Lupkynis (voclosporin)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Lupkynis drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies in the treatment of lupus nephritis (LN).

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the patient has no exclusions to the prescribed therapy.

FDA-Approved Indications

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

Limitations of Use

Safety and efficacy of Lupkynis have not been established in combination with cyclophosphamide. Use of Lupkynis is not recommended in this situation.

POLICY

Exclusions

Coverage will not be provided for members using Lupkynis in combination with cyclophosphamide.

Criteria for Initial Approval

A. Lupkynis (voclosporin) may be considered **medically necessary** for the treatment of lupus nephritis (LN) when all of the following criteria are met:

1. Prior to initiating therapy, the member is positive for autoantibodies relevant to systemic lupus erythematosus (SLE).
2. Member has clinically active lupus renal disease and is receiving background therapy with mycophenolate mofetil (MMF) with corticosteroids.
3. The medication is being prescribed by, or in consultation with, a nephrologist or rheumatologist.
4. Member must have an eGFR ≥ 45ml/min per 1.73 m^2

Approval will be for **12 months.**

Continuation of Therapy

A. The continued treatment with Lupkynis (voclosporin) may be considered **medically necessary** for the treatment of lupus nephritis (LN) in patients who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Approval will be for **12 months.**

Lupkynis is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

Medication Name	Quantity Limit	FDA-recommended dosing
Lupkynis 7.9 mg capsules	180 capsules per 30 days	Recommended dose: 23.7mg twice a day Dose Reduction: • If eGFR <60 mL/min/1.73 m^2 and reduced from baseline by >20% and <30%, reduce the dose by 7.9 mg twice a day. • 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

CLINICAL RATIONALE

Background

Lupus nephritis (LN) is an inflammation of the kidneys that is caused by systemic lupus erythematosus (SLE), a chronic, autoimmune disease that leads to multisystem inflammation and organ injury and most commonly affects women of child-bearing age. Lupus nephritis is one of the most serious complications of SLE and occurs when the immune system mistakenly attacks the kidneys, leading to inflammation and possibly to organ damage. LN most often develops within 5 years from when lupus symptoms first appear. Symptoms include weight gain, swelling, increase in urination (especially at night), blood and foamy appearance in the urine, and high blood pressure. If untreated, kidney failure can occur and may require dialysis or a kidney transplant. It is estimated that approximately 50% of patients with SLE will develop lupus nephritis and 10% to 30% of patients with LN will develop end-stage kidney disease.

Lupkynis is a calcineurin-inhibitor immunosuppressant and the first oral treatment for lupus nephritis and second agent approved for LN, following Benlysta's expanded indication to included treatment of active LN in December 2020. Benlysta is a monoclonal antibody given by IV infusion or subcutaneous injection.

Efficacy

The FDA approved Lupkynis based on evidence from two randomized, controlled, double-blinded clinical trials: Aura-LV (Phase 2) and AURORA (Phase 3). The studies included 533 adults with lupus nephritis who were randomized to receive 23.7 mg of Lupkynis twice daily or placebo in addition to standard of care (mycophenolate mofetil plus low-dose glucocorticoids). In the AURORA study, 357 participants were enrolled and randomized in a 1:1 ratio to receive either Lupkynis 23.7 mg twice daily or placebo in addition to mycophenolate mofetil (MMF) at a dose of 2gm/day and tapered low-dose oral corticosteroids. The dosage of Lupkynis was adjusted based on eGFR and blood pressure in a pre-defined dosage adjustment protocol. Patients with a baseline eGFR ≤ 45ml/min/1.73 m^2 were excluded from the study. The primary efficacy endpoint was the proportion of patients achieving complete renal response at week 52. Complete renal response was defined as follows (both must be met): Urine protein creatinine ratio (UPCR) ≤ 0.5mg/mg and eGFR ≥ 60mL/min/1.73 m^2 or no confirmed decrease from baseline in eGFR of ≥ 20%. AURORA met its primary endpoint with 40.8% of patients in the treatment group showing complete renal response vs 22.5% in the placebo group. In addition, the treatment group was favored in every secondary endpoint: renal response at Week 24, partial renal response at Week 24, Week 52, time to UPCR ≤0.5 mg/mg, and time to 50% reduction in UPCR. The 104-week double-blind AURORA continuation study (AURORA 2) is currently ongoing and is expected to provide longer term safety and efficacy data.

