MEDICAL POLICY STATEMENT

Original Effective Date	Next Annual Review Date	Last Review / Revision Date
09/25/2013	08/11/2016	07/15/2015

Policy Name	Policy Number
Rituxan (rituximab)	SRx-0030

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Rituxan (rituximab)

B. BACKGROUND

The intent of the Rituxan (PA) Program is to encourage appropriate selection of patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies, and also to encourage use of preferred agents.

C. DEFINITIONS

N/A

D. POLICY

I. CareSource will approve the use of Rituxan and consider its use as medically necessary when the following criteria have been met for:

A. **ANCA-associated vasculitis** (e.g. Wegener granulomatosis or microscopic polyangitis) and **ALL** of the following:

1. Prescribed by or under the recommendation of a nephrologist or rheumatologist
2. Age 18 years or older
3. Active severe disease present
4. No active infection
5. Administered in combination with glucocorticoids
6. Patient has failed treatment with cyclophosphamide and a glucocorticoid

B. **Chronic lymphocytic leukemia** and **ALL** of the following:

1. Age 18 years or older
2. No active infection
3. Prescribed by an oncologist or under the recommendation of an oncologist
4. CD20-positive

5. Administered in combination with fludarabine and cyclophosphamide
6. Symptomatic disease, as indicated by **1 or more** of the following:
    a. Autoimmune anemia or thrombocytopenia that is poorly responsive to corticosteroids
    b. Bulky adenopathy
    c. Fatigue
    d. Fever for 2 or more weeks without evidence of infection
    e. Hyperviscosity
    f. Night sweats without evidence of infection
    g. Organomegaly (e.g. hepatomegaly, splenomegaly)
    h. Progressive anemia or thrombocytopenia
    i. Progressive lymphocytosis (i.e. increase of more than 50% over 2-month period or lymphocyte doubling times of less than 6 months)
    j. Unintentional weight loss

C. **Non-Hodgkin lymphoma**, as indicated by **1 or more** of the following:
1. **Initial** course of rituximab and **ALL of the following:**
    a. Age 18 years or older
    b. Prescribed by an oncologist or under the recommendation of an oncologist
    c. No active infection
    d. CD20-positive B-cell non-Hodgkin lymphoma and **1 or more** of the following:
        (1) Diffuse large-cell disease, in combination with first-line chemotherapy with **1 or more** of the following:
            i. CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone)
            ii. EPOCH chemotherapy regimen (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
            iii. Other chemotherapy regimens for patients with poor left ventricular function who cannot tolerate high-dose anthracycline-based therapy
        (2) Follicular disease, in combination with first-line chemotherapy
        (3) Non-progressing low-grade disease with **1 or more** of the following:
            i. Complete response after first-line treatment with 6 to 8 cycles of cyclophosphamide, vincristine, and prednisone
            ii. Partial response after first-line treatment with 6 to 8 cycles of cyclophosphamide, vincristine, and prednisone
            iii. Stable disease after first-line treatment with 6 to 8 cycles of cyclophosphamide, vincristine, and prednisone
        (4) Relapsed or refractory low-grade or follicular disease
2. **Subsequent** course of rituximab and **ALL** of the following:
    a. Age 18 years or older
    b. No active infection
    c. CD20-positive B-cell non-Hodgkin lymphoma and **1 or more** of the following:
        (1) Diffuse large-cell disease with favorable response to prior first-line therapy with rituximab and chemotherapy
        (2) Follicular disease with favorable response to prior first-line therapy with rituximab
        (3) Relapsed or refractory low-grade or follicular disease with favorable response to induction with rituximab
        (4) Non-progressing low-grade disease at time of initial administration of rituximab, with **1 or more** of the following:
            i. Complete or partial response after first-line treatment with 6 to 8 cycles of cyclophosphamide, vincristine, and prednisone

ii. Stable disease after first-line treatment with 6 to 8 cycles of cyclophosphamide, vincristine, and prednisone

D. **Post-transplant lymphoproliferative** disorder and **ALL** of the following:
   1. CD20-positive B-cell disease
   2. No active infection
   3. Prescribed by an oncologist or under the recommendation of an oncologist
   4. Disease activity and treatment scenario includes **1 or more** of the following:
      a. Adult-Failure to respond to reduction of immunosuppressant therapy
      b. Child with **1 or more** of the following:
         (1) Failure to respond to reduction of immunosuppressant therapy
         (2) High risk of rejection with reduction of immunosuppressive therapy
         (3) Persistent or progressive post-transplant lymphoproliferative disorder in absence of allograft rejection

E. **Rheumatoid arthritis** and **ALL** of the following:
   1. Age 18 years or older
   2. Moderate to severe active rheumatoid arthritis
   3. No active infection
   4. Prescribed by a rheumatologist or under recommendation of a rheumatologist
   5. Administered in combination with methotrexate, unless unable to tolerate methotrexate
   6. Inadequate response to two or more tumor necrosis factor antagonist drugs (e.g. adalimumab, etanercept, infliximab)

F. **Thrombotic thrombocytopenic purpura** and **ALL** of the following:
   1. Age 18 years or older
   2. No active infection
   3. Disease severity includes **1 or more** of the following:
      a. Acute disease with either cardiac (e.g. increased troponin) or neurologic pathology
      b. Recurrent disease
      c. Refractory disease (i.e. to plasma exchange and corticosteroids)

