

**Clinical Policy: Rituximab (Rituxan), Rituximab-pvvr (Ruxience), Rituximab-abbs (Truxima), Rituximab-Hyaluronidase (Rituxan Hycela)**

**Reference Number: LA.PHAR.260**

**Effective Date:**

**Last Review Date: 01.21**

**Line of Business: Medicaid**

**Coding Implications**

**Revision Log**

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**

**Rituximab (Rituxan®) is a human monoclonal immunoglobulin G-1 (IgG1) kappa antibody directed against the CD20 antigen.**

**Rituximab-pvvr (Ruxience™) is a CD20-directed cytolytic antibody and biosimilar to Rituxan for the listed Ruxience indications.**

**Rituximab-abbs (Truxima®) is a CD20-directed cytolytic antibody and biosimilar to Rituxan for the listed Truxima indications.**

**Rituximab and hyaluronidase (Rituxan Hycela™) is a combination of rituximab and human hyaluronidase that is used to increase the dispersion and absorption of the co-administered drugs when given subcutaneously.**

**FDA Approved Indication(s)**

<b><u>Indications</u></b>		<b><u>Rituxan</u></b>	<b><u>Ruxience</u></b>	<b><u>Truxima</u></b>	<b><u>Rituxan Hycela*</u></b>
<b><u>Oncology indications (adults)</u></b>					
<b><u>Low-grade and follicular B-cell NHL</u></b>	<b><u>Relapsed or refractory, low-grade [Rituxan, Ruxience, Truxima] or follicular [Rituxan, Ruxience, Truxima, Rituxan Hycela], CD20-positive, B-cell NHL as a single agent</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>
	<b><u>Previously untreated follicular, CD20-positive B-cell NHL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>
	<b><u>Non-progressing (including stable disease), low-grade [Rituxan, Ruxience, Truxima] or follicular [Rituxan Hycela], CD20-positive B-cell NHL as a single agent after first-line CVP chemotherapy</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>	<b><u>X</u></b>

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<u>Indications</u>		<u>Rituxan</u>	<u>Ruxience</u>	<u>Truxima</u>	<u>Rituxan Hycela*</u>
<u>DLBCL (a B-cell NHL)</u>	<u>Previously untreated CD20-positive DLBCL in combination with CHOP or other anthracycline-based chemotherapy regimens</u>	<u>X</u>	<u>X</u>	<u>X</u>	<u>X</u>
<u>CLL (a B-cell NHL)</u>	<u>Previously untreated and treated CD20-positive CLL in combination with FC chemotherapy</u>	<u>X</u>	<u>X</u>	<u>X</u>	<u>X</u>
<u>Non-oncology indications (adults)</u>					
<u>RA</u>	<u>Moderately to severely active RA in combination with MTX in patients who have inadequate response to one or more TNF antagonist therapies</u>	<u>X</u>		<u>X</u>	
<u>GPA, MPA</u>	<u>GPA and MPA in combination with glucocorticoids</u>	<u>X</u>	<u>X</u>	<u>X</u>	
<u>PV</u>	<u>Moderate to severe PV</u>	<u>X</u>			

*Abbreviations: CLL (chronic lymphocytic leukemia), DLBCL (diffuse large B-cell lymphoma), GPA (granulomatosis with polyangiitis; Wegener's granulomatosis), MPA (microscopic polyangiitis), NHL (Non-Hodgkin's lymphoma), PV (pemphigus vulgaris), RA (rheumatoid arthritis).*

*\*Rituxan Hycela limitations of use: 1) Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion; 2) Rituxan Hycela is not indicated for the treatment of non-malignant conditions.*

### Policy/Criteria

Prior authorization required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Rituxan, Ruxience, Truxima, and Rituxan Hycela are medically necessary when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Non-Hodgkin's Lymphoma (includes CLL) (must meet all):

