voclosporin (Lupkynis™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO232

Description

Voclosporin (Lupkynis) is an orally administered calcineurin-inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
voclosporin (Lupkynis)	7.9 mg capsules	Lupus Nephritis	180 capsules/30 days

Initial Evaluation

I. **Voclosporin (Lupkynis)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a rheumatologist or nephrologist; **AND**
   C. **Not** used in combination with biologic(s) [e.g., rituximab (Rituxan), abatacept (Orencia), belimumab (Benlysta)]; **AND**
   D. A confirmed positive autoantibody test [antinuclear (ANA) and/or anti-double-stranded DNA (anti-ds-DNA)]; **AND**
   E. A diagnosis of **Lupus Nephritis (LN); AND**
      1. Biopsy indicating class III (focal), IV (diffuse), or V (membranous) LN; **AND**
      2. Biopsy shows active lesions; **OR**
         i. Biopsy shows active AND chronic lesions; **AND**
      3. Provider attestation indicating medication will be given in combination with mycophenolate (CellCept) for induction and maintenance; **AND**
      4. Provider attestation the member will continue to receive standard therapy (e.g., antimalarials, NSAIDs, immunosuppressives, corticosteroids), unless all are contraindicated or not tolerated; **AND**
      5. Treatment with belimumab (Benlysta) has been ineffective, contraindicated, or not tolerated.

II. Voclosporin (Lupkynis) is considered investigational when used for all other conditions, including but not limited to:
   A. Systemic Lupus Erythematosus (SLE) with absence of lupus nephritis
   B. Severe active central nervous system lupus
   C. Renal transplantation

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. A diagnosis of **Lupus Nephritis (LN)**; **AND**
IV. Member has exhibited improvement or stability of disease symptoms (e.g., reduction in proteinuria, improved/stable serum creatinine, reduction in urinary sediment); **AND**
V. **Not** used in combination with other biologic(s) [e.g., rituximab (Rituxan), abatacept (Orencia), belimumab (Benlysta)]; **AND**
VI. Member will continue to receive standard therapy (e.g., antimalarials, NSAIDs, immunosuppressives, corticosteroids), unless all are contraindicated or not tolerated.

Supporting Evidence

I. LN is a kidney disease that develops in about 40% of patients with SLE. Approximately 10% of patients develop end stage renal disease (ESRD). Kidney failure, dialysis, and kidney transplants are common in this patient population. Patients with SLE with any sign of kidney involvement (glomerular hematuria and/or cellular casts, proteinuria >0.5 g/24 hours [or spot urine protein-to-creatine ratio (UPCR) >500 mg/g], unexplained decrease in glomerular filtration rate (GFR)) are candidates for kidney biopsy to confirm diagnosis/class of LN, which then guides treatment.
   - Class I (minimal mesangial) and Class II (mesangial proliferative): Usually does not need specific immunosuppressive therapy but may be prone to histological transformation to more aggressive disease on repeat biopsy.
   - Class III (focal) and Class IV (diffuse): active, chronic classifications at high risk of developing ESRD, thus are targeted populations for immunosuppressive therapies.
   - Class V (membranous): presents similar to nephrotic syndrome with subendothelial deposits. Patients with Class III or IV disease may have these deposits and can be classified

as Class III or IV in combination with Class V, can also present as pure Class V. Immunosuppressive therapy is indicated.

- Class VI (advanced sclerosing): patients with sclerosing lesions; generally, do not respond to immunosuppressive therapy; treatment requires dialysis and/or kidney transplant.

II. European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) 2019 and 2012 American College of Rheumatology guidelines on LN recommend immunosuppressive therapy for LN starting with an induction phase to achieve a renal response, which is recommended for the first six months of treatment, followed by maintenance therapy. Initial (induction) treatment is recommended with mycophenolate mofetil (MMF) or low-dose intravenous cyclophosphamide, both combined with glucocorticoids (pulses of IV methylprednisolone, then oral prednisone). Subsequent long-term maintenance treatment with MMF or azathioprine should follow, with no, or low-dose (< 7.5 mg/day), glucocorticoids. If a patient fails to respond to the first six months of induction therapy, guidelines suggest switching the immunosuppressive agent in combination with glucocorticoid pulse. Alternatively, calcineurin inhibitors (tacrolimus or cyclosporine) can be used as monotherapy or in combination with MMF as induction/maintenance therapy particularly in refractory cases.

