Original Effective Date: 06/01/2013
Current Effective Date: 11/23/2023
Last P&T Approval/Version: 10/25/2023
Next Review Due By: 10/2024
Policy Number: C2722-A

Benlysta (belimumab)

PRODUCTS AFFECTED

Benlysta (belimumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Systemic lupus erythematosus (SLE), Active lupus nephritis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR ACTIVE LUPUS NEPHRITIS:
1. Documented diagnosis of active systemic lupus erythematosus disease (SLE) or active lupus

nephritis
AND

2. Documentation of laboratory testing that demonstrates the presence of autoantibodies [e.g., ANA, Anti-dsDNA, Anti-Sm, Anti-Ro/SSA, Anti- La/SSB] [DOCUMENTATION REQUIRED]
AND
3. Prescriber attests to an inadequate response or serious side effects to standard therapy for SLE [Current standard therapy includes various combinations of corticosteroids, antimalarial drugs (e.g., Hydroxychloroquine) and/or immunosuppressive agents (e.g., oral cyclophosphamide, azathioprine, methotrexate, and mycophenolate mofetil)]
AND
4. Prescriber attests to or clinical reviewer has found no evidence of concurrent use of another biologic [i.e., Actemra, Cimzia, Enbrel, Humira, Kineret, Orencia, Remicade, Rituxan, Simponi, Stelara]
AND
5. Prescriber attests to or clinical reviewer has found no evidence of severe active central nervous system (CNS) lupus [such as seizures, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis]
AND
6. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR ACTIVE LUPUS NEPHRITIS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms [DOCUMENTATION REQUIRED]
AND
4. Prescriber attests member is currently treated and adherent to standard therapy for SLE

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of treatment: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified rheumatologist, nephrologist, or physician who specializes in the treatment or management of patients with systemic autoimmune diseases. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

5 years of age and older

QUANTITY:

Intravenous administration in adults and pediatric patients with SLE or Lupus Nephritis Initial: 10 mg/kg every 2 weeks for 3 doses; then 10 mg/kg every 4 weeks

Subcutaneous administration in ADULTS with SLE: 200 mg once weekly.
Subcutaneous administration in ADULTS with Lupus Nephritis: 400 mg dose (two 200 mg injections) once weekly for 4 doses, then 200 mg once weekly thereafter
NOTE: Subcutaneous dosing of Benlysta has not been evaluated and is not approved for patients

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non- hospital facility-based location.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Benlysta (belimumab) IV.
For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous, Subcutaneous

DRUG CLASS:
B-Lymphocyte Stimulator (BLyS)-Specific Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of:

- Patients aged 5 years and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy
- Patients aged 5 years and older with active lupus nephritis who are receiving standard therapy.

Limitations of use: The efficacy of BENLYSTA has not been evaluated in patients with severe active central nervous system lupus. Use of BENLYSTA is not recommended in this situation.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Texas (Source: Texas Statutes, Insurance Code)
"Sec. 1369.654. PROHIBITION ON MULTIPLE PRIOR AUTHORIZATIONS.
(a) A health benefit plan issuer that provides prescription drug benefits *may not require an enrollee to receive more than one prior authorization annually* of the prescription drug benefit for *a prescription drug prescribed to treat an autoimmune disease, hemophilia, or Von Willebrand disease*.
(b) This section does not apply to:
(1) opioids, benzodiazepines, barbiturates, or carisoprodol;
(2) prescription drugs that have a typical treatment period of less than 12 months;
(3) drugs that:
(A) have a boxed warning assigned by the United States Food and Drug Administration for use; and
(B) must have specific provider assessment; or

(4) the use of a drug approved for use by the United States Food and Drug Administration in a manner other than the approved use."

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Benlysta (belimumab) 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).

Belimumab has not been evaluated and is not recommended in patients with severe active lupus nephritis or severe active central nervous system lupus or in combination with other biologic products or cyclophosphamide.

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 prevalence of SLE worldwide is 4 to 250 per 100,000; the disease affects women disproportionately (approximately 90 % of the patients are female). The incidence is most frequent in women aged 15 to 25 years. 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 (Finnish Medical Society, 2007).

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. No new drugs have been approved for SLE in over 50 years. Hence, a lot of hope and excitement has been generated by the development of biological agents designed to eliminate B cells either through direct killing (anti-B cell antibodies such as rituximab) or attrition by inhibition of survival (anti-B-lymphocyte stimulator BLyS [also known as BAFF] agents such as belimumab).

Belimumab is a human IgG1g antibody that is the first of the BLyS-specific inhibitor. It blocks the binding of soluble BLyS, a B-cell survival factor, to its receptors on B cells. Belimumab does not bind B cells directly, but by binding BLyS, belimumab inhibits the survival of B cells, including auto-reactive B cells, and reduces the differentiation of B cells into immunoglobulin-producing plasma cells. Clinical trials of various phases have indicated that belimumab is beneficial for patients with SLE (Furie et al, 2008; Wallace et al, 2009; Jacobi et al, 2010; Navarra et al, 2011).

