Belimumab (Benlysta)

**Description of Procedure or Service**

Belimumab (Benlysta) is a human monoclonal antibody drug that specifically recognizes and inhibits the biological activity of B-lymphocyte stimulator, or BLyS. BLyS is a cytokine that belongs to the tumor necrosis factor (TNF) ligand family. It is expressed as transmembrane protein on various cell types including monocytes, dendritic cells, and bone marrow stromal cells and is required for the development of B-lymphocyte cells into mature plasma B cells. Plasma B cells produce anti-bodies, the body's first line of defense against infection. In lupus and certain other autoimmune diseases, elevated levels of BLyS are believed to contribute to the production of autoantibodies –antibodies that attack and destroy the body's own healthy tissues. The presence of autoantibodies appears to correlate with disease severity. Preclinical and clinical studies suggest that belimumab can reduce autoantibody levels in SLE. Benlysta (belimumab) has been approved by the U.S. Food and Drug Administration (FDA) for the adjunctive treatment of active, autoantibody-positive, systemic lupus erythematosus (SLE).

Systemic lupus erythematosus (SLE) is a potentially fatal, autoimmune disease, which is characterized by clinical diversity, alterations in the disease activity over time, and aberrations in multiple components of the immune system including B cells, T cells, as well as cytokines and growth factors, especially the presence of anti-nuclear antibodies (ANA) that are found in over 90 % of the patients. Moreover, anti-double-strand deoxyribonucleic acid (anti-dsDNA) antibodies are found in 50 to 90 % of the patients. The disease affects many parts of the body including the brain, heart, joints, kidneys, lungs, and the skin. When SLE flares, it can present as chest pain, fatigue, fever, hair loss, rash, light sensitivity, as well as swelling in the joints and joint pain. Conventional treatments of SLE include anti-malarials (e.g., chloroquine and hydroxychloroquine), corticosteroids, and non-steroidal anti-inflammatory drugs (e.g., aspirin). While therapeutic advances in immunosuppressive drugs (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate) and support therapy have markedly improved survival, SLE still carries substantially increased rates of mortality and end stage renal disease, which are even more elevated in younger patients.

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

**Policy**

BCBSNC will provide coverage for belimumab (Benlysta) for the treatment of autoantibody-positive systemic lupus erythematosus when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Coverage for belimumab (Benlysta) requires prior review.
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Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Belimumab (Benlysta) is covered

Belimumab may be considered medically necessary for patients:

1. 18 years of age or older; and
2. For the treatment of active, autoantibody-positive, systemic lupus erythematosus [anti-nuclear antibody (ANA) titer ≥ 1:80 or anti-doublestranded DNA (anti-dsDNA) level ≥ 30 IU/mL].

When Belimumab (Benlysta) is not covered

Belimumab is considered not medically necessary for use in patients with:

- Severe active lupus nephritis
- Severe active central nervous system lupus

Belimumab is considered not medically necessary when used in combination with other biologics or intravenous cyclophosphamide.

Belimumab is considered investigational for all other indications, including but not limited to use in children.

Policy Guidelines

Belimumab is for intravenous infusion only. The recommended dosage regimen is 10mg/kg at 2 week intervals for the first 3 doses and at 4 week intervals thereafter.

The efficacy of belimumab has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Belimumab has not been studied in combination with other biologics or intravenous cyclophosphamide.

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including belimumab (Benlysta). Caution should be exercised when considering use in patients with a history of chronic infections. Patients receiving therapy for a chronic infection should not receive belimumab (Benlysta).

Acute hypersensitivity reactions, including anaphylaxis and death, have been reported in association with BENLYSTA. These events generally occurred within hours of the infusion; however they may occur later. Non-acute hypersensitivity reactions including rash, nausea, fatigue, myalgia, headache, and facial edema, have been reported and typically occurred up to a week following the most recent infusion. Hypersensitivity, including serious reactions, has occurred in patients who have previously tolerated infusions of BENLYSTA. Patients with a history of multiple drug allergies may be at increased risk of hypersensitivity/anaphylaxis. The safety and effectiveness of belimumab has not been established in children.

There are no adequate and well-controlled clinical studies using Benlysta in pregnant women. Benlysta should be used during pregnancy only if the potential benefit to the mother justifies the
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potential risk to the fetus. Women of childbearing potential should use adequate contraception during treatment and for at least 4 months after the final treatment. Because maternal antibodies are excreted in human breast milk, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of breastfeeding to the infant and the importance of the drug to the mother.

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 service codes: J0490

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


Policy Implementation/Update Information

7/1/11 New medical policy issued. Belimumab is considered medically necessary for treatment of active, autoantibody-positive, systemic lupus erythematosus.
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12/6/11 Deleted statement: “who are not immunocompromised” under When Covered section. Added statement: “Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including Benlysta. Caution should be exercised when considering use in patients with a history of chronic infections. Patients receiving therapy for a chronic infection should not receive Benlysta” to Policy Guidelines section. Reviewed with medical director. Removed HCPCS code Q2044 from the Billing/Coding section and added J0490 effective 1/1/2012. (lpr)

3/20/12 Under “When Not Covered” first two statements changed to read “not medically necessary” Instead of “investigational” and the last statement continues to read “investigational for all other indications, including but not limited to use in children.” Specialty Matched Consultant Advisory Panel review meeting 2/29/12. No change to policy statement. (lpr)

3/12/13 Specialty Matched Consultant Advisory Panel review meeting 2/20/2013. No change to policy statement. Reference added. (lpr)


3/10/15 Specialty Matched consultant advisory panel review meeting 2/5/2015. No change to policy statement. (lpr)

4/1/16 Specialty Matched consultant advisory panel review meeting 2/24/16. No change to policy statement. –an

12/30/16 Minor changes to description section. No change to policy statement. (an)

3/31/17 Description section updated. Added specific laboratory findings to Item 2 in the When Covered section. Information regarding use during pregnancy and lactation added to Policy Guidelines section. Reference added. Specialty Matched Consultant Advisory Panel review meeting 2/22/2017. (an)

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.