III. Guidelines recommend patients with LN be treated with hydroxychloroquine or an equivalent antimalarial, unless contraindicated, and adjunctive therapies be added to manage LN and attenuate complications of the disease.

IV. The safety and efficacy of voclosporin (Lupkynis) in pediatric patients has not been established.

V. The safety and efficacy of voclosporin (Lupkynis) in combination with biologic therapies [e.g., rituximab (Rituxan), abatacept (Orencia), belimumab (Benlysta)] has not been evaluated.

VI. Per the package insert, use of voclosporin (Lupkynis) is not recommend in patients with a baseline eGFR less than or equal to 45 mL/min/1.73m^2 unless the benefit exceeds the risk, as these patients may be at increased risk for acute and/or chronic nephrotoxicity.

VII. Policy is specific to list MMF as the induction/maintenance therapy due to potential safety concerns of additive toxic effects that may occur when co-administering voclosporin (Lupkynis) and cyclophosphamide. Per the package insert, use of voclosporin (Lupkynis) in combination with cyclophosphamide has not been established and is not recommended. The FDA review of voclosporin (Lupkynis) further adds “given the adverse reaction profile of cyclophosphamide and the lack of efficacy data for voclosporin in combination with cyclophosphamide, the review team concluded that there is reasonable concern about the benefit-risk profile in this situation, thus necessitating this limitation of use”.

VIII. Voclosporin (Lupkynis) was evaluated as an adjunct to standard therapy in a Phase 3, randomized, double-blind, placebo-controlled, 52-week trial in adults (n=357) with biopsy proven LN. The primary efficacy outcome was complete renal response at week 52, defined as a UPCR < 0.5, eGFR ≥ 60 ml/min per 1.73 m2 or a decline in no more than 20% from baseline, no rescue therapy, and a sustained dose ≤than 10 mg of prednisone. The primary endpoint was met

with 73 patients (40.8%) in the voclosporin (Lupkynis) arm achieving renal response compared to 40 patients (22.5%) in the placebo arm (odds ratio 2.7; 95% CI: 1.6-4.3; P<0.001).

- All patients included in the trial were on background therapy with mycophenolate mofetil plus corticosteroids. Patients were 18 years of age and older with antibody positive SLE, ratio of urinary protein to creatinine (UPCR) of 2 or more (average patient had a baseline UPCR of 4), biopsy proven LN 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 within last 6 months. All patients also had biopsy specimens showing active lesions or active and chronic lesions.

IX. As of date there are no head to head trials comparing voclosporin (Lupkynis) to belimumab (Benlysta). Additionally, guidelines do not have recommendations around preferring either agent in the setting of LN. However, given the potential for chronic calcineurin inhibitor-related nephrotoxicity, especially relevant to this patient population with underlying renal disease, and the insufficient long-term controlled safety data beyond one year, the plan requires trial of or contraindication to belimumab (Benlysta) prior to use of voclosporin (Lupkynis).

Investigational or Not Medically Necessary Uses

I. Voclosporin (Lupkynis) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Systemic Lupus Erythematosus (SLE) in absence of lupus nephritis (LN)
   B. Severe active central nervous system lupus
   C. Renal Transplantation

References

1. Lupkynis [Prescribing Information]. Aurinia Pharma U.S., Inc.: Rockville, MD. January 2021.
2. Almaani S, Meara A, Rovin BH. Update on lupus nephritis. Clin J Am Soc Nephrol. 2017;12(5):825-835.
3. Lim SS, Bayakly AR, Helmick CG, Gordon C, Easley KA, Drenkard C. The incidence and prevalence of systemic lupus erythematosus, 2002–2004: The Georgia Lupus Registry. Arthritis Rheumatol 2014;66:357–68.
4. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. Arthritis Care Res (Hoboken). 2012;64(6):797-808.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. Kidney inter., Suppl.2012;2: 139–27.
6. Fanouriakis A, Kostopoulou M, Cheema K, et al. 2019 update of the joint European league against rheumatism and European renal association-European dialysis and transplant association (Eular/era-edta) recommendations for the management of lupus nephritis. Ann Rheum Dis. 2020;79(6):713-723.
7. FDA Center for Drug Evaluation and Research. Application number: 213716Orig1s000. Multi-Discipline review. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/213716Orig1s000MultidisciplineR.pdf

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2021