On March 8, 2011, the U.S. Food and Drug Administration approved belimumab (Benlysta) for the treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus who are

receiving standard therapy, including anti-malarials, corticosteroids, immunosuppressive, and non-steroidal anti-inflammatory drugs. The label for Benlysta includes the following limitations of use: The efficacy of belimumab has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus and has not been studied in combination with other biologics or intravenous cyclophosphamide. Belimumab is administered intravenously over a 1-hourperiod; it should not be administered with live vaccines. The most common side effects associated with the use of belimumab include diarrhea, fever, and nausea. Patients also commonly experienced infusion reactions; thus, pre-treatment with an antihistamine should be considered.

Belimumab is approved at a dosage of 10 mg/kg of body weight to be given at 2-week intervals for the first 3 doses and 4-week intervals thereafter. In several randomized controlled trials examining the effectiveness of belimumab in patients with SLE, the durations of therapy were 52 and 76 weeks (Phung, 2011). In a clinical study of belimumab submitted to the FDA for approval, active SLE disease was defined as a SELENA-SLEDAI (Safety of Estrogens in Lupus Erythematosus: National Assessment- Systemic Lupus Erythematosus Disease Activity Index) score of equal to or greater than 4, and positive autoantibody test results (anti-nuclear antibody [ANA] and/or anti-double- stranded DNA [anti-dsDNA])at screening. Belimumab has also been studied in the treatment of other autoimmune diseases such as lupus nephritis, multiple sclerosis, and rheumatoid arthritis (Aran and Putterman, 2008; Hawker, 2008; Bingham, 2008). Furthermore, belimumab is being considered as one of the novel strategies in immunosuppression following stem cell/solid organ transplantations (Webber et al, 2011). However, in the absence of evidence based on large, randomized, placebo-controlled trials, the role of belimumab for these indications has yet to be established.

On 4/26/2019, The FDA approved Benlysta (belimumab) intravenous (IV)infusion for treatment of children with systemic lupus erythematosus (SLE) – often referred to as simply “lupus” – a chronic disease that causes inflammation and damage to various body tissues and organs.

Belimumab is a B-lymphocyte stimulator protein inhibitor that is thought to decrease the amount of abnormal B cells. It is hypothesized that an abnormal level of B cells is a mechanism of action in lupus. While childhood-onset SLE is rare, when diagnosed, it is generally more active in children and adolescents than adult patients, particularly in how it impacts organs such as the kidneys and central nervous system. As a result of the disease starting early in life, pediatric patients with SLE are at a higher risk for developing increased organ damage and complications from the disease as well as adverse events from the life-long treatments usually required. This is the first time that the FDA has approved a treatment for pediatric patients with SLE. Benlysta has been approved for use in adult patients since 2011.

The approval was based on data from the ‘PLUTO’ study testing over one year the effectiveness and safety as well as the pharmacokinetics (how the drug moves through the body) of a 10-milligram dose of intravenous belimumab plus standard therapy compared with placebo plus standard therapy among children aged 5-11 years. Disease activity improved in 52.8 percent of children treated with Benlysta plus standard therapy compared with 43.6 percent of those who received placebo and standard therapy. Children who were treated with Benlysta IV plus standard therapy also had a lower risk of a severe flare and a longer period of time between severe flares (160 days versus 82 days). The drug’s safety and pharmacokinetic profiles in pediatric patients were consistent with those in adults with SLE.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Benlysta (belimumab) are considered experimental/investigational and therefore, will follow Molina’s Off-Label policy. Contraindications to Benlysta (belimumab) include: anaphylaxis to belimumab, vaccination with live vaccines concurrently with belimumab.

OTHER SPECIAL CONSIDERATIONS:

Informational Note:

-The SLE Responder Index uses the SELENA-SLEDAI score as an objective measure of reduction in global disease activity; the BILAG index to ensure no significant worsening in any specific organ system; and the PGA to ensure that improvements in disease activity are not accompanied by worsening of the subject's condition overall.
-Based on the phase II trial results, a new SLE responder index (SRI) was developed for use in clinical trials. This tries to capture an improvement in disease activity without worsening of the overall condition or the development of significant disease activity in new organ systems. A responder is defined as a ⩾ 4-point reduction in SELENA–SLEDAI score, no new British Isles Lupus Assessment Group (BILAG) A or no >1 new BILAG B domain score and no deterioration from baseline in the Physician's Global Assessment (PGA) by ⩾ 0.3 points [Furie et al. 2009].

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0490	Injection, belimumab,10 mg

AVAILABLE DOSAGE FORMS:
Benlysta SOLR 120MG and 400MG vials
Benlysta Autoinjector & Prefilled syringe 200MG/ML

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Standards, Audit and Guidelines Working Group, The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults, Rheumatology, Volume 57, Issue 1, January 2018, Pages e1–e45

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Age Restrictions Quantity FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q4 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Quantity FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file