1. Diagnosis of any of the following non-Hodgkin's lymphoma (NHL) subtypes (a-m):
  - a. AIDS-related B-cell lymphomas;
  - b. Burkitt lymphoma;
  - c. Castleman's disease;
  - d. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
  - e. Diffuse large B-cell lymphoma (DLBCL);
  - f. Follicular lymphoma (FL);
  - g. Hairy cell leukemia (Rituxan/Ruxience/Truxima only);
  - h. Low- or high-grade B-cell lymphoma;

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- i. MALT lymphoma (gastric or nongastric);
- j. Mantle cell lymphoma;
- k. Marginal zone lymphoma (nodal or splenic);
- l. Post-transplant lymphoproliferative disorder;
- m. Primary cutaneous B-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member meets one of the following (a or b):
  - a. Age  $\geq$  18 years;
  - b. Age  $<$  18 years with aggressive mature B-cell lymphoma;
4. If request is for Rituxan or Truxima, member meets one of the following ( a or b):
  - a. Medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);  
*\*Prior authorization may be required for Ruxience*
  - b. Request is for Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.;
5. If request is for Rituxan Hycela, member has received at least one full dose of Rituxan, Ruxience, or Truxima;
6. Request meets either of the following (a or b):\*
  - a. Dose does not exceed (i or ii):
    - i. Rituxan/Ruxience/Truxima: 500 mg/m<sup>2</sup> per IV infusion (see Section V for cycle regimens);
    - ii. Rituxan Hycela: 1,600 mg/26,800 units per SC injection (see Section V for cycle regimens);
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: 6 months**

#### **B. Rheumatoid Arthritis (must meet all):**

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (see Appendix F);
2. Request is for Rituxan/Ruxience/Truxima;
3. Prescribed by or in consultation with a rheumatologist;
4. Age  $\geq$  18 years;
5. Member meets one of the following (a or b):
  - a. Failure of a  $\geq$  3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
  - b. If intolerance or contraindication to MTX (see Appendix D), failure of a  $\geq$  3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide,

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hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

6. Failure of Inflectra or Renflexis, unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for Inflectra and Renflexis*
7. Documentation of one of the following baseline assessment scores (a or b):
  - a. Clinical disease activity index (CDAI) score (see Appendix G);
  - b. Routine assessment of patient index data 3 (RAPID3) score (see Appendix H);
8. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
9. Rituxan/Ruxience/Truxima will be administered in combination with MTX unless contraindicated or clinically significant adverse effects are experienced;
10. Dose does not exceed two-1,000 mg IV infusions separated by 2 weeks followed by two-1,000 mg IV infusions every 16 weeks.

Approval duration: 6 months

### C. Granulomatosis with Polyangiitis (Wegener's Granulomatosis) and Microscopic Polyangiitis (must meet all):

1. Diagnosis of GPA or MPA;
2. Request is for Rituxan/Ruxience/Truxima;
3. Prescribed by or in consultation with a rheumatologist;
4. For Rituxan: age ≥ 2 years;
5. For age ≥ 18 years: If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
6. Prescribed in combination with a glucocorticoid (e.g. prednisone, prednisolone, dexamethasone);
7. Dose does not exceed (a or b):
  - a. Induction: 375 mg/m<sup>2</sup> weekly for 4 weeks;
  - b. Follow up treatment: two-500 mg infusions separated by 2 weeks, then 500 mg every 6 months.

Approval duration: 6 months

### D. Pemphigus Vulgaris and Pemphigus Foliaceus (must meet all):

1. Diagnosis of PV or pemphigus foliaceus (PF);
2. Request is for Rituxan/Ruxience/Truxima;
3. Prescribed by or in consultation with a dermatologist;
4. Age ≥ 18 years;
5. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
6. Dose does not exceed (a or b):
  - a. Initial: two-1,000 mg infusions separated by 2 weeks;
  - b. Maintenance: 500 mg every 6 months (starting 12 months after initial dose).

