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Subject: Rituxan (rituximab)
Effective Date: November 11, 2008

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: Background, applicable product and disclaimer information is located at the end of this document.

Overview

Rituxan® (rituximab) is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. Rituximab binds specifically to the antigen CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35), a hydrophobic transmembrane protein located on pre-B and mature B lymphocytes. The antigen is also expressed on >90% of B-cell non-Hodgkin's lymphomas (NHL), but is not found on hematopoietic stem cells, pro-B cells, normal plasma cells or other normal tissues. CD20 regulates an early step(s) in the activation process for cell cycle initiation and differentiation, and possibly functions as a calcium ion channel. CD20 is not shed from the cell surface and does not internalize upon antibody binding. Free CD20 antigen is not found in the circulation. 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 pro-inflammatory cytokine production.

Pharmacy Coverage Guidelines

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

A. Non-Hodgkin's Lymphoma

1. Tufts Health Plan will **NOT** require prior authorization for coverage of Rituxan® for the treatment of Non-Hodgkin's Lymphoma, including chronic lymphocytic leukemia (CLL). For any medical billing claim submitted, please utilize ICD-9 codes 200.00 – 200.80 (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® 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**® 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: **Enbrel**® (etanercept), **Humira**™ (adalimumab), or **Remicade**® (infliximab).

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: 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 require prescribers to submit clinical documentation supporting the drug's effectiveness in treating the intended malignancy. 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[®] for conditions other than those listed above without appropriate documentation.

Codes

The following HCPCS/CPT code(s) are:

Code	Description
J9310	Rituximab, 100mg

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.

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**

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. However, for Tufts Health Plan Medicare Preferred Members, the Pharmacy Medical Necessity Guidelines only apply to Medicare Part D covered drugs. Tufts Medicare Preferred defers to Medicare coverage guidelines when reviewing Medicare Part B covered drugs. Medicare's national and local coverage determinations for Part B covered drugs can be accessed via the CMS coverage database at <http://www.cms.hhs.gov/mcd/search.asp>. Medicare general coverage guidelines are located in Chapter 15 of the Medicare Benefit Policy Manual, which can be accessed at <http://www.cms.hhs.gov/Manuals/IOM/list.asp>. Generally, Tufts Medicare Preferred requires prior authorization for the same drugs that require prior authorization for the fully insured Tufts Health Plan offerings. 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.

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.