Clinical Policy: Rituximab (Rituxan)

Reference Number: PA.CP.PHAR.260
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for rituximab (Rituxan®).

FDA Approved Indication(s)
Rituxan is indicated for the treatment of:

- Non-Hodgkin's lymphoma (NHL)
  - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
  - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy
  - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line CVP (cyclophosphamide, vincristine, prednisone) chemotherapy
  - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or other anthracycline-based chemotherapy regimens
- Chronic lymphocytic leukemia (CLL)
  - Previously untreated and previously treated CD20-positive CLL, in combination with fludarabine and cyclophosphamide (FC)
- Rheumatoid arthritis (RA)
  - Moderately- to severely- active RA in adult patients in combination with methotrexate (MTX) and after inadequate response to one or more tumor necrosis factor antagonist therapies
- Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA)
  - GPA and MPA in adult patients in combination with glucocorticoids

Rituxan Hycela is indicated for the treatment of:

- Adult patients with follicular lymphoma (FL)
  - Relapsed or refractory, FL as a single agent
  - Previously untreated FL in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
  - Non-progressing (including stable disease), FL as a single agent after first-line CVP chemotherapy
- Adult patients with diffuse large B-cell lymphoma (DLBCL)
  - Previously untreated DLBCL in combination with CHOP or other anthracycline-based chemotherapy regimens
- Adult patients with CLL

- Previously untreated and previously treated CLL in combination with FC

Limitation(s) of use:
- Rituxan is not recommended for use in patients with severe, active infections.
- Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.
- Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that Rituxan is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Hodgkin's Lymphoma *(includes chronic lymphocytic leukemia)* (must meet all):
1. Diagnosis of non-Hodgkin's lymphoma (NHL) or any of its subtypes
2. Age ≥ 18 years;
3. If request is for Rituxan Hycela, member has received at least one full dose of Rituxan;
4. Request meets any of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. Rituxan: 500 mg/m^2 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 rheumatoid arthritis (RA) ;
2. Request is for Rituxan;
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 methotrexate (MTX) for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effect are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effect are experienced;
6. Failure of etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
7. Rituxan will be administered in combination with MTX unless contraindicated;
8. Prescribed dose does not exceed two-1000 mg infusions separated by 2 weeks followed by two-1000 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;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Rituxan will be administered in combination with glucocorticoid therapy;
6. Prescribed dose does not exceed 375 mg/m^2 once weekly.

Approval duration: up to 4 weeks total

D. NCCN **Compendium Indications (off-label)** (must meet all):

1. Diagnosis of one of the following (a, b, or c):
   1. Primary CNS lymphoma;
   2. Leptomeningeal metastases;
   3. Nodular lymphocyte-predominant Hodgkin lymphoma;
2. Request is for Rituxan;
3. Prescribed by or in consultation with an oncologist;
4. For nodular lymphocyte-predominant Hodgkin Lymphoma, age ≥ 18;
5. 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

E. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

1. Refer to PA.CP.PHAR.57 Global Biopharm policy.

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a) Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
      a. Documentation supports that member is currently receiving Rituxan or Rituxan Hycela for a covered oncology indication and has received this medication for at least 30 days;

2. Member is responding positively to therapy;3. If request is for a dose increase, request meets any of the following (a or b):

   a. New dose does not exceed (i or ii):
      i. Rituxan (a, b, or c):
         a) NHL: 500 mg/m^2 per IV infusion;
         b) RA: Two-1000 mg IV infusions every 16 weeks;

c) GPA/MPA: 375 mg/m^2 IV weekly;

ii. Rituxan Hycela for NHL: 1,600 mg/26,800 units SC (*see Section V for cycle regimens)*;

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 (GPA/MPA: up to 4 weeks total)

