09-J3000-96

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Reviewed:09/11/24

Revised:10/15/24

Subject: Voclosporin (Lupkynis)

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DESCRIPTION:

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of an unknown cause that can affect multiple systems including the musculoskeletal, renal, pulmonary, gastrointestinal, and hematologic systems. The etiology of SLE is not completely understood; however, many of the clinical manifestations are mediated directly or indirectly by antibody formation and the creation of immune complexes.

Diagnosis of SLE is based on classification criteria developed by the American Rheumatism Association now the American College of Rheumatology [ACR]) that uses history, physical examination, and laboratory data for diagnosis. Several disease activity instruments are used in clinical trials. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is comprised of 24 clinical and laboratory manifestations of SLE that are scored based on presence or absence in the previous 10 days. Organ involvement is weighted, and the final score can range from 0-105. A SLEDAI score of 6 or more has been shown to be consistent with active disease requiring therapy. The SLEDAI was modified in the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) trial; this modification, known as SELENA-SLEDAI added clarity to some of the definition of activity in the individual items but did not change the basic scoring system. A clinically meaningful difference has been reported to be an improvement of 7 points or a worsening of 8 points. The British Isles Lupus Assessment Group (BILAG) is an organ specific, 86 question assessment based on the healthcare provider's intention to treat. The assessor scores organ manifestations as improve (=1), same (=2), worse (=3), or new (=4) over the last month.

All patients with SLE should be evaluated for lupus nephritis (LN) at the time of initial diagnosis and then at least annually or upon an SLE flare. Proteinuria is usually the first sign leading to an LN diagnosis; patients may also exhibit hypertension, hematuria, or a decrease in kidney function (i.e. decreased eGFR). A kidney biopsy is used to confirm a diagnosis and stage the disease according to the

classification revised by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) in 2003, as follows:

- Class I – Minimal mesangial lupus nephritis
- Class II – Mesangial proliferative lupus nephritis
- Class III – Focal lupus nephritis (active and chronic; proliferative and sclerosing)
- Class IV – Diffuse lupus nephritis (active and chronic; proliferative and sclerosing; segmental and global)
- Class V – Membranous lupus nephritis
- Class VI – Advanced sclerosis lupus nephritis

Voclosporin (Lupkynis), a calcineurin inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in January 2021 for the treatment of adult patients with active lupus nephritis. Voclosporin inhibits the activation of T cells and can decrease the production of proinflammatory cytokines. It is structurally similar to cyclosporine A, differing in only one amino acid, which increases its potency and rate of elimination. Prior to approval of voclosporin, belimumab was the only approved drug for treatment of LN

The safety and efficacy of voclosporin were evaluated in a randomized controlled trial of patients with systemic lupus erythematosus and biopsy confirmed lupus nephritis (N=357; median age 31 years, 88% women). Patients were randomized to treatment with voclosporin (23.7 mg twice daily with adjustments as needed) in combination with mycophenolate mofetil (2 g/day target dose) and corticosteroids (IV methylprednisolone induction with oral taper to target prednisone dose of 2.5 mg/day) or placebo in combination with mycophenolate mofetil and corticosteroids. The primary endpoint was patients who achieved a complete renal response, defined as urine protein to creatinine ratio of 0.5 mg/mg or less AND estimated GFR (eGFR) of at least 60 mL/min/1.73 m(2), no decrease in baseline eGFR of greater than 20%, OR no treatment- or disease-related eGFR associated event (e.g., blood creatinine increased, creatinine renal clearance decreased, glomerular filtration rate decreased, serum creatinine increased, renal impairment, renal failure, or renal failure acute). Patients must not have received more than 10 mg prednisone for 3 or greater consecutive days or for 7 or greater days in total during weeks 44 through 52 to be considered a responder. Patients who received rescue medication or withdrew from the study were considered non-responders.