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### E. NCCN Compendium Indications (off-label) (must meet all):

1. Diagnosis of any of the following (a-f):
  - a. Acute lymphoblastic leukemia in patients who are CD20-positive;
  - b. Immune checkpoint inhibitor-related toxicities;
  - c. Leptomeningeal metastases from lymphoma;
  - d. Nodular lymphocyte-predominant Hodgkin lymphoma;
  - e. Primary CNS lymphoma;
  - f. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma;
2. Request is for Rituxan/Ruxience/Truxima;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. If request is for Rituxan or Truxima, member meets one of the following (a or b):
  - a. Medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);  
*\*Prior authorization may be required for Ruxience*
  - b. Request is for Stage IV or metastatic cancer or associated conditions. Exception if “clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

### F. Neuromyelitis Optica Spectrum Disorder (off-label) (must meet all):

1. Diagnosis of neuromyelitis optica spectrum disorder (NMOSD);
2. Request is for Rituxan/Ruxience/Truxima;
3. Prescribed by or in in consultation with a neurologist;
4. Age ≥ 18 years;
5. Member has experienced at least one relapse within the previous 12 months;
6. Baseline Expanded Disability Status Scale (EDSS) score ≤ 8;
7. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
8. Rituxan/Ruxience/Truxima is not prescribed concurrently with Soliris<sup>®</sup>, Enspryng<sup>™</sup>, or Uplizna<sup>®</sup>;
9. Request meets one of the following (a, b, or c):
  - a. Dose does not exceed 375 mg/m<sup>2</sup> per week for 4 weeks as induction, followed by 375 mg/m<sup>2</sup> biweekly every 6 to 12 months;
  - b. Dose does not exceed 1,000 mg biweekly every 6 to 12 months;
  - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

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### G. Immune Thrombocytopenia (off-label) (must meet all):

1. Diagnosis of immune thrombocytopenia (ITP);
  2. Request is for Rituxan/Ruxience/Truxima;
  3. Prescribed by or in consultation with a hematologist;
  4. Current (within 30 days) platelet count is < 30,000/ $\mu$ L or member has an active bleed;
  5. Member meets one of the following (a or b):
    - a. Failure of a systemic corticosteroid;
    - b. Member has intolerance or contraindication to systemic corticosteroids, and failure of an immune globulin, unless contraindicated or clinically significant adverse effects are experienced (see Appendix B);
- \*Prior authorization may be required for immune globulins*
6. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
  7. Rituximab is not prescribed concurrently with a thrombopoietin receptor agonist (e.g., Nplate<sup>®</sup>, Promacta<sup>®</sup>, Doptelet<sup>®</sup>);
  8. Request meets one of the following (a, b, or c):
    - a. Dose does not exceed 375 mg/m<sup>2</sup> per week for 4 weeks;
    - b. Dose does not exceed 1,000 mg on days 1 and 15;
    - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 1 month

### H. Other diagnoses/indications

1. Members with any of the following diagnoses may be covered if the off-label criteria policy is met:
  - a. Myasthenia gravis;
  - b. Nephrotic syndrome;
2. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
3. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

## II. Continued Approval

### A. Immune Thrombocytopenia (off-label):

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

### B. All Other Indications in Section I (must meet all):

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;



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- b) Relapse: 1,000 mg IV once then 500 mg IV 16 weeks later, then 500 mg IV every 6 months;
- v. NMOSD (Rituxan/Truxima): 375 mg/m<sup>2</sup> or 1,000 mg biweekly every 6 to 12 months;
- b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

### C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.  
Approval duration: Duration of request or 6 months (whichever is less); or
2. Members with any of the following diagnoses may be covered if the off-label criteria policy is met:
  - a. Myasthenia gravis;
  - b. Nephrotic syndrome;
3. If request is for Rituxan or Truxima, medical justification supports inability to use Ruxience (e.g., contraindications to excipients in Ruxience);
4. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

