BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

belimumab (Benlysta®)

Policy # 00295
Original Effective Date: 04/13/2011
Current Effective Date: 05/21/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of belimumab (Benlysta®)‡ for the treatment of systemic lupus erythematosus (SLE) in adult patients who are receiving standard therapy to be **eligible for coverage**.

Patient Selection Criteria
Coverage eligibility for the use of belimumab (Benlysta) for the treatment of systemic lupus erythematosus (SLE) will be considered when all of the following patient selection criteria are met:

- Patient is ≥ 18 years of age; and
- Patient has diagnosis of active systemic lupus erythematosus (SLE); and
- Patient is autoantibody-positive (ANA or anti- double-stranded deoxyribonucleic acid [anti-dsDNA]); and
- Patient is receiving standard therapy (corticosteroids, antimalarials, non-steroidal anti-inflammatory drugs [NSAIDs], immunosuppressives); and
- Patient is NOT receiving other biologics or intravenous (IV) cyclophosphamide.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of belimumab (Benlysta) when patient selection criteria are not met OR for use in any other indication (including, but not limited to severe active lupus nephritis or severe active central nervous system lupus) not listed in the above patient selection criteria to be **investigational.***

Background/Overview

Belimumab (Benlysta) is a new molecular entity that targets a novel pathway for the treatment of SLE. Benlysta is a recombinant, fully human, IgG1λ monoclonal antibody that binds and inhibits the biological activity of soluble B lymphocyte stimulator (BLyS), protein. B lymphocyte stimulator is a member of the tumor necrosis factor (TNF) ligand family and is also known as B-cell activating factor belonging to the TNF family (BAFF). It plays a role in B cell selection and survival and is expressed by a variety of cell types, including neutrophils, monocytes, macrophages, dendritic cells, and T cells. There are 3 receptors for BLyS. B lymphocyte stimulator receptor 3 (BR3) is the only BLyS receptor found on newly formed and mature

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primary B cells, and BLyS is its only ligand. Blockade by belimumab (Benlysta) is expected to affect these cells more than memory B cells and plasma cells, which have other ligand activators.

Systemic Lupus Erythematosus
Systemic lupus erythematosus is a chronic inflammatory disease of unknown cause that can affect the mucocutaneous, gastrointestinal, hematologic, musculoskeletal, neurologic, psychiatric, pulmonary, renal, and reproductive systems. Immunologic abnormalities are a prominent feature of the disease. For example, autoantibodies against dsDNA (i.e. anti-dsDNA) and Smith nuclear antigen (i.e. anti-Sm) are highly specific for SLE. Increases in anti-dsDNA titers, erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP), and a decrease in serum complement levels, often precede active SLE.

Currently, three drugs are FDA-approved for the treatment of SLE: prednisone, aspirin, and hydroxychloroquine. Other drugs commonly used in the treatment of SLE include NSAIDs and immunosuppressive agents, such as cyclophosphamide, methotrexate, azathioprine, and mycophenolate.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
In March 2011, the FDA approved belimumab (Benlysta) to treat patients with active, autoantibody-positive lupus (systemic lupus erythematosus) who are receiving standard therapy, including corticosteroids, antimalarials, immunosuppressives, and nonsteroidal anti-inflammatory drugs.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Two clinical studies involving 1,684 patients with lupus demonstrated the safety and effectiveness of Benlysta. The studies diagnosed patients with active lupus and randomized them to receive Benlysta plus standard therapy, or an inactive infused solution (placebo) plus standard therapy. The studies excluded patients who had received prior B-cell targeted therapy or IV cyclophosphamide, and those who had active lupus involving the kidneys or central nervous system.

Patients treated with Benlysta and standard therapies experienced less disease activity than those who received a placebo and standard of care medicines. Results suggested, but did not definitively establish, that some patients had a reduced likelihood of severe flares, and some reduced their steroid doses.

African American patients and patients of African heritage participating in the two studies did not appear to respond to treatment with Benlysta. The studies lacked sufficient numbers to establish a definite conclusion. To address this concern, the sponsor has agreed to conduct an additional study of people with those backgrounds to further evaluate the safety and effectiveness of Benlysta for this subgroup of lupus patients.

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Those receiving Benlysta during clinical studies reported more deaths and serious infections compared with placebo. The drug should not be administered with live vaccines. The manufacturer is required to provide a Medication Guide to inform patients of the risks associated with Benlysta.

The most common side effects in the studies included nausea, diarrhea, and fever (pyrexia). Patients also commonly experienced infusion reactions, so pre-treatment with an antihistamine should be considered.

References

1. Drugs at FDA. belimumab (Benlysta). 2014
2. Package insert belimumab (Benlysta). April 2014

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2013 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0490
ICD-9 Diagnosis	710.0
ICD-9 Procedure	No codes

Policy History

Original Effective Date: 04/13/2011
Current Effective Date: 05/21/2014
04/07/2011 Medical Policy Committee review
04/13/2011 Medical Policy Implementation Committee approval. New policy
04/12/2012 Medical Policy Committee review
04/25/2012 Medical Policy Implementation Committee approval.
04/04/2013 Medical Policy Committee review

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04/24/2013	Medical Policy Implementation Committee approval. No change to coverage. No changes to coverage. A few cosmetic changes. Consolidated the When Services Are Considered Investigational section.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 05/2015

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.