Safety

Adverse events were similar in both groups (Lupkynis 20.8% vs. placebo 21.3%) in AURORA with infection being most commonly reported (Lupkynis 10.1% vs placebo 11.2%). The most common AEs occurring in ≥10% treated with Lupkynis in both studies included: decrease in 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 dosage modification (71%) or discontinuation (14%). Patients who received Lupkynis showed no significant decrease at week 52 in eGFR or increase in blood pressure, lipids, or glucose. Voclosporin does not appear to exhibit the cardiovascular and metabolic adverse effects seen in other CNIs, such as tacrolimus.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

- Lupkynis [package insert]. Victoria, Canada: Aurinia Pharmaceuticals Inc.; January 2021.
- Anders H, Saxena R, Zhao M et al. Lupus nephritis. Nat Rev Dis Primers. 2020; 6(7):1-25.
- Arriens C, Polyakova S, Adzerikho I et al. AURORA phase 3 study demonstrates voclosporin statistical superiority over standard of care in lupus nephritis (LN). Ann Rheum Dis. 2020; 79:172-73. URL:https://ard.bmj.com/content/79/Suppl_1/172.2?int_source=trendmd&int_medium=cpc&int_campaign=usage-042019 Available from Internet. Accessed 2021 January 7.
- Benlysta prescribing information. Research Triangle Park, NC: GlaxoSmithKline; 2020 December.
- Rovin BH, Solomons N, Pendergraft WF 3rd, Dooley MA, Tumlin J, Romero-Diaz J, Lysenko L, Navarra SV, Huizinga RB; AURA-LV Study Group. A randomized, controlled double-blind study comparing the efficacy and safety of dose-ranging voclosporin with placebo in achieving remission in patients with active lupus nephritis. Kidney Int. 2019 Jan;95(1):219-231
- 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):713-23.

- Food and Drug Administration (FDA). Drugs@FDA. URL: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Available from Internet. Accessed 2021 January 27.
- Furie R, Rovin BH, Houssiau F et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. N Engl J Med. 2020; 383(12):1117-28.
- Hahn BH, McMahon MA, Wilkinson A et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. Arthritis Care Res. 2012; 64(6):797-808.
- Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Glomerulonephritis. Kidney Int. 2012; 2(2):221-32.
- Morales E, Galindo M, Praga M. Update on lupus nephritis: looking for a new vision. Nephron. 2021; 145(1):1-13.
- National Institute of Health and Care Excellence (NICE). URL: http://www.nice.org.uk. Available from Internet. Accessed 2021 February 1.
- National Institutes of Health U.S. National Library of Medicine. Systemic lupus erythematosus. 2020. URL: https://medlineplus.gov/genetics/condition/systemic-lupus-erythematosus/. Available from Internet. Accessed 2021 January 27.
- Parikh S, Almaani S, Brodsky S et al. Update on lupus nephritis: core curriculum 2020. Am J Kidney Dis. 2020; 76(2):265-81.
- Rovin BH, Caster DJ, Cattran DC et al. Management and treatment of glomerular diseases (part 2): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2019; 95(2):281-95.
- RxPipeline. Available with subscription at https://www.caremark.com/wps/portal/client. Accessed 2021 January 27.
- Teng YO, Parikh SV, Saxena A, et al. O11 AURORA phase 3 study demonstrates voclosporin statistical superiority over standard of care in lupus nephritis (LN) Lupus Science & Medicine. 2020; 7: https://lupus.bmj.com/content/7/Suppl_1/A14.1?int_source=trendmd&int_medium=cpc&int_campaign=usage-042019 Available from Internet. Accessed 2021 January 7.
- Tice JA, Agboola F, Herron-Smith S et al. Belimumab and voclosporin for lupus nephritis: effectiveness and value. Draft evidence report. Published January 2021. URL: https://icer.org/wp-content/uploads/2020/11/ICER_Lupus-Nephritis_Draft-Evidence-Report_012221.pdf. Available from Internet. Accessed 2021 January 27.
- Weening JJ, D'Agati VD, Schwartz MM et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. Kidney International. 2004; 65(2): 521-530.

*Some content reprinted from CVSHealth

POLICY HISTORY

Policy #: 05.04.34
Original Effective Date: June 4, 2021
Reviewed: April 2022
Revised:
Current Effective Date: June 4, 2021