### III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy –LA.PMN.53 for Medicaid or evidence of coverage documents.

### IV. Appendices/General Information

#### Appendix A: Abbreviation/Acronym Key

AAN: American Academy of Neurology

ARR: annualized relapse rate

CDAI: clinical disease activity index

CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone

CLL: chronic lymphocytic leukemia

CVP: cyclophosphamide, vincristine, prednisone

DLBCL: diffuse large B-cell lymphoma

DMARD: disease-modifying antirheumatic drug

EDSS: Expanded Disability Status Scale

FC: fludarabine and cyclophosphamide

FDA: Food and Drug Administration

FL: follicular lymphoma

GPA: granulomatosis with polyangiitis (Wegener's granulomatosis)

ITP: immune thrombocytopenia

MALT: mucosa-associated lymphoid tissue

MPA: microscopic polyangiitis

MS: multiple sclerosis

MTX: methotrexate

NCCN: National Comprehensive Cancer Network

NHL: Non-Hodgkin's lymphoma

NMOSD: neuromyelitis optica spectrum disorder

PF: pemphigus foliaceus

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**PPMS: primary progressive MS**

**PV: pemphigus vulgaris**

**RA: rheumatoid arthritis**

**RAPID3: routine assessment of patient  
index data 3**

**RCT: randomized controlled trial**

**RRMS: relapsing-remitting MS**

**SLL: small lymphocytic lymphoma**

### Appendix B: Therapeutic Alternatives

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.*

<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<b><u>RA</u></b>		
<b><u>azathioprine (Azasan<sup>®</sup>, Imuran<sup>®</sup>)</u></b>	<b><u>1 mg/kg/day PO QD or divided BID</u></b>	<b><u>2.5 mg/kg/day</u></b>
<b><u>Cuprimine<sup>®</sup> (d-penicillamine) Off- label</u></b>	<b><u>Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD</u></b>	<b><u>1,500 mg/day</u></b>
<b><u>cyclosporine (Sandimmune<sup>®</sup>, Neoral<sup>®</sup>)</u></b>	<b><u>2.5 – 4 mg/kg/day PO divided BID</u></b>	<b><u>4 mg/kg/day</u></b>
<b><u>hydroxychloroquine (Plaquenil<sup>®</sup>) Off-label</u></b>	<b><u>Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD</u></b>	<b><u>5 mg/kg/day</u></b>
<b><u>leflunomide (Arava<sup>®</sup>)</u></b>	<b><u>100 mg PO QD for 3 days, then 20 mg PO QD</u></b>	<b><u>20 mg/day</u></b>
<b><u>methotrexate (Rheumatrex<sup>®</sup>)</u></b>	<b><u>7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week</u></b>	<b><u>30 mg/week</u></b>
<b><u>Ridaura<sup>®</sup> (auranofin)</u></b>	<b><u>6 mg PO QD or 3 mg PO BID</u></b>	<b><u>9 mg/day</u></b>
<b><u>sulfasalazine (Azulfidine<sup>®</sup>)</u></b>	<b><u>2 g/day PO in divided doses</u></b>	<b><u>3 gm/day</u></b>
<b><u>Enbrel(etanercept)</u></b>	<b><u>25 mg SC twice weekly or 50 mg SC once weekly</u></b>	<b><u>50 mg/week</u></b>
<b><u>Humira (adalimumab)</u></b>	<b><u>40 mg SC every other week (may increase to once weekly)</u></b>	<b><u>40 mg/week</u></b>
<b><u>GPA, MPA</u></b>		
<b><u>glucocorticoids</u></b>	<b><u>Varies</u></b>	<b><u>Varies</u></b>
<b><u>ITP</u></b>		
<b><u>corticosteroids</u></b>	<b><u>Varies</u></b>	<b><u>Varies</u></b>
<b><u>immune globulins (e.g., Carimune<sup>®</sup> NF, Flebogamma<sup>®</sup> DIF 10%, Gammagard<sup>®</sup> S/D,</u></b>	<b><u>Refer to prescribing information</u></b>	<b><u>Refer to prescribing information</u></b>

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<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<u>Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®)</u>		

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

### Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Fatal infusion reactions (Rituxan, Ruxience, Truxima)
  - Severe mucocutaneous reactions, hepatitis B virus reactivation, progressive multifocal leukoencephalopathy (Rituxan, Ruxience, Truxima, Rituxan Hycela).

