

Utilization Review Policy 216

Policy: Biosimilars - Rituxan

• Rituxan® (rituximab injection for intravenous use – Genentech)

EFFECTIVE DATE: 1/1/2021

LAST REVISION DATE: 09/18/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Rituximab products are CD20-directed cytolytic antibodies. All approved rituximab intravenous products are indicated for treatment of the following conditions: 1-3,22

- 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.
- 2. **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in adults, in combination with glucocorticoids.
- 3. **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.
 - for relapsed or refractory, low-grade or follicular, CD20-positive, B-cell disease.
 - 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.
 - for previously untreated diffuse large B-cell, CD20-positive disease, in combination with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) or other anthracycline-based chemotherapy regimens.
- 2. **Pemphigus vulgaris**, for adults with moderate to severe disease.
- Rheumatoid arthritis, in adult patients with moderately to severely active disease, in combination with methotrexate for patients who have had an inadequate response to one or more tumor necrosis factor inhibitors.

In addition to the above indications, <u>Rituxan intravenous</u> is also indicated for treatment of the following conditions:¹

- **1. Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in <u>patients ≥ 2 years of age</u>, in combination with glucocorticoids.
- **2. B-cell lymphoma,** in patients ≥ 6 months of age with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma, Burkitt lymphoma, Burkitt-like lymphoma, or mature B-cell acute leukemia in combination with chemotherapy.

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

clinically inactive components are allowed. At this time, the biosimilars have 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. 4-21

- Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis: Guidelines from the American College of Rheumatology (ACR) [2021] list rituximab among the alternatives for induction or maintenance of remission. Various regimens are recommended with a typical maximum of 1,000 mg/infusion. For maintenance dosing, at least 4 months should separate doses. The optimal dose of rituximab for remission maintenance remains uncertain. Although scheduled maintenance is conditionally recommended over the use of CD19+ B-cell counts and/or ANCA titers to guide retreatment, there are data to support both approaches.
- Immune Thrombocytopenia (ITP): Guidelines from the American Society of Hematology for ITP (2019) mention rituximab as an alternative for children and adults with ITP who do not respond to first-line treatment, and for adults who are corticosteroid-dependent.¹⁷
- **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. 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. The guidelines mention rituximab for use in MS.
- **Neuromyelitis Optica Spectrum Disorders (NMOSD):** The Neuromyelitis Optica Study Group (NEMOS) published revised recommendations for the treatment of NMOSD in 2023 and recommend rituximab as a treatment option for aquaporin-4 (AQP4)-immunoglobulin G (IgG) positive NMOSD and double-negative NMOSD.²⁰
- Oncology indications covered in National Comprehensive Cancer Network (NCCN) guidelines:
 - Acute Lymphoblastic Leukemia: Guidelines (version 2.2025 June 27, 2025) list rituximab
 in multiple regimens for Philadelphia chromosome (Ph)-negative disease for patients with
 CD20-positive disease.¹¹ 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.
 - B-Cell Lymphomas: In the guidelines (version 2.2025 February 10, 2025), rituximab is included in multiple treatment regimens across the spectrum of disease.⁸ Guidelines for pediatric aggressive mature B-cell lymphomas (version 2.2025 April 28, 2025) include rituximab intravenous as a component of treatment regimens for induction therapy/initial treatment and as subsequent therapy for relapsed or refractory disease.⁹ For primary cutaneous lymphomas (version 3.2025 June 10, 2025), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.¹⁰ For Castleman disease, rituximab is broadly recommended in the guidelines (version 2.2025 January 28, 2025) for unicentric and multicentric Castleman disease as initial therapy and second-line and subsequent therapy either as monotherapy or in combination with other treatments.²⁸
 - CLL/Small Lymphocytic Lymphoma: Rituximab features prominently in the guidelines (version 3.2025 – April 2, 2025) and is included in multiple treatment regimens across the spectrum of disease.⁷

