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Subject: Rituxan (rituximab)
Effective Date: May 10, 2011

Clinical Documentation and Prior Authorization Required	√	Type of Review - Case Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	MED	Administrative Process (Internal Use Only)	RN/MD

Note: This pharmacy medical necessity guideline applies to commercial products. For Tufts Health Plan Medicare Preferred members, please refer to the Tufts Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

Overview

FDA-APPROVED INDICATIONS

Rituxan (rituximab) is indicated for the treatment of patients with:

Chronic Lymphocytic Leukemia (CLL):

- In combination with fludarabine and cyclophosphamide (FC, for the treatment of patients with previously untreated and previously treated CD-20 positive CLL.

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 chemotherapy.
- Previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP or other anthracycline-based chemotherapy regimens.

Rheumatoid Arthritis (RA):

- In combination with methotrexate for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies.

Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA)

- In combination with glucocorticoids for the treatment of adult patients with Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA).

Pharmacy Coverage Guidelines

Tufts Health Plan may authorize coverage of **Rituxan** (rituximab) for the following:

A. Non-Hodgkin's Lymphoma or Chronic Lymphocytic Leukemia

1. Tufts Health Plan will **NOT** require prior authorization for coverage of Rituxan (rituximab) for the treatment of Non-Hodgkin's Lymphoma or chronic lymphocytic leukemia (CLL).

For any medical billing claim submitted, please utilize ICD-9 codes 200.00 – 200.88 (lymphosarcoma and reticulosarcoma and other specified malignant tumors), 202.80 – 202.88 (Non-Hodgkin's type NEC), or 204.10 – 204.12 (chronic lymphoid/lymphocytic leukemia) as the primary diagnosis codes when using Rituxan (rituximab) for the treatment of Non-Hodgkin's Lymphoma.

Note: For coverage of all other cancers, see **Off-label Use Coverage for Other Cancer Diagnoses**

B. Rheumatoid Arthritis

Tufts Health Plan may authorize coverage of **Rituxan** (rituximab) in combination with methotrexate for Members when the following criteria are met:

1. Diagnosis from a rheumatologist of active rheumatoid arthritis
- AND**
2. The Member has a documented inadequate response to an appropriate trial with at least one tumor necrosis factor (TNF) antagonist therapy: **Cimzia**[®] (certolizumab pegol), **Enbrel**[®] (etanercept), **Humira**[™] (adalimumab), **Remicade**[®] (infliximab) or **Simponi**[™] (golimumab).

C. Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA)

Tufts Health Plan may authorize coverage of **Rituxan** (rituximab) for Members when the following criteria are met:

1. Diagnosis from a rheumatologist of Wegener's granulomatosis or microscopic polyangiitis
- AND**
2. The Member is concurrently taking glucocorticoids (e.g., prednisone).

Note:

Authorization for Wegener's granulomatosis or microscopic polyangiitis will be limited to 6 months.

- Additional authorization may be given if documentation of an objective measurable effect is provided indicating clinical improvement of condition. Subsequent authorizations may be given in 6-month intervals.

D. Off-label Use Coverage for Other Cancer Diagnoses

Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia, or in the medical literature, or by the Massachusetts commissioner of Insurance (commissioner) under the provisions of the "Sullivan Law": (M.G.L. c.175, s.47K).

Tufts Health Plan may authorize coverage for use for other cancer diagnoses provided effective treatment with such drug is recognized as a "Medically Accepted Indication" according to the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium as indicated by a Category 1 or 2A for quality of evidence and level of consensus.

Note: Tufts Health Plan requires prescribers to submit clinical documentation supporting the drug's effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s).

In cases where the requested off-label use for the diagnosis is not recognized by the NCCN Drugs and Biologics Compendium, Tufts Health Plan will follow the Centers for Medicare and Medicaid Services

(CMS) guidance, unless otherwise directed by the commissioner, and accept clinical documentation referenced in one of the other "Standard Reference Compendia" noted below or supported by clinical research that appears in a regular edition of a "Peer-Reviewed Medical Literature" noted below.