### Appendix D: General Information

- Definition of MTX or disease-modifying antirheumatic drug (DMARD) failure
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to RA therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living
- Off-label use in multiple sclerosis (MS):
  - The off-label use of rituximab in relapsing-remitting MS (RRMS) and primary progressive MS (PPMS) is supported by Class IIb recommendations in Micromedex with the following clinical evidence:
    - RRMS: 1 randomized controlled trial (RCT) (N = 104) found there was a significant difference in T1-weighted lesion count at 24 weeks and annualized relapse rate (ARR) at 24 weeks (but not at 48 weeks) for patients receiving rituximab compared to placebo. Important limitations of this study are poor methodological quality and high risk of attrition bias resulting from a high dropout rate (40% in placebo and 15.9% in rituximab).

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- PPMS: 1 RCT (N = 439) found there was no significant difference in confirmed disability progression for patients receiving rituximab compared to placebo.
  - In the 2018 MS guidelines, the American Academy of Neurology (AAN) does not prefer any one disease-modifying therapy over another for the treatment of RRMS, except for Gilenya<sup>®</sup>, Tysabri<sup>®</sup>, and Lemtrada<sup>®</sup> for highly active disease. The recommended agent in PPMS is Ocrevus<sup>®</sup>. AAN makes the following comments on rituximab:
    - RRMS:
      - Rituximab is probably more effective than placebo in decreasing the risk of relapse at 1 year.
      - There is insufficient evidence to determine the efficacy of rituximab compared with placebo in decreasing the ARR at 1 year.
      - Rituximab is probably more effective than placebo in decreasing the volume of T2 lesions from baseline to week 36.
    - PPMS: The randomized controlled trial of rituximab in PPMS was promising but inconclusive.
  - Off-label use in NMOSD:
    - Rituxan is considered a standard first-line treatments for NMOSD per clinical reviews and the 2010 European Federation of Neurological Societies guideline. Comparative analyses shows that rituximab significantly reduces attack frequency and stabilizes or reduces neurological disabilities while achieving long-term safety. Neurological disability was assessed via the EDSS score, which ranges from 0 (no disability) to 10 (death).
      - In a 5-year follow-up of 30 patients from a 2-year retrospective case series, 18 (60%) were relapse free and 28 (93%) had improved or stabilized disability as evidenced by improvement in the EDSS score. The mean (SD) pretreatment versus posttreatment annualized relapse rate (ARR) was 2.4 (1.5) versus 0.3 (1.0) (p < 0.001). No serious adverse events resulted in discontinuation of therapy.
      - In a 1-year RCT with 68 patients who had a baseline EDSS score ≤ 7, rituximab demonstrated a higher proportion decrease in ARR (SD) than azathioprine (0.83 (0.37) compared to 0.56 (0.50), p = 0.022). The mean change in EDSS score (SD) was -0.98 (1.14) with rituximab versus -0.44 (0.54) with azathioprine (p < 0.001). There were no statistically significant difference in adverse effects.
      - A 2019 meta-analysis that included 26 studies and 577 patients showed a significant mean decrease in the ARR after rituximab therapy (-1.56 (95% CI -1.82 to -1.29). There was no significant correlation found between AQP4-IgG serostatus and ARR or EDSS.