- Graft-Versus-Host Disease (GVHD): The hematopoietic cell transplantation guidelines (version 2.2025 June 3, 2025) list rituximab among the agents used for steroid-refractory chronic GVHD. Among the agents FDA-approved for use in chronic GVHD, Jakafi® (ruxolitinib tablets) is the only agent given a category 1 recommendation for chronic GVHD. Other alternatives with a category 2A recommendation include Niktimvo™ (axatilimab-csfr), Rezurock® (belumosudil), and Imbruvica® (ibrutinib), Orencia® (abatacept), alemtuzumab, calcineurin inhibitors (e.g., tacrolimus, cyclosporine), etanercept, extracorporeal photopheresis, hydroxychloroquine, imatinib, interleukin-2, low-dose methotrexate, mammalian target of rapamycin inhibitors (e.g., sirolimus), mycophenolate mofetil, pentostatin, and rituximab.
- Hairy Cell Leukemia: Guidelines (version 1.2025 September 26, 2024) recommend rituximab as a component in a preferred primary regimen, and in multiple regimens for relapsed/refractory disease (including in patients with progressive disease after relapsed/refractory therapy).¹²
- Hematopoietic Cell Transplant: Guidelines (version 2.2025 June 3, 2025) list rituximab in combination with cyclophosphamide and fludarabine as a non-myeloablative regimen for conditioning for allogeneic transplantation.¹⁵
- Histiocytic Neoplasms Rosai-Dorman Disease: Guidelines (version 1.2025 June 20, 2025) recommend rituximab as first-line or subsequent therapy, irrespective of mutation, as a single agent.²⁹
- Hodgkin Lymphoma: Guidelines (version 2.2025 January 30, 2025) recommend rituximab ± chemotherapy and/or radiation (depending on the clinical presentation) in the first-line setting for nodular lymphocyte-predominant disease.¹³ Rituximab is also used for relapsed/refractory disease and for maintenance. Guidelines for pediatric disease (version 2.2025 June 9, 2025) include rituximab in regimens for primary treatment of nodular lymphocyte-predominant disease.²⁵
- Primary Central Nervous System Lymphoma: Guidelines for central nervous system cancers (version 1.2025 – June 3, 2025) recommend rituximab in multiple regimens for induction therapy and relapsed or refractory primary central nervous system lymphoma.²⁴
- Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma: Guidelines (version 1.2026 – June 24, 2025) include rituximab in regimens across the spectrum of disease (primary therapy, previously treated disease, and maintenance).¹⁴
- Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors: NCCN (version 1.2025 December 20, 2024) and the American Society of Clinical Oncology (ASCO) guidelines (2021) recommend rituximab as an option for corticosteroid-refractory dermatologic and hematologic immune mediated adverse events, as well as for myasthenia gravis, immune-mediated encephalitis, myositis, and stage 3 acute kidney injury/elevated serum creatinine.^{26,27}
- **Pemphigus Vulgaris:** British guidelines (2017) list rituximab in combination with corticosteroids as a first-line therapy.²³
- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend the addition of a biologic (which includes rituximab) or a targeted synthetic disease modifying antirheumatic drug (DMARD) for a patient taking the maximum tolerated dose of methotrexate who is not at target.¹⁶
- **Systemic Lupus Erythematosus (SLE):** European League Against Rheumatism recommendations for the management of SLE (2023) mention rituximab as a therapeutic option for patients who are refractory to standard immunosuppressive therapies. ²¹

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

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). 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.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does <u>not</u> necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a [®] below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a * below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rituxan is recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Truxima, Ruxience, Riabni

Non-Preferred Products(s): Rituxan

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any <u>one</u> of the items listed below (A, B, C, D or E). Chart notes documenting the issue must be provided at time of request:

- A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR
- B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR
- C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR
- D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR
- E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

1. Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis. ^

Criteria. Patient must meet the following criteria (A or B):

- A) Induction Treatment. Approve for 1 month if the patient meets ALL of the following (i and ii):
 - i. The patient has an ANCA-associated vasculotide; IC-ISGP AND Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis [GPA] {Wegener's granulomatosis (WG)} or microscopic polyangiitis [MPA]).
 - ii. The requested agent is being administered in combination with glucocorticoids. IC-L
- B) Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis (Note: This includes patients who received induction treatment using rituximab infusion 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; IC-ISGP AND
 - ii. If the patient previously received a course of therapy, at least 16 weeks will elapse between courses. IC-ISGP

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

- **A)** Initial Therapy: Approve one of the following:
 - i. 375 mg/m² per dose administered intravenously for 4 doses separated by at least 7 days;
 OR
 - ii. Up to two 1,000-mg intravenous doses separated by at least 2 weeks.
- **B**) Follow-Up Treatment of a Patient Who Has Received Induction Treatment for ANCA-Associated Vasculitis: Approve one of the following (i or ii):
 - i. ≥ 18 years of age: Up to 1,000 mg administered by intravenous infusion for 6 doses; OR
 - ii. <18 Years of age: Up to 250 mg/m² administered by intravenous infusion for 2 doses.

2. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma. A evicore

Criteria. Approve for 1 year.

Dosing. Approve up to 500 mg/m² administered as an intravenous infusion on 1 day of each cycle.

3. B-Cell Lymphoma. A eviCore

(Note: Examples of B-cell lymphomas include follicular lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, Burkitt lymphoma, Castleman 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.)

Criteria. Approve for 1 year.

Dosing. Approve one of the following regimens (A <u>or</u> B):

- **A)** Approve up to 375 mg/m² per dose administered intravenously with doses separated by at least 7 days; OR
- **B**) Approve up to 375 mg/kg² on two days of each cycle.

4. Pemphigus Vulgaris. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A, B or C):

- A) <u>Initial Treatment</u>. Approve for 1 month.
- **B)** Patient is Being Treated for a Relapse of Pemphigus Vulgaris. Approve for 1 month (which is adequate duration to administer one course of therapy) if subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product.

 IC-ISGP
 - <u>Note</u>: 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.
- **C)** Patient is Being Treated for Maintenance of Pemphigus Vulgaris. Approve for 1 year if subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product. IC-ISGP
 - <u>Note</u>: 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.

Dosing. Approve the following (A <u>or</u> B):

- A) <u>Initial Treatment or Treatment of a Relapse</u>: 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 every 6 months.

5. Rheumatoid Arthritis (RA). ^

Criteria. Approve if the patient meets ONE of the following (A, B or C):

- **A)** <u>Initial Therapy</u>. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months. ^{IC-EC}
 - <u>Note</u>: Examples of conventional synthetic DMARDs 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 already has a 3-month trial of at least one biologic other than the requested drug. A biosimilar of the requested biologic <u>does not count</u>. Refer to Appendix A for examples of biologics used for rheumatoid arthritis. A patient who has already tried a biologic is not required to "step back" and try a conventional synthetic DMARD.
- B) Patient has already Received One Course of Rituximab for Rheumatoid Arthritis (RA). Approve for 1 month (which is adequate duration to administer one course of therapy) if 16 weeks or greater will elapse between treatment courses. IC-ISGP

 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.
- C) Patient Has Already Received Two or More Courses of a Rituximab Product for Rheumatoid Arthritis. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets the following (i and ii):
 - i. 16 weeks or greater will elapse between treatment courses; IC-ISGP 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. Patient meets at least ONE of the following (a or b):
 - Patient experienced a beneficial clinical response when assessed by at least one objective measure; IC-ISGP OR
 Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).
 - 2. Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths. IC-ISGP

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

OTHER USES WITH SUPPORTIVE EVIDENCE

6. Acute Lymphoblastic Leukemia. @ eviCore

Criteria. Approve for 1 year if the patient has CD20-positive disease.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

7. Graft Versus Host Disease. @

Criteria. Approve for the duration noted 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. Patient has chronic graft-versus-host disease; AND
 - ii. Patient has tried at least one systemic medication for graft versus host disease; OR Note Examples of systemic medications include systemic corticosteroids (methylprednisolone, prednisone), Jakafi (ruxolitinib), Rezurock (belumosudil), Niktimvo (axatilimab-csfr), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib), imatinib, hydroxychloroquine, methotrexate, Nipent (pentostatin), interleukin-2 (e.g., Proleukin [aldesleukin]), sirolimus, or an etanercept product.
- **B)** Patient has Already Received a Course of a Rituximab Product for Graft-Versus-Host Disease. Approve for 1 year if the patient meets at least ONE of the following (i or ii):
 - i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a rituximab product); OR Note: An example of objective measures is normalization of liver function tests, red blood cell count, or platelet count, or resolution of fever or rash.
 - **ii.** Compared with baseline (prior to initiating a rituximab product), patient experienced an improvement in at least one symptom, such as improvement in skin, oral mucosal, ocular, or gastrointestinal symptoms (e.g., nausea, vomiting, anorexia).