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Rituxan (rituximab) is a genetically engineered chimeric murine/human monoclonal IgG1 kappa antibody directed against the CD20 antigen. Rituximab is a monoclonal antibody that targets the CD20 antigen expressed on the surface of pre-B and mature B-lymphocytes. Upon binding to CD20, rituximab mediates B-cell lysis. Possible mechanisms of cell lysis include complement dependent cytotoxicity and antibody dependent cell mediated cytotoxicity. The antibody induced apoptosis in the DHL 4 human B cell lymphoma cell line. B cells are believed to play a role in the pathogenesis of rheumatoid arthritis (RA) and associated chronic synovitis. In this setting, B cells may be acting at multiple sites in the autoimmune/inflammatory process, including through production of rheumatoid factor (RF) and other autoantibodies, antigen presentation, T-cell activation, and/or proinflammatory cytokine production.

Formulations:

IV formulation:

Rituxan: 10 mg/mL; 100 mg/10 mL or 500 mg/50 mL single-use vials

Appendices

Appendix A: Abbreviation Key

ALL: acute lymphoblastic leukemia
CLL: chronic lymphocytic leukemia
CRP: C-reactive protein
ESR: elevation in the erythrocyte sedimentation rate
GPA: granulomatosis with polyangiitis (Wegener's granulomatosis)
MPA: microscopic polyangiitis
MTX: methotrexate
PTLD: Post-transplant lymphoproliferative disorder;
RA: rheumatoid arthritis
SLL: small lymphocytic lymphoma

Appendix B: The 2010 ACR Classification Criteria for RA

Add score of categories A through D. A score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint Involvement**	**Score**
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA	2
	High positive RF *or* high positive ACPA	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal CRP and normal ESR	0
	Abnormal CRP or normal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix C: Definition of MTX or disease-modifying antirheumatic drug (DMARD) failure
In RA, failure of MTX or DMARD is defined as ≤ 50% decrease in swollen joint count, ≤ 50% decrease in tender joint count, and ≤ 50% decrease in ESR, or ≤ 50% decrease in CRP.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9310	Injection, rituximab, 100 mg

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
C79.32	Secondary malignant neoplasm of cerebral meninges
C81.00-C81.99	Hodgkin lymphoma
C82.00-C82.99	Follicular lymphoma
C83.00-C83.99	Non-follicular lymphoma
C84.60-C84.99	Mature T/NK –cell lymphomas
C85.10-C85.89	Other specified and unspecified types of non-Hodgkin lymphoma
C86.0-C86.5	Other specified types of T/NK-cell lymphoma
C88.0	Waldenstrom macroglobulinemia
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)
C91.00-C91.02	Acute lymphoblastic leukemia (ALL)

ICD-10-CM Code	Description
C91.10-C91.12	Chronic lymphocytic leukemia of B-cell type
C91.40-C91.42	Hairy cell leukemia
M05.00-M06.9	Rheumatoid arthritis
M31.30, M31.31	Wegener's granulomatosis
M31.7	Microscopic polyangiitis
D36.0	Benign neoplasm of lymph nodes
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD) (code first complications of transplanted organs and tissue (T86.-)
D59.1	Other autoimmune hemolytic anemias
D69.3	Immune thrombocytopenic purpura
D69.41	Evans syndrome
T86.09	Complications of bone marrow transplant
T86.11	Kidney transplant rejection
T86.19	Other complications of kidney transplant
T86.298	Other complications of heart transplant
T86.39	Unspecified complication of heart-lung transplant
T86.5	Complications of stem cell transplant
Z85.71	Personal history of Hodgkin lymphoma
Z85.72	Personal history of non-Hodgkin lymphomas
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: summarized NCCN and FDA approved uses for improved clarity for Non-Hodgkin's Lymphoma; added specialist involvement in care into one criteria set; removed diagnosis requirement for ACR criteria in RA; revised conventional DMARD requirement in RA to require at least one conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine); off-label criteria added for additional NCCN-recommended diagnoses; removed off-label criteria for autoimmune hemolytic anemia and immune thrombocytopenia, will instead defer to off-label policy; approval durations updated; references reviewed and updated.	02.27.18	

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