Appendix F: The 2010 ACR Classification Criteria for RA

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**Add score of categories A through D; a score of  $\geq 6$  out of 10 is needed for classification of a patient as having definite RA.**

<b><u>A</u></b>	<b><u>Joint involvement</u></b>	<b><u>Score</u></b>
	<b><u>1 large joint</u></b>	<b><u>0</u></b>
	<b><u>2-10 large joints</u></b>	<b><u>1</u></b>
	<b><u>1-3 small joints (with or without involvement of large joints)</u></b>	<b><u>2</u></b>
	<b><u>4-10 small joints (with or without involvement of large joints)</u></b>	<b><u>3</u></b>
	<b><u>&gt; 10 joints (at least one small joint)</u></b>	<b><u>5</u></b>
<b><u>B</u></b>	<b><u>Serology (at least one test result is needed for classification)</u></b>	
	<b><u>Negative rheumatoid factor (RF) and negative anti-citrullinated protein antibody (ACPA)</u></b>	<b><u>0</u></b>
	<b><u>Low positive RF or low positive ACPA</u></b> <i>* Low: <math>&lt; 3 \times</math> upper limit of normal</i>	<b><u>2</u></b>
	<b><u>High positive RF or high positive ACPA</u></b> <i>* High: <math>\geq 3 \times</math> upper limit of normal</i>	<b><u>3</u></b>
<b><u>C</u></b>	<b><u>Acute phase reactants (at least one test result is needed for classification)</u></b>	
	<b><u>Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)</u></b>	<b><u>0</u></b>
	<b><u>Abnormal CRP or abnormal ESR</u></b>	<b><u>1</u></b>
<b><u>D</u></b>	<b><u>Duration of symptoms</u></b>	
	<b><u>&lt; 6 weeks</u></b>	<b><u>0</u></b>
	<b><u><math>\geq 6</math> weeks</u></b>	<b><u>1</u></b>

### Appendix G: Clinical Disease Activity Index (CDAI) Score

**The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.**

<b><u>CDAI Score</u></b>	<b><u>Disease state interpretation</u></b>
<b><u><math>\leq 2.8</math></u></b>	<b><u>Remission</u></b>
<b><u>2.8 to <math>\leq 10</math></u></b>	<b><u>Low disease activity</u></b>
<b><u>10 to <math>\leq 22</math></u></b>	<b><u>Moderate disease activity</u></b>
<b><u><math>&gt; 22</math></u></b>	<b><u>High disease activity</u></b>

### Appendix H: Routine Assessment of Patient Index Data 3 (RAPID3) Score

**The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.**

<b><u>RAPID3 Score</u></b>	<b><u>Disease state interpretation</u></b>
<b><u><math>\leq 3</math></u></b>	<b><u>Remission</u></b>
<b><u>3.1 to 6</u></b>	<b><u>Low disease activity</u></b>

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<u>6.1 to 12</u>	<u>Moderate disease activity</u>
<u>&gt; 12</u>	<u>High disease activity</u>