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

8. Hairy Cell Leukemia. @ eviCore

Criteria. Approve for 1 year.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

9. Hematopoietic Cell Transplantation. @

Criteria. Approve for 1 month (which is adequate duration to administer one course of therapy) if the medication will be used as part of a conditioning regimen for allogeneic transplant.

Dosing. Approve one course of therapy, which consists of one dose of 375 mg/m^2 before transplant and three doses of $1,000 \text{ mg/m}^2$ separated by at least 7 days after transplant.

10. Hodgkin Lymphoma. @ eviCore

Criteria. Approve for 1 year if the patient has nodular lymphocyte-predominant disease.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

11. Immune Thrombocytopenia (ITP). ^

Criteria. Approve if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 1 month if the patient has tried one other therapy.

 Note: Examples of therapies for ITP include intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, Alvaiz (eltrombopag), Doptelet (avatrombopag), Nplate (romiplostim), Promacta (eltrombopag), Tavalisse (fostamatinib), and splenectomy.
- **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; IC-ISGP 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 <u>Note</u>: Examples of a response include a platelet count increase from baseline following treatment with a rituximab product.
 - The prescriber has determined that the patient has relapsed. ^{IC-ISGP}

 Note: Examples of a relapse include the patient experiences thrombocytopenia after achievement of a remission.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

12. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors. @

Criteria. Approve for the duration noted if the patient meets the following (A or B):

<u>Note</u>: Examples of checkpoint inhibitors are Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), and Libtayo (cemiplimab-rwlc intravenous infusion).

- A) Initial Therapy. Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):
 - **a.** According to the prescriber, patient developed an immunotherapy-related toxicity; AND
 - **b.** Patient developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor; AND
 - **c.** Patient is symptomatic despite a trial of at least ONE systemic corticosteroid.

<u>Note</u>: Examples of a corticosteroid include methylprednisolone and prednisone.

B) Patient has Already Received a Course of a Rituximab Product. Approve for 1 month.

Dosing. Approve dosing that meets the following (A <u>or</u> B):

- **A)** Approve up to 500 mg/m² or up to 1000 mg administered intravenously for 2 doses separated by at least 14 days; OR
- **B)** Approve up to 375 mg/m² administered intravenously for 4 doses separated by at least 7 days.

13. Multiple Sclerosis. ^

Criteria. Approve for 1 year if the patient meets ONE of the following (A <u>or</u> B):

- **A)** Initial Therapy. Approve if the patient meets ALL the following (i and ii):
 - According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to at least ONE other disease-modifying agent for multiple sclerosis; AND
 - <u>Note</u>: See <u>Appendix B</u> for examples of disease-modifying agents used for multiple sclerosis.
 - b. At least 6 months will elapse between treatment courses. ^{IC-ISGP}

 <u>Note</u>: 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.
- **B)** Patient is Currently Receiving Rituximab. Approve if the patient meets one of the following criteria (i or ii):
 - a. <u>Patient has been receiving Rituximab for < 1 year</u>. Approve if at least 6 months will elapse between treatment courses; IC-ISGP OR
 - <u>Note</u>: 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.
 - b. <u>Patient has been receiving Rituximab for 1 year or more</u>. Approve for 1 year if the patient meets ALL of the following (a <u>and</u> b):
 - At least 6 months will elapse between treatment courses; ^{IC-ISGP} AND
 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.
 - ii. Patient meets ONE of the following [(1) or (2)]:
 - 1. Patient experienced a beneficial clinical response when assessed by at least one objective measure; IC-ISGP OR
 - Note: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization or reduced worsening on the Expanded Disability Status Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-3 (NEDA-3) or NEDA-4; improvement on the fatigue symptom and impact questionnaire-relapsing multiple

sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Items Multiple Sclerosis Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and or attenuation of brain volume loss.

2. Patient experienced stabilization, slow progression, or improvement in at least one symptoms such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation. IC-ISGP

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.

