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 $\geq 45$ml/min per $1.73 \text{ m}^2$

**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**

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Quantity Limit</th>
<th>FDA-recommended dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lupkynis 7.9 mg capsules</td>
<td>180 capsules per 30 days</td>
<td>Recommended dose: 23.7mg twice a day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dose Reduction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If eGFR &lt;60 mL/min/1.73 m$^2$ and reduced from baseline by $&gt;20%$ and $&lt;30%$, reduce the dose by 7.9 mg twice a day.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 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 $\geq 80%$ of baseline; do not exceed the starting dose</td>
</tr>
</tbody>
</table>

**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 m² 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 m² 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**


*Some content reprinted from CVSHealth

<table>
<thead>
<tr>
<th>POLICY HISTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Policy #:</strong></td>
</tr>
<tr>
<td><strong>Original Effective Date:</strong></td>
</tr>
<tr>
<td><strong>Reviewed:</strong></td>
</tr>
<tr>
<td><strong>Revised:</strong></td>
</tr>
<tr>
<td><strong>Current Effective Date:</strong></td>
</tr>
</tbody>
</table>