Pharmacy Policy Bulletin

Title: Belimumab (Benlysta®)/Voclosporin (Lupkynis™)

Policy #: Rx.01.203

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **belimumab (Benlysta®) and voclosporin (Lupkynis™)** as provided under the member's prescription drug benefit.

Description:

Systemic lupus erythematosus (SLE) is an autoimmune disorder that is very heterogeneous with respect to its severity and the organs affected. Approximately 1.5 million Americans, primarily women of childbearing age, have a form of lupus. SLE represents approximately 70% of all lupus cases. Common clinical manifestations of SLE include pain, extreme fatigue, hair loss, cognitive issues, rashes (often the classic “butterfly rash”), arthritis and arthralgias. More severe clinical manifestations include renal, hematologic, or central nervous system involvement. SLE is often associated with relapses (which can be acute or chronic) and remissions.

Lupus nephritis (LN) is a form of glomerulonephritis that constitutes one of the most severe organ manifestation of systemic lupus erythematosus (SLE). Most patients with SLE who develop LN do so within 5 years of an SLE diagnosis and in many cases, LN is the presenting manifestation resulting in the diagnosis of SLE. Treatment of LN usually involves immunosuppressive therapy, typically with mycophenolate mofetil or cyclophosphamide and with glucocorticoids, although these treatments are not uniformly effective. Within 10 years of an initial SLE diagnosis, 5 to 20% of patients with LN develop end-stage kidney disease.

BLyS, a B-cell survival factor, is overexpressed in patients with systemic lupus erythematosus (SLE) and other autoimmune diseases. Belimumab is an inhibitor that targets B-lymphocyte stimulator (BLyS) protein, which may reduce the number of abnormal B cells by blocking the binding of BLyS to its receptors on B-cells. An intravenous (IV) formulation of belimumab was approved by the FDA in 2011.

A subcutaneous formulation of the medication was approved by the FDA in July 2017.

Benlysta® (belimumab) is indicated for the treatment of:

- Patients aged 5 years and older with active, autoantibody-positive 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. Benlysta has not been studied in combination with other biologics. Use of Benlysta is not recommended in these situations.

Voclosporin is a calcineurin-inhibitor immunosuppressant. Activation of lymphocytes involve an increase in intracellular calcium concentrations that bind to the calcineurin regulatory site and activate calmodulin binding catalytic subunit and through dephosphorylation, activates the transcription factor Nuclear Factor of Activated T-Cell Cytoplasmic (NFATc).

The immunosuppressant activity results in inhibition of lymphocyte proliferation, T-cell cytokine production, and expression of T-cell activation surface antigens.

Lupkynis™ (voclosporin) is indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis

Policy:

Systemic Lupus Erythematosus

INITIAL CRITERIA Belimumab (Benlysta®) is approved when ALL of the following are met:

1. Diagnosis of active systemic lupus erythematosus; and
2. Autoantibody positive (i.e., anti-nuclear antibody [ANA] titer greater than or equal to 1:80 or anti-dsDNA level greater than or equal to 30 IU/mL), antibodies to DNA [Anti-dsDNA], Anti-Smith [Anti-Sm]); and
3. Currently receiving at least one standard of care treatment for active systemic lupus erythematosus (eg, antimalarials [e.g., hydroxychloroquine], corticosteroids, NSAIDs, or immunosuppressants); and
4. Prescribed by or in consultation with a rheumatologist; and
5. Member is 5 years of age or older

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Belimumab (Benlysta®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Lupus Nephritis

INITIAL CRITERIA Belimumab (Benlysta®) is approved when ALL of the following are met:

1. Member has active lupus nephritis confirmed by kidney biopsy; and
2. Member is receiving standard therapy for lupus nephritis (e.g., corticosteroids, immunosuppressants, azathioprine); and
3. Prescribed by or in consultation with a rheumatologist or nephrologist; and
4. Member is 5 years of age or older

INITIAL CRITERIA Voclosporin (Lupkynis™) is approved when ALL of the following are met:

1. Diagnosis of active lupus nephritis; and
2. Member is 18 years of age or older; and
3. Used in combination with mycophenolate mofetil and corticosteroids; and
4. Prescribed by or in consultation with nephrologist or rheumatologist

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Belimumab (Benlysta®) or Voclosporin (Lupkynis™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

Lupkynis™ (Voclosporin)

Malignancies and serious infections: Increased risk for developing malignancies and serious infections with LUPKYNIS or other immunosuppressants that may lead to hospitalization or death.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Anders HJ, Saxena R, Zhao MH, Parodis I, Salmon JE, Mohan C. Lupus nephritis. Nat Rev Dis Primers. 2020 Jan 23;6(1):7. doi: 10.1038/s41572-019-0141-9. PMID: 31974366. Accessed February 01, 2023.

Benlysta® [Package Insert]. Rockville, MD: Human Genome Sciences, Inc.; February 2023. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=2fa3c528-1777-4628-8a55-a69dae2381a3&type=display. Accessed April 17, 2023.

Gladman DD, Pisetski DS, Curtis MR. Clinical manifestations of systemic lupus erythematosus in adults. UpToDate. Waltham, MA: UpToDate Inc. https://www-uptodate-com.proxy1.lib.tju.edu/contents/overview-of-the-clinical-manifestations-of-systemic-lupus-erythematosus-in-adults?source=search_result&search=lupus&selectedTitle=1~150. Accessed on April 17, 2023.

Lupus facts and statistics. Lupus Foundation of America Web Site. https://resources.lupus.org/entry/facts-and-statistics. Published 2017. Accessed April 17, 2023.

Lupkynis™ (voclosporin) [prescribing information]. Rockville, MD: Aurinia Pharma U.S., Inc.; January 2021. Available from: https://d1io3yog0oux5.cloudfront.net/auriniapharma/files/pages/lupkynis-prescribing-information/FPI-0011+Approved+USPI++MG.pdf. Accessed April 17, 2023.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Benlysta®	belimumab
Lupkynis™	voclosporin

Cross References:

Rx.01.33 Off-Label Use

Rx.01.76 Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit

Policy Version Number:	9.00
P&T Approval Date:	March 16, 2023
Policy Effective Date:	July 01, 2023
Next Required Review Date:	March 16, 2024