14. Neuromyelitis Optica (NMO) Spectrum Disorder. @

Criteria. Approve for 1 month.

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

- A) Up to 375 mg/m² administered intravenously for 4 doses separated by at least 7 days; OR
- B) Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

15. Primary Central Nervous System Lymphoma. @ eviCore

Criteria. Approve for 1 year.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

16. Rosai-Dorfman Disease. @ eviCore

Criteria. Approve for 1 year if the patient is \geq 18 years of age.

Dosing. Approve the requested dose.

17. Systemic Lupus Erythematous (SLE) [Lupus]. @

Criteria. Approve for the duration noted if the patient meets ONE of the following (A <u>or</u> B): <u>Note</u>: This includes nephrotic syndrome in a patient with SLE.

- A) Initial Therapy. Approve for 1 month (adequate duration to receive one course) if the patient has has tried at least ONE standard immunomodulating or immunosuppressant agent Note: Examples of standard immunomodulating or immunosuppressant agents include hydroxychloroquine, corticosteroids (e.g., prednisone, methylprednisolone), methotrexate, azathioprine, mycophenolate, and cyclophosphamide.
- **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.

18. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. @ eviCore

Criteria. Approve for 1 year.

Dosing. Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

19. Antibody-Mediated Rejection (AMR).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- i. <u>Initial Therapy</u>. Approve for 1 month if the patient meets ONE of the following (i <u>or</u> ii):
 - i. The requested medication is being used as second-line treatment or as part of a combination treatment for AMR in a kidney, lung, or cardiac transplant patient; OR
 - **ii.** The requested medication is being used as part of a desensitization protocol in a highly sensitized patient awaiting donor transplant.
- **ii.** Patient has Already Received a Course of a Rituximab Product for Antibody-Mediated Rejection. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for antibody-mediated rejection.

Dosing.²⁸⁻²⁹ Approve ONE of the following (A or B):

- A) Up to 375 mg/m² administered intravenously with doses separated by at least 7 days; OR
- **B)** Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.
- **20.** Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy. * (Note: Examples include dermatomyositis, polymyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy, inclusion body myositis, nonspecific myositis).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** <u>Initial Therapy</u>. Approve for 1 month if the patient has refractory disease and has failed all first-line therapies.
- **B)** Patient has Already Received a Course of a Rituximab Product for Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for immune-mediated myopathy/idiopathic inflammatory myopathy.

Dosing.³⁰⁻³³ Approve ONE of the following (A or B):

- A) Up to 375 mg/m² administered intravenously with doses separated by at least 7 days; OR
- **B)** Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

21. Hemophilia (Acquired).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i or ii):
 - i. The patient has acquired or refractory hemophilia and the requested medication is being used as first-line therapy in combination with corticosteroids; OR
 - **ii.** The patient has refractory disease and the requested medication is being used as a second-line agent.
- **B**) Patient has Already Received a Course of a Rituximab Product for Hemophilia (Acquired). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for hemophilia (acquired).

Dosing.³⁴ Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

22. Thrombotic Thrombocytopenic Purpura (Acquired).

Criteria. Approve for the duration noted 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 severe, relapsed, or refractory disease; AND
 - ii. The patient has failed first-line therapy (i.e., plasma exchange and glucocorticoids).
- **B)** Patient has Already Received a Course of a Rituximab Product for Thrombotic

 Thrombocytopenic Purpura (Acquired). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for thrombotic thrombocytopenic purpura (acquired).

Dosing. 34-35 Approve ONE of the following (A or B):

- **A)** Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days; OR
- **B)** Approve 100 mg administered intravenously with doses separated by at least 5 days.

23. Immunoglobulin G4-Related Disease (IgG4-RD).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i or ii):
 - i. The patient has refractory or relapsed disease and the requested medication is being used as second-line therapy after failure of all first-line therapies; OR
 - ii. The patient has an absolute contraindication to glucocorticoid use.
- **B)** Patient has Already Received a Course of a Rituximab Product for Immunoglobulin G4-Related Disease (IgG4-RD). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for immunoglobulin G4-related disease (IgG4-RD).