G. **Waldenstrom macroglobulinemia**, as indicated by **1 or more** of the following:
   1. **Initial** course of rituximab and **ALL** of the following:
      a. Age 18 years or older
      b. No active infection
      c. Prescribed by an oncologist or under the recommendation of an oncologist
      d. Symptoms related to **1 or more** of the following:
         (1) Amyloidosis
         (2) Bulky adenopathy
         (3) Cold agglutinin disease or cryoglobulinemia (eg, Raynaud phenomenon, acrocyanosis)
         (4) Cytopenias (e.g. hemolytic anemia, thrombocytopenia)
         (5) Hyperviscosity (e.g. retinal changes)
         (6) Hyperviscosity (eg, retinal changes, confusion)
         (7) Neuropathy (motor or sensory)
         (8) Constitutional symptoms (eg, night sweats, weight loss)
         (9) Hepatosplenomegaly
   2. **Subsequent** course of rituximab and **ALL** of the following:
      a. Age 18 years or older
      b. Prescribed by an oncologist or under the recommendation of an oncologist
      c. No active infection
      d. Partial or complete response to initial course of rituximab as evidenced by **ALL** of the following:

(1) Fifty percent or greater reduction in adenopathy and/or organomegaly, if present with initial treatment, on physical examination or CT scan
(2) Fifty percent or greater reduction of serum monoclonal IgM protein by serum electrophoresis
(3) No new symptoms or signs of disease

e. Response to initial rituximab course lasted at least 12 months

H. **Immune thrombocytopenia**, as indicated by **ALL** of the following:
1. No active infection
2. Prescribed by a hematologist or under the recommendation of hematologist
3. Disease activity and treatment scenario includes **1 or more** of the following:
   a. For adults: platelet count less than 30,000/m3 (30 $x10^9$/L)
   b. For children or adults: significant or persistent bleeding associated with low platelet count (eg, less than 50,000/m3 (50 $x10^9$/L))
4. Failure of or contraindication to therapy with **1 or more** of the following:
   a. Anti-D immunoglobulin
   b. Corticosteroids
   c. IVIG
   d. Splenectomy

I. **Graft Versus Host Disease**, as indicated by **ALL** of the following:
1. No active infection
2. Third line of therapy or greater

J. **Castleman's Disease** , as indicated by **ALL** of the following:
1. No active infection

All other uses of Rituxan are considered experimental/investigational and therefore, will follow CareSource's Off-Label policy.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Note: Patient is required to have completed the trial listed in the above criteria unless the patient is unable to tolerate or has a contraindication. Documentation such as chart notes or pharmacy claims may be requested.

Refer to the product package insert for dosing, administration and safety guidelines.

For Medicare Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

If there is no NCD or LCD present, reference the CareSource Policy for coverage.

CONDITIONS OF COVERAGE
Place of Service
Office, Outpatient
Note: CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

HCPCS J9310
CPT

AUTHORIZATION PERIOD
Approved initial authorizations are valid for 6 months. Continued treatment may be considered when the member has shown biological response to treatment. A reauthorization after successful initiation period will be placed for 1 year. **ALL** authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

F. REVIEW/REVISION HISTORY

Date Issued:	08/20/2013
Date Reviewed:	08/20/2013, 09/25/2013, 07/15/2014, 07/15/2015
Date Revised:	08/20/2013 – Change in diagnosis
	07/15/2014 – Added diagnosis TTP and additional criteria to CD20+ CLL
	07/15/2015 – Added MCG 19th edition criteria

G. REFERENCES

1. MCG Ambulatory Care 19th Edition, Copyright © 2015 MCG Health, LLC
2. Rituxan (rituximab). Physician Prescribing Information [Internet] Genentech, Inc. 2014 August Accessed at: http://www.rituxan.com
3. Rituximab (Rituxan - Hoffman-La Roche Ltd.) New indication: granulomatosis with polyangiitis and microscopic polyangiitis, remission induction (adults). CEDC final recommendation [Internet] Canadian Agency for Drugs and Technologies in Health. 2012 Aug Accessed at: http://www.cadth.ca/en/products/cdr/cdr-overview
4. Stone JH, Merkel PA, Spiera R, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med 2010; 363:221.
5. Jones RB, Tervaert JW, Hauser T, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. N Engl J Med 2010; 363:211.
6. Ratanatharathorn V, Carson E, Reynolds C, et al. Anti-CD20 chimeric monoclonal antibody treatment of refractory immune-mediated thrombocytopenia in a patient with chronic graft-versus-host disease. Ann Intern Med 2000; 133:275.
7. Canninga-van Dijk MR, van der Straaten HM, Fijnheer R, et al. Anti-CD20 monoclonal antibody treatment in 6 patients with therapy-refractory chronic graft-versus-host disease. Blood 2004; 104:2603.
8. Cutler C, Miklos D, Kim HT, et al. Rituximab for steroid-refractory chronic graft-versus-host disease. Blood 2006; 108:756.
9. Kim SJ, Lee JW, Jung CW, et al. Weekly rituximab followed by monthly rituximab treatment for steroid-refractory chronic graft-versus-host disease: results from a prospective, multicenter, phase II study. Haematologica 2010; 95:1935.
10. Bower M, Powles T, Williams S, et al. Brief communication: rituximab in HIV-associated multicentric Castleman disease. Ann Intern Med 2007; 147:836.
11. Hoffmann C, Schmid H, Müller M, et al. Improved outcome with rituximab in patients with HIV-associated multicentric Castleman disease. Blood 2011; 118:3499.

This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC.

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.