Treatment with voclosporin resulted in significantly higher proportion of patients achieving a complete renal response at both 24 weeks (32.4% vs 19.7%; OR 2.2, 95% CI 1.3 to 3.7) and 52 weeks (40.8% vs 22.5%; OR 2.7, 95% CI 1.6 to 4.3) compared to placebo in combination with mycophenolate mofetil and corticosteroids. The most common adverse reactions reported in clinical trials ≥10% included: decreased GFR, hypertension, diarrhea, headache, anemia, cough, and urinary tract infection. Decreases in GFR were mostly observed during the first 3 months of treatment with voclosporin and resolved with dosing modification (71%) or discontinuation (14%). Overall, hypertension was reported in 66 patients receiving voclosporin, but serious hypertension was limited to just 7 patients. Voclosporin does not appear to exhibit the cardiovascular and metabolic adverse effects seen in other CNIs, such as tacrolimus.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of voclosporin (Lupkynis) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Indication for use is lupus nephritis
2. Member has biopsy-proven lupus nephritis of International Society of Nephrology and Renal Pathology Society class III (focal lupus nephritis) or IV (diffuse lupus nephritis) with or without coexisting class V (membranous lupus nephritis), or pure class V lupus nephritis – laboratory documentation must be provided
3. Use will be in combination with mycophenolate and a corticosteroid (unless contraindicated or not tolerated)
4. Voclosporin is prescribed by or in consultation with a nephrologist or rheumatologist
5. Member is 18 years of age or older
6. Dose does not exceed 23.7 mg twice daily

Approval duration:6 months

Continuation of voclosporin (Lupkynis) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another healthplan in the past two years for treatment of active lupus nephritis, **OR** the member has previously met all indication-specific criteria
2. Member has achieved a beneficial response to treatment with voclosporin
3. Voclosporin is prescribed by or in consultation with a nephrologist or rheumatologist
4. Member is 18 years of age or older
5. Dose does not exceed 23.7 mg twice daily

Approval duration:1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 23.7 mg orally, twice a day.

Dose Adjustments

- If eGFR <60 mL/min/1.73 m2 and reduced from baseline by >20% and <30%, reduce the dose by 7.9 mg twice a day. Re-assess eGFR within two weeks; if eGFR is still reduced from baseline by >20%, reduce the dose again by 7.9 mg twice a day.
- If eGFR <60 mL/min/1.73 m2 and reduced from baseline by ≥30%, discontinue LUPKYNIS. Re-assess eGFR within two weeks; consider re-initiating LUPKYNIS at a lower dose (7.9 mg twice a day) only if eGFR has returned to ≥80% of baseline.
- For patients that had a decrease in dose due to eGFR, consider increasing the dose by 7.9 mg twice a day for each eGFR measurement that is ≥80% of baseline; do not exceed the starting dose.
- Patients with severe renal impairment: the recommended dose is 15.8 mg twice daily
- Patients with mild and moderate hepatic impairment: the recommended dose is 15.8 mg twice daily

Drug Availability

- Capsules: 7.9 mg

PRECAUTIONS:

Boxed Warning

- Increased risk for developing malignancies and serious infections that may lead to hospitalization or death

Contraindications

- Patients concomitantly using strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)
- Known serious or severe hypersensitivity reaction

Precautions/Warnings

- Nephrotoxicity (acute and/or chronic): May occur due to concomitant nephrotoxic drugs. Monitor renal function; consider dosage reduction
- Hypertension: May require antihypertensive therapy; monitor relevant drug interactions
- Neurotoxicity: Including risk of posterior reversible encephalopathy syndrome (PRES); monitor for neurologic abnormalities; reduce dosage or discontinue
- Hyperkalemia: Risk may be increased with other agents associated with hyperkalemia; monitor serum potassium levels.
- QT Prolongation: Consider obtaining electrocardiograms and monitoring electrolytes in patients at high risk.

- Immunizations: Avoid live vaccines.
- Pure Red Cell Aplasia: Consider discontinuation

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non chemotherapeutic, nos

ICD-10 Diagnosis Codes That Support Medical Necessity

M32.14	Glomerular disease in systemic lupus erythematosus

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT.**

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Systemic lupus erythematosus is a systemic autoimmune disease than can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage.

RELATED GUIDELINES:

Belimumab (Benlysta) Injection,09-J1000-35

OTHER:

None

REFERENCES:

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2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 9/1/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 9/1/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 9/1/24].
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/11/24.

GUIDELINE UPDATE INFORMATION:

06/15/21	New Medical Coverage Guideline.
07/15/22	Revision to position statement,
10/15/23	Review and revision to guideline, consisting of updating position statement and references.
10/15/24	Review and revision to guideline, consisting of updating position statement and references.