Dosing. ³⁶⁻³⁷ Approve ONE of the following (A or B):

- A) Up to 375 mg/m² administered intravenously with doses separated by at least 7 days; OR
- **B)** Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

24. Minimal Change Disease.

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B)

- **A)** Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i or ii):
 - i. The patient meets ALL of the following (a, b, and c):
 - **a.** The patient is < 18 years of age; AND
 - **b.** The patient has steroid-dependent, steroid-sensitive nephrotic syndrome; AND
 - **c.** The patient meets one of the following (1 or 2):
 - **1.** The patient has continuing frequent relapses despite optimal combinations of prednisone and corticosteroid-sparing agents; OR
 - 2. The patient has had serious adverse effects of therapy; OR
 - ii. The patient meets ALL of the following (a, b and c):
 - **a.** The patient is ≥ 18 years of age; AND
 - **b.** The patient has frequently relapsing or glucocorticoid-dependent minimal change disease; AND
 - **c.** The patient has failed to attain a durable remission with cyclophosphamide or calcineurin inhibitors.
- **B)** Patient has Already Received a Course of a Rituximab Product for Minimal Change Disease. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for minimal change disease.

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

- **A)** Approve up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks; OR
- **B)** Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

25. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** <u>Initial Therapy</u>. Approve for 1 month if the patient has failed intravenous immune globulin (IVIG), glucocorticoids, and plasma exchange.
- B) Patient has Already Received a Course of a Rituximab Product for Chronic Inflammatory

 Demyelinating Polyneuropathy (CIDP). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for chronic inflammatory demyelinating polyneuropathy (CIDP).

Dosing.³⁹ Approve up to 375 mg/m² administered intravenously with doses separated by at least 7 days.

26. Sjogren's Syndrome.

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** <u>Initial Therapy</u>. Approve for 1 month if the patient has tried corticosteroids and other immunosuppressive agents and these agents were ineffective.
- **B)** Patient has Already Received a Course of a Rituximab Product for **Sjogren's Syndrome**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **Sjogren's syndrome**.

Dosing.⁴⁰⁻⁴¹ Approve up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

27. Systemic Sclerosis.

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

- **A)** <u>Initial Therapy</u>. Approve for 1 month if the patient has tried corticosteroids and other immunosuppressive agents and these agents were ineffective.
- **B)** Patient has Already Received a Course of a Rituximab Product for **Systemic Sclerosis**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **systemic sclerosis**.

Dosing.⁴⁰⁻⁴¹ Approve up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

28. Susac Syndrome.

Criteria. Approve for the duration noted 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 severe or extremely severe disease presentation; AND
 - ii. According to the prescriber, initial treatments are inadequate.
 <u>Note</u>: Examples of initial treatments include corticosteroids and intravenous immunoglobulin (IVIG).
- **B)** Patient has Already Received a Course of a Rituximab Product for **Susac Syndrome**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **Susac Syndrome**.

Dosing.²⁷ Approve ONE of the following (A <u>or</u> B):

- A) Approve up to a single dose of 500 mg given once and then repeated in 6 months; OR
- **B)** Approve up to a dose of 250 mg once then repeated in 2 weeks followed by 500 mg every 6 months.

Conditions Not Recommended for Approval.

Coverage of rituximab intravenous products is not recommended in the following situations:

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
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52452 and Rituximab Intravenous Products Utilization Review Policy	08/28/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52452, and Rituximab Intravenous Products Utilization Review Policy.	12/11/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does <u>not</u> necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Multiple indications – changed "prescribing physician" to "prescriber" *B-Cell Lymphoma: Pediatric Aggressive Mature B-cell Lymphoma was added as an example of a B-cell lymphoma * Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis: 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). * Acute Lymphoblastic Leukemia (ALL): 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.	06/12/2020

