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

Reference Number: ERX.SPA.109  
Effective Date: 10.01.16  
Last Review Date: 02.19

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-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)**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Rituxan</th>
<th>Truxima</th>
<th>Rituxan Hycela*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oncology indications (adults)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-grade and follicular B-cell NHL</td>
<td>Relapsed or refractory, low-grade [Rituxan, Truxima] or follicular [Rituxan, Truxima, Rituxan Hycela], CD20-positive, B-cell NHL as a single agent.</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Previously untreated follicular, CD20-positive B-cell NHL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Non-progressing (including stable disease), low-grade [Rituxan, Truxima] or follicular [Rituxan Hycela], CD20-positive B-cell NHL as a single agent after first-line CVP chemotherapy.</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DLBCL (a B-cell NHL)</td>
<td>Previously untreated CD20-positive DLBCL in combination with CHOP or other anthracycline-based chemotherapy regimens.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CLL (a B-cell NHL)</td>
<td>Previously untreated and treated CD20-positive CLL in combination with FC chemotherapy.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>Non-oncology indications (adults)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>Moderately to severely active RA in combination with MTX in patients who have inadequate response to one or more TNF antagonist therapies.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>GPA, MPA</td>
<td>GPA and MPA in combination with glucocorticoids.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>PV</td>
<td>Moderate to severe PV.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Rituxan, 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. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
      b. Follicular lymphoma (FL);
      c. Low- or high-grade B-cell lymphoma;
      d. MALT lymphoma (gastric or nongastric);
      e. Marginal zone lymphoma (nodal or splenic);
      f. Mantle cell lymphoma;
      g. Diffuse large B-cell lymphoma (DLBCL);
      h. Burkitt lymphoma;
      i. AIDS-related B-cell lymphomas;
      j. Post-transplant lymphoproliferative disorder;
      k. Castleman’s disease;
      l. Hairy cell leukemia (Rituxan/Truxima only);
      m. Primary cutaneous B-cell lymphoma:
   2. Prescribed by or in consultation with an oncologist or hematologist;
   3. Age ≥ 18 years;
   4. If request is for Rituxan Hycela, member has received at least one full dose of Rituxan or Truxima;
   5. Request meets any of the following (a or b):
      a. Dose does not exceed (i or ii):
         i. Rituxan/Truxima: 500 mg/m² per IV infusion;
         ii. Rituxan Hycela: 1,600 mg/26,800 units SC;
      b. 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

B. Rheumatoid Arthritis (must meet all):
   1. Diagnosis of RA;
   2. Request is for Rituxan/Truxima;
   3. Prescribed by or in consultation with a rheumatologist;
   4. Age ≥ 18 years;
   5. Member meets one of the following (a or b):
      a. Failure of a ≥ 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 ≥ 3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug (DMARD; e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   6. Failure of 2 of the following, each used for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced: etanercept (Enbrel® is preferred),
adalimumab (Humira® is preferred), Kevzara®, infliximab (Remicade® is preferred),
golimumab (Simponi Aria® is preferred);
*Prior authorization is required for etanercept, adalimumab, Kevzara, infliximab, and golimumab

7. Rituxan/Truxima will be administered in combination with MTX unless contraindicated or
clinically significant adverse effects are experienced;
8. 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/Truxima;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Rituxan/Truxima will be administered in combination with glucocorticoid therapy;
6. Dose does not exceed (a or b):
   a. Induction: 375 mg/m² 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/Truxima;
3. Prescribed by or in consultation with a dermatologist;
4. Age ≥ 18 years;
5. 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).

Approval duration: 6 months

E. NCCN Compendium Indications (off-label) (must meet all):
1. Diagnosis of any of the following:
   a. Primary CNS lymphoma;
   b. Leptomeningeal metastases from lymphoma;
   c. Nodular lymphocyte-predominant Hodgkin lymphoma;
   d. Acute lymphoblastic leukemia;
   e. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma;
   f. Immune checkpoint inhibitor-related toxicities;
2. Request is for Rituxan/Truxima;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. 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. 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. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III
   (Diagnoses/Indications for which coverage is NOT authorized).
II. Continued Therapy