### V. Dosage and Administration

<u>Drug Name</u>	<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Rituxan, Ruxience, Truxima</u>	<u>Low-grade and follicular B-cell NHL</u>	<p><u>375 mg/m<sup>2</sup> IV infusion according to the following schedules:</u></p> <ul style="list-style-type: none"> <li>• <u>Relapsed or refractory, low-grade or follicular, CD20+, B-cell NHL</u> <ul style="list-style-type: none"> <li>○ <u>Once weekly for 4 or 8 doses</u></li> <li>○ <u>Retreatment: once weekly for 4 doses</u></li> </ul> </li> <li>• <u>Previously untreated, follicular, CD20+, B-cell NHL:</u> <ul style="list-style-type: none"> <li>○ <u>Administer on Day 1 of each cycle of chemotherapy for up to 8 doses;</u></li> <li>○ <u>If complete or partial response, initiate Rituxan/Truxima maintenance treatment as a single-agent every 8 weeks for 12 doses to start 8 weeks following completion of a rituximab product in combination with chemotherapy.</u></li> </ul> </li> <li>• <u>Non-progressing, low-grade, CD20+, B-cell NHL, after first-line CVP chemotherapy:</u> <ul style="list-style-type: none"> <li>○ <u>Following completion of 6-8 cycles of CVP chemotherapy, administer once weekly for 4 doses at 6-month intervals to a maximum of 16 doses.</u></li> </ul> </li> </ul>	<u>375 mg/m<sup>2</sup> IV infusion</u>
<u>Rituxan</u>	<u>Low-grade and follicular B-cell NHL</u>	<ul style="list-style-type: none"> <li>• <u>Rituxan in combination with Zevalin for low-grade or follicular B-cell NHL:</u> <ul style="list-style-type: none"> <li>○ <u>250 mg/m<sup>2</sup> IV within 4 hrs prior to administration of Indium-111-(In-111-) Zevalin and Yttrium-90-(Y-90) Zevalin.</u></li> <li>○ <u>Administer rituximab and In-111-Zevalin 7-9 days prior to rituximab and Y-90-Zevalin.</u></li> <li>○ <u>Refer to the Zevalin package insert for full prescribing information regarding the Zevalin therapeutic regimen.</u></li> </ul> </li> </ul>	<u>375 mg/m<sup>2</sup> IV infusion</u>

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<u>Drug Name</u>	<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Rituxan Hycela</u>	<u>Follicular B-cell NHL</u>	<p><b><u>1,400 mg rituximab and 23,400 units hyaluronidase SC according to the following schedules:</u></b></p> <p><b><u>First dose must be with IV Rituxan/Truxima if indicated with an asterisk (*).</u></b></p> <ul style="list-style-type: none"> <li>• <b><u>Relapsed or refractory FL:</u></b> <ul style="list-style-type: none"> <li>○ <b><u>Once weekly for 3 or 7 weeks (i.e., 4 or 8 weeks in total)*</u></b></li> <li>○ <b><u>Retreatment: once weekly for 3 weeks (i.e., 4 weeks in total)*</u></b></li> </ul> </li> <li>• <b><u>Previously untreated FL:</u></b> <ul style="list-style-type: none"> <li>○ <b><u>Administer on Day 1 of Cycles 2–8 of chemotherapy (every 21 days), for up to 7 cycles (i.e., up to 8 cycles in total)*</u></b></li> <li>○ <b><u>If complete/partial response, initiate Rituxan Hycela maintenance treatment as a single-agent every 8 weeks for 12 doses to start 8 weeks following completion of Rituxan Hycela in combination with chemotherapy</u></b></li> </ul> </li> <li>• <b><u>Non-progressing FL after first-line CVP chemotherapy:</u></b> <ul style="list-style-type: none"> <li>○ <b><u>Following completion of 6–8 cycles of CVP chemotherapy, administer once weekly for 3 weeks (i.e., 4 weeks in total) at 6 month intervals to a maximum of 16 doses*</u></b></li> </ul> </li> </ul>	<b><u>1,400 mg/23,400 units SC per injection</u></b>
<u>Rituxan, Ruxience, Truxima</u>	<u>DLBCL (a B-cell NHL)</u>	<b><u>375 mg/m<sup>2</sup> IV infusion on Day 1 of each cycle of chemotherapy for up to 8 doses total.</u></b>	<b><u>375 mg/m<sup>2</sup> IV infusion</u></b>
<u>Rituxan Hycela</u>	<u>DLBCL (a B-cell NHL)</u>	<p><b><u>First dose must be with IV Rituxan</u></b></p> <ul style="list-style-type: none"> <li>• <b><u>1,400 mg rituximab and 23,400 units hyaluronidase SC on Day 1 of Cycles 2–8 of CHOP chemotherapy for up to 7 cycles (i.e., up to 6–8 cycles in total)</u></b></li> </ul>	<b><u>1,400 mg/23,400 units SC per injection</u></b>
<u>Rituxan, Ruxience, Truxima</u>	<u>CLL (a B-cell NHL)</u>	<b><u>375 mg/m<sup>2</sup> IV infusion on the day prior to initiation of FC chemotherapy, then 500 mg/m<sup>2</sup> on Day 1 of cycles 2-6 (every 28 days).</u></b>	<b><u>500 mg/m<sup>2</sup> per day</u></b>
<u>Rituxan Hycela</u>	<u>CLL</u>	<b><u>First dose must be with IV Rituxan</u></b>	<b><u>1,600 mg/26,800</u></b>