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	* Graft Versus Host Disease (GVHD): 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 immunosuprressant or be concurrently receiveing an immunosuppressant in combination with rituximab	
Policy revision	Riabni: This newly approved biosimilar was added to the policy. There are no changes to the criteria, which apply to all rituximab products included in this policy.	01/12/2021
Policy revision	Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: An alternative dosing regimen (up to 250 mg/m² for two doses, then up to 250 mg/m² not more frequently than once every 6 months) was added. Acute Lymphoblastic Leukemia: The Dosing was updated to require a minimum of 7 days between doses (previously was 14 days). Hairy Cell Leukemia: The requirement of relapsed or refractory disease was removed. Primary Central Nervous System Lymphoma: This condition of approval was added to the policy. Systemic Lupus Erythematous (SLE) [Lupus]: A note was added to clarify this includes nephrotic syndrome in a patient with SLE.	07/07/2021
Policy revision	Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: The minimum amount of time required between doses was removed from the Dosing (not needed since addressed in clinical criteria). For initial therapy, up to two 1,000-mg intravenous doses separated by at least 2 weeks was added as an alternative induction dose. For follow-up treatment of a patient who has received induction treatment, the dosing was separated by age (≥ 18 or < 18 years of age); previously, dosing applied to all patients regardless of age. For a patient ≥ 18 years of age, the dose is up to 1,000 mg intravenously, whereas the dose is based on body surface area (250 mg/m²) if < 18 years of age. Alternative induction doses were removed from the criteria (not needed).	7/21/2021
Policy revision	B-Cell Lymphoma: High-grade B-cell lymphoma was added as an example of a B-Cell Lymphoma. To align with guidelines, dosing was updated to approve up to two doses per cycle. Rheumatoid Arthritis: Note was clarified to state that a previous trial of a biologic applies to one biologic other than the requested drug. A biosimilar of the requested biologic does not count. A requirement was added for a patient who has already received two or more courses of a rituximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. Graft-Versus-Host Disease: For initial therapy, the initial approval was changed to be for 1 month (previously was for 1 year). A requirement was added for a patient who has already received a course of a rituximab product to have at least one objective or subjective response to therapy. Multiple Sclerosis: For the required previous trial of at least one other disease-modifying agent for multiple sclerosis, it was clarified that inadequate efficacy or significant intolerance was according to the prescriber. Examples of disease-modifying agents used for multiple sclerosis were moved to an appendix (previously listed as examples in a note within the criteria). For a patient who has been receiving a rituximab product for 1 year or longer, response criteria were developed for reauthorization in which the patient either experienced a beneficial clinical response when assessed by at least one objective measure (with examples provided in a Note), or the patient experienced stabilization, slowed progression, or improvement in at least one symptom such as	08/04/2022

	motor function, fatigue, vision, bowel/bladder function, spasticity,	
	walking/gait, or pain/numbness/tingling sensation.	
Policy revision Policy revision	Removed the following indications: Pre-transplant to suppress panel reactive anti-HLA antibodies in patients with high Panel Reactive Antibody (PRA) Levels to Human Leukocyte Antigens (HLA); Dermatomyositis or Polymyositis; and Grave's Disease/Ophthalmopathy. Added the following indications: Antibody-Mediated Rejection (AMR); Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy; Hemophilia (Acquired); Thrombotic Thrombocytopenic Purpura (Acquired); Immunoglobulin G4-Related Disease (IgG4-RD); Minimal Change Disease; Chronic Inflammatory Demyelinating Polyneuropathy (CIDP); Sjogren's Syndrome and Systemic Sclerosis. Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis: Dosing was updated to specify a total of four doses for initial therapy. For follow up treatment, a total of six doses was specified for patients ≥ 18 years of age and two doses for patients < 18 years of age. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors: This condition of approval was added. Neuromyelitis Optica Spectrum Disorder: A total of four weekly doses for a regimen of 375 mg/m² intravenous was specified.	03/01/2023
Policy review	No criteria changes.	09/04/2024
	Review based on commercial policy annual review	00/10/2
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
Aspirus Update	Moved Riabni to preferred product status effective 1/1/25. Riabni will no longer be targeted by the policy.	12/3/2024
Aspirus Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025
Policy revision	B-Cell Lymphoma: The nomenclature acquired immune deficiency (AIDS)-related B-cell lymphoma was updated to human immunodeficiency virus (HIV)-related B-cell lymphoma. Rheumatoid Arthritis: The requirements for a patient who has already received one or more courses of therapy were modified to a patient has already received two or more courses of a rituximab product and a patient has already received two or more courses of a rituximab product. For patients already receiving one course, the requirements are 16 weeks or greater will lapse between treatment courses and the medication will not be used concurrently with another biologic or with a targeted synthetic DMARD. In addition to these requirements, a patient who has already received two or more courses will either experience a beneficial clinical response when assessed by at least one objective measure or experience an improvement in at least one symptom. Graft-Versus-Host-Disease (GVHD): A requirement was added that patient has chronic GVHD. The requirement patient has tried at least one conventional systemic treatment was modified to at least one systemic medication. Jakafi (ruxolitinib), Rezurock (belumosudil), Niktimvo (axatilimab-csfr), hydroxychloroquine, methotrexate, interleukin-2, sirolimus, and etanercept were added, and antithymocyte globulin and infliximab were removed from the Note of examples of systemic medications. Hematopoietic Cell Transplantation: This was added as a new condition of approval.	09/18/2025

