Clinical Policy: Voclosporin (Lupkynis)

Reference Number: CP.PHAR.504
Effective Date: 01.22.21
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Voclosporin (Lupkynis™) is a calcineurin inhibitor.

FDA Approved Indication(s)

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

Limitation(s) 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/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Lupkynis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Lupus Nephritis (must meet all)**:**

1. Diagnosis of LN with kidney biopsy confirming one of the following (a, b, or c):
   a. LN class III (focal);
   b. LN class IV (diffuse segmental or global);
   c. LN class V (membranous);
2. Prescribed by or in consultation with a nephrologist or rheumatologist;
3. Age ≥ 18 years;
4. Member has a confirmed diagnosis of systemic lupus erythematosus;
5. Inadequate response to dual therapy with systemic corticosteroid (e.g., prednisone, methylprednisolone) and one of the following (a or b):
   a. Mycophenolate and cyclophosphamide, each for 6 months, unless clinically significant adverse effects are experienced;
   b. Member has contraindication to mycophenolate and cyclophosphamide, and inadequate response to azathioprine for 6 months, unless contraindicated or clinically significant adverse effects are experienced;
6. Evidence of one of the following (a or b):
   a. Urine protein/creatinine ratio (UPCR) ≥ 1.5 mg/mg;
   b. UPCR ≥ 2 mg/mg and LN Class V;
7. Prescribed in combination with a background immunosuppressive therapy (e.g., mycophenolate, azathioprine) and a systemic corticosteroid (e.g., prednisone);
8. Dose does not exceed 47.4 mg (6 capsules) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Lupus Nephritis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):
   a. Reduced level of proteinuria measured by UPCR ≤ 0.5 mg/mg from baseline with low dose steroids (e.g., prednisone);
   b. No reduction from baseline in eGFR of greater than 20% with low dose steroids (e.g., prednisone);
   c. eGFR ≥ 60 ml/min/1.73 m^2 with low dose steroids (e.g., prednisone);
3. Prescribed in combination with a background immunosuppressive therapy (e.g., mycophenolate, azathioprine) and a systemic corticosteroid (e.g., prednisone);
4. If request is for a dose increase, new dose does not exceed 47.4 mg (6 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
LN: lupus nephritis
UPCR: urine protein/creatinine ratio

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
mycophenolate mofetil (MMF) (off-label)	Induction: 2 to 3 g/ per day PO plus methylprednisolone IV for 3 days then prednisone tapered is recommended for class III/IV disease. For class V disease without proliferative changes but with nephrotic range proteinuria, 2 to 3 g per day PO plus prednisone 0.5 mg/kg/day is recommended.	3 g per day PO or IV
azathioprine (off-label)	Maintenance: 2 mg/kg/day PO +/- low dose daily glucocorticoids	2 mg/kg per day
methylprednisolone	Induction: 500 to 1,000 mg per day IV for 3 doses, followed by 0.5 to 1 mg/kg/day PO prednisone which is then tapered after a few weeks to lowest effective dose that controls the disease. Proteinuria treatment: 4 to 48 mg PO per day administered in 4 divided doses or 10 to 40 mg IV or IM	Varies
prednisone	Maintenance: 40 mg/day to 80 mg/day PO until urine is protein-free; slowly taper as indicated. LN treatment: 0.5 to 1 mg/kg/day PO after induction therapy with methylprednisolone and other induction drugs. Taper dose as directed.	Varies
prednisolone	Proteinuria treatment: 40 mg/day to 80 mg/day PO until urine is protein-free, then slowly taper as indicated.	Varies
triamcinolone	Proteinuria treatment: Initially, 60 mg IM, titrate to patient response and relief duration. Usual dose range is 40 to 80 mg IM per day.	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients concomitantly using strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)
  - Known serious or severe hypersensitivity reaction to Lupkynis or any of its excipients

- Boxed warning(s): malignancies and serious infection

Appendix D: General information

- *2019 update of the EULAR recommendations for the management of systemic lupus erythematosus – renal:* Mycophenolate (1a/A**)** or low-dose intravenous cyclophosphamide (2a/B**)** are recommended as initial (induction) treatment, as they have the best efficacy/toxicity ratio. For maintenance therapy mycophenolate (1a/A**)** or azathioprine (1a/A**)** should be used. Mycophenolate may be combined with low dose of a calcineurin inhibitor in severe nephrotic syndrome **(**2b/C**)** or incomplete renal response **(**4/C**),** in the absence of uncontrolled hypertension, high chronicity index at kidney biopsy and/or reduced GFR.
    - Tacrolimus is not a recommended induction agent, and consensus was not reached regarding the use of calcineurin inhibitors in patients whose nephritis fails to improve or worsens after 6 months of induction with cyclophosphamide, mycophenolate mofetil, or both. Tacrolimus may be a consideration if nephritis is worsening in patients treated for 3 months with glucocorticoids plus either cyclophosphamide or mycophenolate mofetil. In refractory or relapsing disease, rituximab may be considered. Guidelines recommend rituximab for some patients whose nephritis fails to improve or worsens after 6 months of induction with cyclophosphamide, mycophenolate mofetil, or both.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
LN	23.7 mg PO BID	47.4 mg/day

VI. Product Availability

Capsule: 7.9 mg

VII. References

1. Lupkynis Prescribing Information. Rockville, MD: Aurinia Pharmaceuticals, Inc.; January 2021. Available at: https://www.lupkynis.com/. Accessed February 14, 2021.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT03021499, Aurinia Renal Response in Active Lupus With Voclosporin (AURORA) Available at: https://www.clinicaltrials.gov/ct2/show/NCT03021499. Accessed June 22, 2020.
3. Weening J, Vivette D, Schwartz M, et al. The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. JASN February 2004, 15(2)241-250.
4. Drug Monographs. Clinical Pharmacology. Tampa, FL: Gold Standard Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com. Accessed June 22, 2020.
5. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Annals of the Rheumatic Diseases 2019;78:736-745.
6. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum.* 2012; 64:2677.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	06.22.20	08.20
Drug is now FDA approved - criteria updated per FDA labeling: eGFR requirement removed, cyclophosphamide as an option for concurrent immunosuppressive therapy w/Lupkynis removed as this is not recommended per the labeling, and concurrently prescribed with "non-biologic" immunosuppressive therapy was changed to "background" immunosuppressive therapy; rheumatology specialist added, criterion for diagnosis of SLE added, clarification of maximum dose as 6 capsules/day added; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154.	02.23.21	05.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.