

Title: rituximab (Rituxan)

Origination: 08/26/09	Revised: 11/23/11	Annual Review: 12/15/11
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Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Background Information:

Reference Statement

- Guidelines will be compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

Medication Summary

- Rituximab is indicated for adults with moderately-to-severely active rheumatoid arthritis (RA) who have failed methotrexate combination therapy or sequential administration of other DMARDs **and** one or more tumor necrosis factor (TNF) antagonist therapies. It should only be used for Members who have high disease activity and poor prognostic features.
- Rituximab is a genetically engineered chimeric murine/human monoclonal antibody that binds to CD20 antigen on normal and malignant B-lymphocytes. As a result, rituximab triggers a host cytotoxic immune response against CD20-positive cells resulting in cell apoptosis. B-cells are believed to play a role in the development and progression of rheumatoid arthritis (RA) through production of rheumatoid factor (RF) and other autoantibodies, antigen presentation, T cell activation, and/or pro-inflammatory cytokine production. Treatment with rituximab causes near complete depletion of peripheral B lymphocytes within two (2) weeks of the first dose and continues for at least six (6) months until subsequent gradual recovery.
- Rituximab is dosed as two (2) 1000mg intravenous (IV) infusions given on days 1 and 15 (two weeks apart). Methylprednisolone (100mg IV or its equivalent) should be given 30 minutes prior to each infusion to reduce the incidence and severity of infusion reactions. Although the safety and efficacy of more than one (1) treatment course (two infusions) has not been established, prospective data of patients receiving multiple treatment courses (3 to 5 courses) has shown consistent and sustained efficacy relative to the original baseline with no additive adverse effects.

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Background Information, continued:

Eligibility Criteria

- Member must be eligible and have applicable benefits.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusions

- Members with a history of hypersensitivity to Rituximab or any of its ingredients.
- Concurrent administration of multiple biological response modifiers [including, but not limited to: Kineret (anakinra), Remicade (infliximab), Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)]. Only one (1) agent at a time will be covered for the treatment of Rheumatoid Arthritis.

Additional Information

- Requests received **for Medicare Members** will be reviewed using Center for Medicare & Medicaid Services (CMS) “LCD for Rituximab (Rituxan - L29271)” – Refer to Attachment A or view on-line at:
http://www.cms.hhs.gov/mcd/results_index.asp?from=%27lmpcontractor%27&contractor=197&name=First+Coast+Service+Options%2C+Inc%2E+%2809102%2C+MAC+%2D+Part+B%29&letter_range=4&retired

Procedure:

- 1.0 Request for *therapy (initiation and continuation)* with Rituxan requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying one (1) of the following diagnoses:
 - 1.1 Rheumatoid Arthritis:
 - 1.1.1 Diagnosis of moderate to severe RA; **AND**
 - 1.1.2 Combination therapy with methotrexate (MTX) unless Member has contraindication or intolerance to MTX; **AND**
 - 1.1.3 Previous failure with oral DMARDS; **AND**

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Procedure, continued:

- 1.0 Request for *therapy (initiation and continuation)* with Rituxan requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying one (1) of the following diagnoses, continued:
 - 1.1 Rheumatoid Arthritis, continued:
 - 1.1.4 **For Commercial Members (excludes Medicare or Miami Dade County)** - Member shows inadequate response, or intolerance to, an adequate dose **both** Humira (adalimumab) **AND** Enbrel (etanercept);
 - 1.1.5 Age greater than 18 years old; **AND**
 - 1.1.6 Member has NOT received Rituxan in previous four (4) months;
 - 1.1.7 If criteria are met, Rituxan is approvable for six (6) months;
 - 1.2 Non-Hodgkin's Lymphoma:
 - 1.2.1 Rituxan is approvable for six (6) months;
 - 1.3 Primary CNS Cancers:
 - 1.3.1 Rituxan is approvable for six (6) months;
 - 1.4 Hodgkin's Lymphoma:
 - 1.4.1 Rituxan is approvable for six (6) months;
 - 1.5 Multiple myeloma:
 - 1.5.1 Rituxan is approvable for six (6) months;
 - 1.6 Chronic lymphocytic leukemia:
 - 1.6.1 Rituxan is approvable for six (6) months;
 - 1.7 Relapsed or refractory waldenstrom macroglobulinemia:
 - 1.7.1 Rituxan is approvable for six (6) months;
 - 1.8 Thrombocytopenic purpura:
 - 1.8.1 Rituxan is approvable for six (6) months;
 - 1.9 Wegener's Granulomatosis and Microscopic Polyangiitis (MPA) in combination with glucocorticoids:
 - 1.9.1 Rituxan is approvable for six (6) months.

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References:

1. Saag, KG. et al. American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis. *Arthritis & Rheumatism (Arthritis Care & Research)*. 2008; 59, 762–784.
2. Rituxan (package insert). South San Francisco, CA: Biogen Idec, Inc. and Genentech, Inc. September 2008.
3. Cohen SB, Emery P, Greenwald MW, et al. for the REFLEX Trial Group. Rituximab for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy: results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. *Arthritis Rheum*. 2006; 54(9): 2793-2806.
4. Saag, KG. et al. American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis. *Arthritis & Rheumatism* 2008; 59: 762-784.
5. Thurlings R, et al. Disease activity–guided rituximab therapy in rheumatoid arthritis. The effects of re-treatment in initial nonresponders versus initial responders. *Arthritis & Rheumatism* 2008; 58: 3657-3664.
6. Keystone E, Fleischmann RM, Emery P, et al. Safety and efficacy of additional courses of rituximab in patients with active rheumatoid arthritis an open-label extension analysis. *Arthritis & Rheumatism* 2007; 56: 3896-3908.
7. Smolen JS, Betteridge N, Breedveld FC, et al. Consensus statement on the use of rituximab in patients with rheumatoid arthritis *Ann Rheum Dis* 2006; 10.1136/ard.2006.061002.
8. Kremer JM, Tony HP, Tak PP, Luggen M, Mariette X, Hessey E, McCabe D, Safa-Leathers S. Efficacy of rituximab in active RA patients with an inadequate response to one or more TNF inhibitors. *Ann Rheum Dis*. 2006;65(suppl II):326.
9. van Vollenhoven RF, Cohen S, Pavelka K, et al. Response to rituximab in patients with rheumatoid arthritis is maintained by repeat therapy: results of an open-label trial [abstract]. *Ann Rheum Dis*.2006; 65: 510.
10. van Vollenhoven RF, Emery P, Bingham C, et al. Long-term safety data from extended follow-up and repeat use of rituximab in rheumatoid arthritis [abstract]. *Ann Rheum Dis*. 2007; 66 (suppl II):88.

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References, continued:

11. Kremer JM, Tony HP, Genovese MC, Tak PP, Luggen M, Bombardieri S, Hesse E, Safa-Leathers S. Repeat treatment with rituximab in active RA patients: long-term efficacy in patients with one versus two or more prior TNF inhibitors. *Ann Rheum Dis.* 2007;66(suppl):432.
12. Centers for Medicare & Medicaid Services, US Department of Health and Human Services. Local Coverage Determination (LCD) for Rituximab (Rituxan - L29271). 1st Quarter 2009 update. Revision 1, effective 02/02/2009.
13. Facts and Comparisons 4.0, St. Louis, MO. Walters Kluwer Health URL: www.factsandcomparisons.com. Updated 2010.
14. National Comprehensive Cancer Network, Inc. (NCCN) Practice Guidelines in Oncology Version 2.2010, March 2010. Available at: www.nccn.org/professionals/physician_gls/f_guidelines.asp

Disclaimer Information:

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.