

Evidence Based Guideline

Monoclonal Antibodies for Non-Hodgkin Lymphoma & Acute Myeloid Leukemia

File Name: monoclonal_antibodies_for_non_hodgin_lymphoma_&_acute_myeloid_leukemia
Guideline Number: EBG.MED1489
Origination: 7/2009
Last CAP Review: N/A
Next CAP Review: 3/2010
Last Review: 7/2009

Description of Procedure or Service

Rituximab (Rituxan®) is a chimeric murine/human monoclonal antibody directed against the surface antigen CD20, which is expressed on all normal B lymphocytes and more than 90% of B-cell non-Hodgkin lymphomas (NHL). Rituximab induces lysis of B cells (normal and malignant) that express CD20, and also sensitizes B cells to the cytotoxic effect of chemotherapy.

Alemtuzumab (Campath®) is a recombinant, humanized, monoclonal antibody directed against the cell surface protein CD52, which is expressed on most normal and malignant B and T lymphocytes, but not on hematopoietic stem cells. Therefore, it has the potential for broad application in treating B- and T-cell malignancies. Its mechanism of action appears to involve complement-mediated cell lysis, antibody-dependent cellular toxicity, and the induction of apoptosis.

Gemtuzumab (Mylotarg®) is a recombinant, humanized monoclonal antibody directed against the CD33 antigen, which is expressed on the surface of leukemic blasts in more than 80% of patients with acute myeloid leukemia (AML), and by normal cells committed to the myeloid lineage, but not by pluripotent hematopoietic stem cells. Binding of the anti-CD33 antibody with the CD33 antigen results in formation of a complex that is internalized and eventually leads to DNA double-strand breaks and cell death.

The following policy considers labeled and off-label indications for the uses of rituximab, alemtuzumab, and gemtuzumab in NHL and AML in the non-stem-cell transplant setting.

*****Note: This Evidence Based Guideline is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Evidence Based Guideline for the Use of Monoclonal Antibodies for the Treatment of Non-Hodgkin Lymphoma & Acute Myeloid Leukemia

1. Rituximab (Rituxan®) may be appropriate to treat patients with B-cell non-Hodgkin lymphoma (NHL) in any of the following:
 - a. when used with cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy as first-line treatment of follicular NHL,*
 - b. when used with cyclophosphamide, vincristine, doxorubicin, and prednisone (CHOP) chemotherapy as first-line treatment of follicular NHL,
 - c. to treat relapsed or refractory, low-grade or follicular, CD20+ B-cell NHL,*

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- d. to treat low-grade NHL in those with stable disease or who achieve a partial or complete response following first-line treatment with CVP chemotherapy,*
 - e. when used with CHOP or other anthracycline-based chemotherapy as first-line treatment for patients with diffuse large B-cell lymphoma (DLBCL),*
 - f. for recurrent, aggressive CD20-positive NHL,
 - g. for previously untreated or relapsed/refractory mantle cell lymphoma,
 - h. as combination therapy in previously untreated B-cell chronic lymphocytic leukemia (B-CLL).
2. Alemtuzumab (Campath®) may be appropriate as a single agent for the treatment of B-cell chronic lymphocytic leukemia (B-CLL)* in patients with a chromosome deletion of 17p or in patients not suitable for treatment with fludarabine (see Note in Benefits Application).
 3. Gemtuzumab ozogamicin (Mylotarg®) may be appropriate for the treatment of patients with CD33-positive acute myeloid leukemia (AML) in first relapse who are 60 years of age or older and who are not considered candidates for other cytotoxic chemotherapy.*

*Indicates an indication approved by the U.S. Food and Drug Administration

Medical Evidence regarding the Use of Monoclonal Antibodies for the Treatment of Non-Hodgkin Lymphoma & Acute Myeloid Leukemia indicates it is not recommended in the following situations:

1. For conditions other than those listed above.
2. Alemtuzumab (Campath®) is not recommended for the treatment of malignancies other than B-cell CLL.
3. Gemtuzumab ozogamicin (Mylotarg®) is not recommended for:
 - a. treatment of patients with AML and who are younger than 60 years of age,
 - b. treatment of newly diagnosed AML,
 - c. treatment of second or subsequent relapse of AML,
 - d. use in combination with cytotoxic chemotherapy.

Note: In September 2007, the U.S. Food and Drug Administration (FDA) expanded the approved labeling for alemtuzumab to include its use in previously untreated patients with B-cell CLL (previous label approved only for treatment of B-cell CLL in treatment-experienced patients, specifically those who had been treated with an alkylating agent and whose disease was not responding adequately to fludarabine therapy).

Treatment of B-cell chronic lymphocytic leukemia (B-CLL) with monoclonal antibody therapy is used in patients with non-localized disease (i.e., Ann Arbor stage II-IV).

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the policy.

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Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J9010, J9300, J9310

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual, 2.03.05, 5/14/09

Senior Medical Director 7/2009

Policy Implementation/Update Information

9/28/09 New evidence based guideline adopted from the BCBSA. Reviewed with Senior Medical Director 7/20/09. (btw)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.