"Standard Reference Compendia"

1. American Hospital Formulary Service – Drug Information (AHFS-DI)
2. Thomson Micromedex DrugDex
3. Clinical Pharmacology (Gold Standard)

"Peer Reviewed Medical Literature"

- American Journal of Medicine
- Annals of Internal Medicine
- Annals of Oncology
- Annals of Surgical Oncology
- Biology of Blood and Marrow Transplantation
- Blood
- Bone Marrow Transplantation
- British Journal of Cancer
- British Journal of Hematology
- British Medical Journal
- Cancer
- Clinical Cancer Research
- Drugs
- European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)
- Gynecologic Oncology
- International Journal of Radiation, Oncology, Biology, and Physics
- The Journal of the American Medical Association
- Journal of Clinical Oncology
- Journal of the National Cancer Institute
- Journal of the National Comprehensive Cancer Network (NCCN)
- Journal of Urology
- Lancet
- Lancet Oncology
- Leukemia
- The New England Journal of Medicine
- Radiation Oncology

When Tufts Health Plan evaluates the evidence in published, peer-reviewed medical literature, consideration will be given to the following:

1. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
4. Whether the study is appropriate to address the clinical question.
 - a) whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover.);
 - b) that non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,
 - c) that case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

Limitations

1. Tufts Health Plan will not authorize the use of Rituxan (rituximab) for conditions other than those listed above without appropriate documentation.

Codes

The following HCPCS/CPT code(s) are:

Code	Description
J9310	Injection, rituximab, 100 mg

References

1. Rituxan[®] (rituximab) package insert, Genentech 2006
2. Genentech website, www.gene.com
3. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, Non-Hodgkin's Lymphomas. V.3.2008. www.nccn.org. Accessed October 10, 2008.
4. Food and Drug Administration. FDA approves Rituxan to treat two rare disorders. URL: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm251946.htm>. Available from Internet. Accessed 2011 April 20.
5. National Institute of Allergy and Infectious Diseases (NIAID). Wegener's Granulomatosis. URL: <http://www.niaid.nih.gov/topics/wegeners>. Available from Internet. Accessed 2011 April 21.
6. National Institutes of Health: Genetic and Rare Diseases Information Center (GARD). Microscopic polyangiitis. URL: http://rarediseases.info.nih.gov/GARD/Condition/3652/Microscopic_polyangiitis.aspx. Accessed 2011 April 21.
7. The Johns Hopkins Vasculitis Center. Microscopic polyangiitis. URL: <http://www.hopkinsvasculitis.org/types-vasculitis/microscopic-polyangiitis>. Available from Internet. Accessed 2011 April 21.
8. Rituxan (rituximab) [package insert]. South San Francisco, CA: Genentech, Inc.; April 2011.

Approval History

Reviewed by the Pharmacy and Therapeutics Committee on May 9, 2006.

Subsequent Endorsement Date(s) and Changes Made:

1. May 8, 2007: No changes
2. March 4, 2008:
 - Added ICD-9 diagnoses codes 200.00 – 200.80 to criteria #1 for Non-Hodgkin's Lymphoma.
3. November 11, 2008:
 - Added ICD-9 diagnoses codes 204.10 – 204.12 (chronic lymphoid/lymphocytic leukemia) to criteria #1 for Non-Hodgkin's Lymphoma.
4. January 13, 2009:
 - Removed **Section B** and inserted updated language for **Off-label Use Coverage for Other Cancer Diagnoses**
5. November 10, 2009:
 - Added Cimzia (certolizumab pegol) and Simponi (golimumab) to tumor necrosis factor (TNF) antagonist therapy prerequisites for rheumatoid arthritis.
6. January 1, 2010:
 - Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred).
7. May 11, 2010:
 - Added approval for Chronic Lymphocytic Leukemia and updated pharmacy coverage guidelines.
8. September 14, 2010:
 - Added ICD-9 diagnoses codes 200.81 – 200.88 to criteria #1 for Non-Hodgkin's Lymphoma.
9. January 11, 2011:

- Administrative Update: Effective 4/1/2011, Off-label Use Coverage for Other Cancer Diagnoses language updated. Tufts Health Plan requires prescribers to submit clinical documentation supporting the drug's effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s)

10. May 10, 2011:

- Added coverage guidelines for the treatment of Wegener's granulomatosis and microscopic polyangiitis.

Background, Product and Disclaimer Information

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for Tufts Health Plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a Member's benefit document and in coordination with the Member's physician(s). Tufts Health Plan makes coverage decisions on a case-by-case basis considering the individual Member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the Tufts Health Plan service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Tufts Health Plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

Pharmacy Medical Necessity Guidelines apply to all fully insured Tufts Health Plan offerings unless otherwise noted in this policy or the Member's benefit document. Check the applicable formulary in the Pharmacy section of our Web site at <http://www.tuftshealthplan.com/providers> to determine if the drug requires you to get prior authorization. This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member's benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLinkSM Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Medicare Preferred, please refer to Tufts Medicare Preferred Prior Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to Member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.