positive, a tyrosine kinase inhibitor is required prior to approval of rituximab. Rituximab is also required to be prescribed by or in consultation with an oncologist.</p> <p><b>Hairy Cell Leukemia:</b> This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve if the patient has relapsed or refractory disease, and if the agent is prescribed by or in consultation with an oncologist.</p>	11/20/2019

	<p><b>Hodgkin Lymphoma:</b> This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve if the patient has nodular lymphocyte-predominant disease, and if the agent is prescribed by or in consultation with an oncologist.</p> <p><b>Multiple Sclerosis:</b> A criterion that excludes concomitant use with another disease-modifying agent for multiple sclerosis was added. Previously, this was addressed in the Conditions Not Recommended for Coverage and applied to all indications. A criterion was added that requires at least 6 months to elapse between treatment courses. Previously, this was addressed in the dosing section.</p> <p><b>Neuromyelitis Optica:</b> This approval condition was broadened to more generally state Neuromyelitis Optica Spectrum Disorders. The approval duration was changed from 1 year to 1 month.</p> <p><b>Systemic Lupus Erythematosus (SLE):</b> Criteria were added to require a trial of at least one standard immunomodulating or immunosuppressant agent. Since patients with neuropsychiatric symptoms of SLE or lupus nephritis are generally included in this criterion, specific criteria that applied to these patients were removed from the policy.</p> <p><b>Waldenstrom’s Macroglobulinemia/Lymphoplasmacytic Lymphoma:</b> This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve if the agent is prescribed by or in consultation with an oncologist.</p> <p><b>Other Cancer-related Indications:</b> This criterion was deleted from the policy. Indication-specific criteria were added to the policy for these conditions.</p> <p><b>Conditions Not Recommended for Approval:</b> The following situations are now addressed in the criteria section for the related condition and were removed from this section of the policy: Concurrent Use with A Biologic Disease-Modifying Antirheumatic Drug (DMARD) or Targeted Synthetic DMARD and Current Use with Disease-Modifying Agents Used for Multiple Sclerosis (MS).</p>	
<p>Early annual revision</p>	<p><b>Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis:</b> For follow-up treatment of patients who have received induction treatment for ANCA-associated vasculitis, the maintenance dose was changed to be up to 1,000 mg per dose (previously was up to 500 mg). For the criterion applying to patients who achieved disease control, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). For patients who have already received rituximab for induction therapy, criteria were clarified to note this applies to those receiving any rituximab product (previously listed as rituximab).</p> <p><b>B-Cell Lymphoma:</b> Pediatric Aggressive Mature B-cell Lymphoma was added as an example of a B-cell lymphoma.</p> <p><b>Rheumatoid Arthritis:</b> For the criterion applying to patients who responded to therapy, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). For patients who have already received one or more courses of therapy, criteria were clarified to note this applies to those receiving any rituximab product (previously listed as rituximab).</p> <p><b>Pemphigus Vulgaris:</b> An example of a corticosteroid (prednisone) was moved to a note in the policy (previously listed as an example within the criteria). For the criterion that refers to subsequent infusions, criteria were clarified to note this applies to those receiving any rituximab product (previously listed as rituximab).</p> <p><b>Acute Lymphoblastic Leukemia (ALL):</b> To align with updated NCCN guidelines, the requirement that patients who are Philadelphia-chromosome-positive try a tyrosine kinase inhibitor prior to rituximab was removed from the policy.</p> <p><b>Graft Versus Host Disease (GVHD):</b> To align with updated NCCN guidelines and other policies, criteria were changed to require at least one conventional systemic treatment prior to a rituximab product. Previously, criteria required that the patient had tried at least one other immunosuppressant or be concurrently receiving an immunosuppressant in combination with rituximab.</p> <p><b>Immune Thrombocytopenia (ITP):</b> For the criteria applying to patients who responded to therapy and patients who relapsed, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). For patients who have already received one or more courses of therapy, criteria were clarified to note this applies to those receiving any rituximab product (previously listed as rituximab).</p> <p><b>Multiple Sclerosis:</b> An example of the time required between courses of therapy was moved to a note (previously listed as an example within the criteria).</p> <p><b>Systemic Lupus Erythematosus (SLE) [Lupus]:</b> For patients who have already received one or more courses of therapy, criteria were clarified to note this applies to those receiving any rituximab product (previously listed as rituximab).</p>	<p>06/03/2020</p>

**APPENDIX**

	<b>Mechanism of Action</b>	<b>Examples of Inflammatory Indications for Products*</b>
<b>Biologics</b>		
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, PsO, PsA, RA
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
<b>Simponi®, Simponi® Aria™</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC IV formulation: AS, PsA, RA
<b>Actemra®</b> (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA IV formulation: PJIA, RA, SJIA
<b>Kezara®</b> (sarilumab SC injection)	Inhibition of IL-6	RA
<b>Orencia®</b> (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: PJIA, PSA, RA IV formulation: PJIA, PsA, RA
<b>Rituximab IV Products</b> (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
<b>Ilaris</b> (canakinumab SC injection)	Inhibition of IL-1β	SJIA
<b>Kineret®</b> (anakinra SC injection)	Inhibition of IL-1	RA, SJIA <sup>^</sup>
<b>Stelara®</b> (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
<b>Siliq™</b> (brodalumab SC injection)	Inhibition of IL-17	PsO
<b>Cosentyx™</b> (secukinumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
<b>Taltz®</b> (ixekizumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
<b>Ilumya™</b> (tildrakizumab-asnm SC injection)	Inhibition of IL-23	PsO
<b>Skyrizi™</b> (risankizumab-rzsa SC injection)	Inhibition of IL-23	PsO
<b>Tremfya™</b> (guselkumab SC injection)	Inhibition of IL-23	PsO
<b>Entyvio™</b> (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
<b>Targeted Synthetic DMARDs</b>		
<b>Otezla®</b> (apremilast tablets)	Inhibition of PDE4	PsO, PsA
<b>Olumiant®</b> (baricitinib tablets)	Inhibition of the JAK pathways	RA
<b>Rinvoq®</b> (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
<b>Xeljanz®, Xeljanz XR</b> (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

\* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn’s disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; <sup>^</sup> Off-label use of SJIA supported in guidelines.