A. All Indications in Section I (must meet all):
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Rituxan, Truxima or Rituxan Hycela for a covered oncology indication and has received this medication for at least 30 days;
2. Meets one of the following (a or b):
   a. Member is responding positively to therapy;
   b. If PV or PF, member has experienced relapse;
3. If request is for a dose increase, request meets either of the following (a or b):
   a. New dose does not exceed the following:
      i. NHL:
         a) Rituxan/Truxima: 500 mg/m² per IV infusion;
         b) Rituxan Hycela: 1,600 mg/26,800 units SC;
      ii. RA (Rituxan/Truxima): Two-1,000 mg IV infusions every 16 weeks;
      iii. GPA/MPA (Rituxan/Truxima):
         a) Induction: 375 mg/m² IV weekly for up to 4 weeks total;
         b) Follow-up treatment: Two-500 mg IV infusions separated by two weeks, then 500 mg IV every 6 months;
      iv. PV or PF (Rituxan/Truxima) (a or b):
         a) Maintenance: 500 mg IV every 6 months (starting 12 months after initial dose);
         b) Relapse: 1,000 mg IV once then 500 mg IV 16 weeks later, then 500 mg IV every 6 months;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone
CVP: cyclophosphamide, vincristine, prednisone
CLL: chronic lymphocytic leukemia
CVP: cyclophosphamide, vincristine, prednisone
DLBCL: diffuse large B-cell lymphoma
DMARD: disease-modifying antirheumatic drug
FC: fludarabine and cyclophosphamide
FDA: Food and Drug Administration
FL: follicular lymphoma
GPA: granulomatosis with polyangiitis
(Wegener’s granulomatosis)
MALT: mucosa-associated lymphoid tissue
MPA: microscopic polyangiitis
MTX: methotrexate
Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>azathioprine (Azasan®, Imuran®)</td>
<td>1 mg/kg/day PO QD or divided BID</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>Cuprimine® (d-penicillamine) Off-label</td>
<td>Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD</td>
<td>1,500 mg/day</td>
</tr>
<tr>
<td>cyclosporine (Sandimmune®, Neoral®)</td>
<td>2.5 – 4 mg/kg/day PO divided BID</td>
<td>4 mg/kg/day</td>
</tr>
<tr>
<td>hydroxychloroquine (Plaquenil®) Off-label</td>
<td>Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD</td>
<td>5 mg/kg/day</td>
</tr>
<tr>
<td>leflunomide (Arava®)</td>
<td>100 mg PO QD for 3 days, then 20 mg PO QD</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>methotrexate (Rheumatrex®)</td>
<td>7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week</td>
<td>30 mg/week</td>
</tr>
<tr>
<td>Ridaura® (auranofin)</td>
<td>6 mg PO QD or 3 mg PO BID</td>
<td>9 mg/day</td>
</tr>
<tr>
<td>sulfasalazine (Azulfidine®)</td>
<td>2 g/day PO in divided doses</td>
<td>3 gm/day</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>25 mg SC twice weekly or 50 mg SC once weekly</td>
<td>50 mg/week</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>40 mg SC every other week (may increase to once weekly)</td>
<td>40 mg/week</td>
</tr>
<tr>
<td>Kevzara (sarilumab)</td>
<td>200 mg SC once every two weeks</td>
<td>200 mg every 2 weeks</td>
</tr>
<tr>
<td>Simponi Aria (golimumab)</td>
<td>Initial dose: 2 mg/kg IV at weeks 0 and 4 Maintenance dose: 2 mg/kg IV every 8 weeks</td>
<td>2 mg/kg every 8 weeks</td>
</tr>
<tr>
<td>Remicade (infliximab)</td>
<td>In conjunction with MTX Initial dose: 3 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 3 mg/kg IV every 8 weeks</td>
<td>10 mg/kg every 8 weeks or 3 mg/kg every 4 weeks</td>
</tr>
</tbody>
</table>

*Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks.

GPA, MPA

<table>
<thead>
<tr>
<th>glucocorticoids</th>
<th>Varies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
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</tr>
</tbody>
</table>

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, Truxima)
  - Severe mucocutaneous reactions, hepatitis B virus reactivation, progressive multifocal leukoencephalopathy (Rituxan, Truxima, Rituxan Hycela).

Appendix D: General Information
- Definition of MTX/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

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| Rituxan, Truxima | Low-grade and follicular B-cell NHL | 375 mg/m² IV infusion according to the following schedules:  
  - Relapsed or refractory, low-grade or follicular, CD20+, B-cell NHL  
    o Once weekly for 4 or 8 doses  
    o Retreatment: once weekly for 4 doses  
  - Previously untreated, follicular, CD20+, B-cell NHL:  
    o Administer on Day 1 of each cycle of chemotherapy for up to 8 doses;  
    o 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.  
  - Non-progressing, low-grade, CD20+, B-cell NHL, after first-line CVP chemotherapy:  
    o 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. | 375 mg/m² IV infusion |
| Rituxan | Low-grade and follicular B-cell NHL | 375 mg/m² IV infusion in combination with Zevalin for low-grade or follicular B-cell NHL:  
  o 250 mg/m² IV within 4 hrs prior to administration of Indium-111-(In-111-) Zevalin and Yttrium-90-(Y-90) Zevalin.  
  o Administer rituximab and In-111-Zevalin 7–9 days prior to rituximab and Y-90-Zevalin.  
  o Refer to the Zevalin package insert for full prescribing information regarding the Zevalin therapeutic regimen. | 375 mg/m² IV infusion |
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| **Rituxan Hycela**         | Follicular B-cell NHL       | 1,400 mg rituximab and 23,400 units hyaluronidase SC according to the following schedules:  
First dose must be with IV Rituxan/Truxima if indicated with an asterisk (*).  
- Relapsed or refractory FL:  
  - Once weekly for 3 or 7 weeks (i.e., 4 or 8 weeks in total)*  
  - Retreatment: once weekly for 3 weeks (i.e., 4 weeks in total)*  
- Previously untreated FL:  
  - 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)*  
  - 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  
- Non-progressing FL after first-line CVP chemotherapy:  
  - 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*  | 1,400 mg/23,400 units SC per injection |
| **Rituxan**                | DLBCL (a B-cell NHL)        | 375 mg/m² IV infusion on Day 1 of each cycle of chemotherapy for up to 8 doses total. | 375 mg/m² IV infusion                                |
| **Rituxan Hycela**         | DLBCL (a B-cell NHL)        | **First dose must be with IV Rituxan**  
- 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 8 cycles in total)  | 1,400 mg/23,400 units SC per injection |
| **Rituxan**                | CLL (a B-cell NHL)          | 375 mg/m² IV infusion on the day prior to initiation of FC chemotherapy, then 500 mg/m² on Day 1 of cycles 2-6 (every 28 days). | 500 mg/m² per day                                   |
| **Rituxan Hycela**         | CLL (a B-cell NHL)          | **First dose must be with IV Rituxan**  
- 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)  | 1,600 mg/26,800 units SC per injection |
| **Rituxan**                | RA                          | 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. | 1000 mg per week                                     |
| **Rituxan**                | GPA/MPA                     | Induction:  
  - 375 mg/m² IV once weekly for 4 weeks in combination with glucocorticoids  
Follow-up treatment if disease control with induction treatment:  
  - 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:  | Induction: 375 mg/m² per week  
Follow-up treatment: 500 mg/dose (see regimen for dosing frequency) |
### CLINICAL POLICY
Rituximab, Rituximab-abbs, Rituximab-Hyaluronidase