Immune Thrombocytopenia (ITP): Alvaiz (eltrombopag), Doptelet (avatrombopag), Nplate (romiplostim), Promacta (eltrombopag), Tavalisse (fostamatinib) were added to the Note of examples of therapies for ITP.

Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors: Requirements were added that, according to the prescriber, the patient developed an immunotherapy-related toxicity and developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor. An additional dosing regimen of up to 1,000 mg administered intravenously for 2 doses separated by at least 14 days was added.

Rosai-Dorfman Disease: This was added as a new condition of approval. Pemphigus Vulgaris: For a patient being treated for a relapse, the

approval duration was changed from 1 year to 1 month. For maintenance

therapy dosing, added a frequency of every 6 months.

APPENDIX A

	Mechanism of Action	Examples of Inflammatory Indications*		
Biologics				
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC		
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA		
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA		
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC		
Simponi°, Simponi° Aria™ (golimumab SC	Inhibition of TNF	SC formulation: AS, PsA, RA, UC		
injection, golimumab IV infusion)		IV formulation: AS, PJIA, PsA, RA		
Actemra® (tocilizumab IV infusion, tocilizumab SC	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA		
injection)		IV formulation: PJIA, RA, SJIA		
Kevzara ° (sarilumab SC injection)	Inhibition of IL-6	RA		
Orencia® (abatacept IV infusion, abatacept SC	T-cell costimulation	SC formulation: JIA, PSA, RA		
injection)	modulator	IV formulation: JIA, PsA, RA		
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic	RA		
	antibody			
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA		
Stelara ® (ustekinumab SC injection, ustekinumab	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC		
IV infusion)		IV formulation: CD, UC		
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO PsO		
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA		
Taltz [®] (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA		
Ilumya [™] (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO		
Skyrizi [™] (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsO PsO		
Tremfya ™ (guselkumab SC injection)	Inhibition of IL-23	PsO		
Entyvio ™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC		
Targeted Synthetic DMARDs				
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA		
Olumiant [®] (baricitinib tablets)	Inhibition of JAK pathways	RA		
Rinvoq * (upadacitinib extended-release tablets)	Inhibition of JAK pathways	RA		
Xeljanz [®] (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC		
Xeljanz * XR (tofacitinib extended-release tablets)	Inhibition of 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; JIA – Juvenile idiopathic arthritis; PSO – Plaque psoriasis; PSA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; ^ Off-label use of Kineret in JIA supported in guidelines; DMARDs – Disease-modifying antirheumatic drug.

APPENDIX B

MPPENDIA D			
Medication	Mode of Administration		
Aubagio® (teriflunomide tablets)	Oral		
Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)		
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral		
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)		
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)		
Extavia® (interferon beta-1b subcutaneous injection)	Injection (self-administered)		
Gilenya® (fingolimod capsules)	Oral		
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)		
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)		
Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion		
Mavenclad® (cladribine tablets)	Oral		
Mayzent [®] (siponimod tablets)	Oral		
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion		
Plegridy® (peginterferon beta-1a subcutaneous or intramuscular injection)	Injection (self-administered)		
Ponvory [™] (ponesimod tablets)	Oral		
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)		
Tecfidera® (dimethyl fumarate delayed-release capsules, generic)	Oral		
Tysabri [®] (natalizumab intravenous infusion)	Intravenous infusion		
Vumerity® (diroximel fumarate delayed-release capsules)	Oral		
Zeposia® (ozanimod capsules)	Oral		