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<u>Drug Name</u>	<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
	<u>(a B-cell NHL)</u>	<ul style="list-style-type: none"> <li><u>1,600 mg/26,800 units on Day 1 of Cycles 2–6 (every 28 days) for a total of 5 cycles (i.e., 6 cycles in total)</u></li> </ul>	<u>units SC per injection</u>
<u>Rituxan, Truxima</u>	<u>RA</u>	<u>Two 1000 mg IV infusions separated by 2 weeks (i.e., day 1 and day 15), followed by two-1000 mg IV infusions every 16 weeks. Rituxan is given in combination with MTX.</u>	<u>1000 mg per week</u>
<u>Rituxan, Ruxience, Truxima</u>	<u>GPA/MPA</u>	<p><u>Induction:</u></p> <ul style="list-style-type: none"> <li><u>375 mg/m<sup>2</sup> IV once weekly for 4 weeks in combination with glucocorticoids</u></li> </ul> <p><u>Follow-up treatment if disease control with induction treatment:</u></p> <ul style="list-style-type: none"> <li><u>Two 500 mg IV infusions separated by 2 weeks, followed by 500 mg IV every 6 months thereafter based on clinical evaluation. Follow up treatment should be initiated:</u> <ul style="list-style-type: none"> <li><u>Within 24 weeks after the last Rituxan induction infusion or based on clinical evaluation, but no sooner than 16 weeks after the last Rituxan induction infusion.</u></li> <li><u>Within the 4 week period following achievement of disease control if induction was achieved with other immunosuppressants.</u></li> </ul> </li> </ul>	<p><u>Induction:</u></p> <p><u>375 mg/m<sup>2</sup> per week</u></p> <p><u>Follow-up treatment:</u></p> <p><u>500 mg/dose (see regimen for dosing frequency)</u></p>
<u>Rituxan</u>	<u>PV</u>	<p><u>Initial and maintenance therapy:</u></p> <ul style="list-style-type: none"> <li><u>Two 1,000 mg IV infusions separated by 2 weeks with a tapering course of glucocorticoids, then 500 mg IV at month 12 and every 6 months thereafter or based on clinical evaluation</u></li> </ul> <p><u>Relapse:</u></p> <ul style="list-style-type: none"> <li><u>1,000 mg IV once. Subsequent infusions may be administered no sooner than 16 weeks following the previous infusion.</u></li> </ul>	<p><u>Initial/relap se: 1000 mg/dose</u></p> <p><u>Maintenanc e: 500 mg/6 months</u></p>

**VI. Product Availability**

<u>Drug Name</u>	<u>Availability</u>
<u>Rituximab (Rituxan)</u>	<u>Single-dose vials for IV injection: 100 mg/10 mL, 500 mg/50 mL</u>

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<u>Drug Name</u>	<u>Availability</u>
<u>Rituximab-pvvr (Ruxience)</u>	<u>Single-dose vials for IV injection: 100 mg/10 mL, 500 mg/50 mL</u>
<u>Rituximab-abbs (Truxima)</u>	<u>Single-dose vials for IV injection: 100 mg/10 mL, 500 mg/50 mL</u>
<u>Rituximab-hyaluronidase (Rituxan Hycela)</u>	<u>Single-dose vials for SC injection: 1,400 mg/23,400 units, 1,600 mg/26,800 units</u>

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