



Louisiana

voclosporin (Lupkynis™)

Policy # 00748

Original Effective Date: 06/14/2021

Current Effective Date: 06/14/2021

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.

Note: belimumab (Benlysta®) is addressed separately in medical policy 00295.

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 voclosporin (Lupkynis™)† for the treatment of lupus nephritis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of voclosporin (Lupkynis) will be considered when all of the following patient selection criteria are met:

- Initial (6 months)
 - Patient has a diagnosis of systemic lupus erythematosus that is autoantibody positive (ANA [anti-nuclear antibody] or anti-double-stranded deoxyribonucleic acid [anti-dsDNA]); AND
 - Patient has a diagnosis of active lupus nephritis; AND
 - Diagnosis is confirmed by kidney biopsy demonstrating Class III, IV, or V (alone or in combination) lupus nephritis; AND
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - Patient is ≥18 years of age; AND
 - Patient's eGFR is >45 mL/min/1.73 m²; AND
 - Lupkynis will be used in combination with mycophenolate mofetil plus a systemic corticosteroid; AND
 - Lupkynis will NOT be used in combination with cyclophosphamide.

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- Continuation
 - Patient has received an initial authorization for Lupkynis; AND
 - Patient has demonstrated a beneficial response to Lupkynis for the treatment of active lupus nephritis (e.g., improvement in urine protein:creatinine ratio or no confirmed decrease from baseline in eGFR of $\geq 20\%$); AND
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - Lupkynis will continue to be used in combination with mycophenolate mofetil plus a systemic corticosteroid; AND
 - Lupkynis will NOT be used in combination with cyclophosphamide.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of voclosporin (Lupkynis) when the diagnosis is not confirmed by a kidney biopsy demonstrating Class III, IV, or V lupus nephritis to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of voclosporin (Lupkynis) when the patient has not demonstrated a beneficial response to the drug to be **not medically necessary.****

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 voclosporin (Lupkynis) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Lupkynis is a calcineurin inhibitor indicated in combination with mycophenolate mofetil (MMF) and corticosteroids for the treatment of lupus nephritis. It is an immunosuppressant that leads to inhibition of lymphocyte proliferation, T-cell cytokine production, and expression of T-cell

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activation surface antigens to prevent disease progression in patients with lupus nephritis. The recommended starting dosage of Lupkynis is 23.7 mg twice daily, in combination with MMF and corticosteroids. Capsules should be swallowed whole on an empty stomach on a 12-hour schedule (minimum of 8 hours between doses). If the patient does not experience therapeutic benefit by 24 weeks of therapy, consideration should be given to discontinuing Lupkynis.

Lupus nephritis (LN) is a renal complication of systemic lupus erythematosus (SLE) that is characterized by an inflammatory response to immune complexes in the kidney. It occurs in approximately 40% of patients with SLE and it may be diagnosed prior to SLE. Patients with SLE should be screened regularly for LN via urinalysis and assessment of kidney function. When these screenings are abnormal, kidney biopsy can confirm the diagnosis and determine the classification of disease. Treatment of LN may include corticosteroids, cyclophosphamide, mycophenolate mofetil, and hydroxychloroquine. Response to treatment is often slow and relapses are reported in nearly 50% of patients. LN may worsen over time, with 10-30% of patients developing kidney failure requiring dialysis or kidney transplantation. New treatment options for LN include belimumab (Benlysta®)‡ and Lupkynis. Clinical practice guidelines have not yet been updated to include these therapies, but they may provide an additional treatment option in patients who cannot tolerate or do not respond to standard therapy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Lupkynis was approved in January 2021 for use in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. 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.

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The safety and efficacy of Lupkynis were investigated in a 52-week randomized, double-blind, placebo-controlled trial in patients with a diagnosis of systemic lupus erythematosus and with biopsy-proven active Class III or IV LN (alone or in combination with Class V LN) or Class V LN. Patients with Class III or IV LN (alone or in combination with Class V LN) were required to have a urine protein to creatinine (UPCR) ratio of ≥ 1.5 mg/mg; patients with Class V LN were required to have a UPCR of ≥ 2 mg/mg.

A total of 357 patients with LN were randomized in a 1:1 ratio to receive either Lupkynis 23.7 mg twice daily or placebo. Patients in both arms received background treatment with MMF and corticosteroids and were prohibited from using other immunosuppressants and from changing/commencing angiotensin II receptor blockers or angiotensin converting enzyme inhibitors. Patients with a baseline eGFR ≤ 45 mL/min/1.73 m² were not enrolled in the study. Dosage of Lupkynis was adjusted based on eGFR and blood pressure in a pre-defined dosage adjustment protocol. The mean (SD) daily dose in the study was 41.3 (± 9.7) mg/day.

The primary efficacy endpoint was the proportion of patients achieving complete renal response at Week 52. Complete renal response was defined as both a UPCR of ≤ 0.5 mg/mg and an eGFR ≥ 60 mL/min/1.73m² or no confirmed decrease from baseline in eGFR of $>20\%$ or no treatment or disease-related eGFR-associated event at the time of assessment. Additionally, patients must not have received more than 10 mg prednisone for ≥ 3 consecutive days or for ≥ 7 days in total during Weeks 44-52 in order to be considered a responder. A higher proportion of patients in the Lupkynis arm than the placebo arm achieved complete renal response at week 52 (40.8% of the Lupkynis patients vs 22.5% of the placebo patients, $p < 0.001$).

References

1. Lupkynis [package insert]. Aurinia Pharma U.S., Inc. Rockville, MD. Updated January 2021.
2. Lupus Nephritis: Diagnosis and Classification. UpToDate. Updated March 2021.
3. Lupkynis Drug Evaluation. Express Scripts. Updated February 2021.

Policy History

Original Effective Date: 06/14/2021

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05/06/2021 Medical Policy Committee review

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05/12/2021 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 05/2022

*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.

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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: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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.

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