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituxan</td>
<td>PV</td>
<td>Initial and maintenance therapy:</td>
<td>Initial/relapse: 1000 mg/dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Two 1000 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</td>
<td>Maintenance: 500 mg/6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapse:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• 1000 mg IV once. Subsequent infusions may be administered no sooner than 16 weeks following the previous infusion.</td>
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</tr>
</tbody>
</table>

### VI. Product Availability

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

### VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy split from USS.SPMN.44 Rheumatoid Arthritis and Ankylosing Spondylitis Treatments and converted to new template. All safety criteria removed. Added dosing. RA: added age requirement; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; if the former are contraindicated, to require trial of methotrexate; if the former is contraindicated, added sulfasalazine as an alternative. In addition to RA, all other FDA-approved indications are added as well as NCCN compendia uses. Re-auth: combined into All Indications; added dosing and reasons to discontinue. Approval durations are 3 and 6 months for oncology and 6 and 12 months for all other indications.</td>
<td>08.16</td>
<td>09.16</td>
</tr>
<tr>
<td>Converted to new template. NHL: The FDA CLL labeled indication is added under NHL. Nodal marginal zone lymphoma is added under NCCN uses. Maximum dose is added. Safety information is removed. Duration is increased to 6 months. RA diagnostic criteria modified from requiring one or more of the following: ≥ 5 inflamed joints, elevation in the erythrocyte sedimentation rate (ESR) and/or serum C-reactive protein (CRP) concentration; positive rheumatoid factor</td>
<td>07.17</td>
<td>08.17</td>
</tr>
</tbody>
</table>
and/or anticyclic citrullinated peptide (CCP) antibodies (present in most patients), evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarticular swelling to the ACR diagnostic criteria. Off-label uses for autoimmune hemolytic anemia, immune thrombocytopenia purpura and graft-versus-host disease added. Other requests for off-label uses are referred to the off-label use policy. References updated.

4Q17 Annual Review
Added age requirement per PI and safety guidance; RA: removed requirement for submission of diagnostic lab since a specialist is required to prescribe or be consulted; NHL: created appendix D for approvable indications; Removed Class IIb DrugDex off-label uses: Warm and Cold Autoimmune Hemolytic Anemia, Immune Thrombocytopenia Purpura, Graft-versus-Host Disease; Removed UpToDate references; Added Rituxan Hycela to policy.

10.05.17 11.17

2Q 2018 annual review: revised conventional DMARD requirement in RA to require at least one conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine); modified trial and failure of preferred agents for RA; off-label criteria added for additional NCCN-recommended diagnoses; references reviewed and updated.

02.27.18 05.18

Criteria added for new indication pemphigus vulgaris; added Rituxan Hycela to COC; myasthenia gravis and nephrotic syndrome diagnoses added to policy as covered diagnoses if off-label criteria is met; references reviewed and updated.

07.31.18 11.18

1Q 2019 annual review: Rituxan biosimilar Truxima is added and applied to all policy criteria applicable to Rituxan; NHL criteria is edited to include all FDA approved or NCCN recommended NHL subtypes; additional NCCN recommended uses other than NHL are added to section I.E. (NCCN compendium uses); hematologist added for all oncology indications; GPA/MPA dosing updated to delineate induction versus follow-up treatment and approval duration is edited from 4 weeks total to 6/12 months; PF off-label criteria is added; references reviewed and updated.

01.15.19 02.19

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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