Drug Coverage Policy

Effective Date.....6/15/2024
Coverage Policy Number.....IP0122
Policy Title.....Lupkynis

Lupus – Lupkynis

- **Lupkynis™ (voclosporin capsules – Aurinia)**

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Lupkynis, a calcineurin inhibitor immunosuppressant, is indicated in combination with a background immunosuppressive therapy regimen for the treatment of active **lupus nephritis** in adults.[1]

Lupkynis safety and efficacy have not been established in combination with cyclophosphamide and this combination is not recommended.

Guidelines

European League Against Rheumatism (EULAR) guidelines for SLE (2023) recommend hydroxychloroquine for all patients, unless contraindicated.[2] Depending on the type and severity of organ involvement, glucocorticoids can be used but dosing should be minimized or withdrawn. Methotrexate, azathioprine, mycophenolate, and/or biologic agents (Benlysta® [belimumab intravenous or subcutaneous infusion], Saphnelo® [anifrolumab-fnia intravenous infusion]) should be considered in patients who do not respond to hydroxychloroquine ± glucocorticoids. EULAR also states biologic agents (Benlysta, Saphnelo) should also be considered as second-line therapy for the treatment of active skin disease. Patient with active proliferative lupus nephritis should also consider combination therapy with biologic agents (Benlysta, Lupkynis). In general, the pharmacological interventions are directed by patient characteristics and the type/severity of organ involvement.

Guidelines for the management of lupus nephritis from Kidney Disease: Improving Global Outcomes (KDIGO) [2024] recommend Benlysta or Lupkynis in combination with other medications plus glucocorticoids as initial treatment options for patients with active Class III or IV (± Class V) biopsy confirmed lupus nephritis (strong recommendation, moderate certainty of evidence).[3] No preference is given between the treatment protocol options; however, the KDIGO guidelines do provide individual patient clinical factors to consider, including but not limited to, kidney function and histology, risk of disease flare, proteinuria, background suppression, and need for parenteral therapy.

Medical Necessity Criteria

Lupkynis is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Lupus Nephritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Diagnosis of lupus nephritis has been confirmed on biopsy; AND
       Note: For example, World Health Organization class III, IV, or V lupus nephritis.
     - **iii.** The medication is being used concurrently with an immunosuppressive regimen; AND
       Note: For example, mycophenolate mofetil or azathioprine with a systemic corticosteroid.
     - **iv.** Patient has an estimated glomerular filtration rate (eGFR) > 45 mL/min/m^2; AND
     - **v.** The medication is prescribed by or in consultation with a nephrologist or rheumatologist.
   - **B)** Patient is Currently Receiving Lupkynis. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The medication is being used concurrently with an immunosuppressive regimen; AND
       Note: For example, mycophenolate mofetil or azathioprine with a systemic corticosteroid.
     - **iii.** Patient has responded to Lupkynis, as determined by the prescriber; AND
       Note: Examples of a response include improvement in organ dysfunction, reduction in flares, reduction in corticosteroid dose, decrease of anti-double stranded DNA (anti-dsDNA) titer, and improvement in complement levels (i.e., C3, C4).
     - **iv.** The medication is prescribed by or in consultation with a nephrologist or rheumatologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Biologics or with Cyclophosphamide.** Lupkynis has not been studied in combination with other biologics or cyclophosphamide.[1] Safety and efficacy have not been established with these combinations. See Appendix for examples of biologics that should not be taken in combination with Lupkynis.

2. **Plaque Psoriasis.** In a Phase III trial, voclosporin was inferior to cyclosporine, which is an established therapy for plaque psoriasis.[4] Numerous other FDA-approved therapies are available with established efficacy for plaque psoriasis.

References

1. Lupkynis™ capsules [prescribing information]. Rockville, MD: Aurinia; January 2021.
2. Franouriakis 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.
3. Rovin BH, Adler SG, Barratt J, et al. Executive summary of the KDIGO 2021 guideline for the management of glomerular diseases. *Kidney Int*. 2021;100(4):753-779.
4. Li Y, Palmisano M, Sun D, Zhou Sl. Pharmacokinetic disposition difference between cyclosporine and voclosporin drives their distinct efficacy and safety profiles in clinical studies. *Clin Pharmacol*. 2020;12:83-96.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision,	**Updated** coverage policy title from *Voclosporin* to *Lupus - Lupkynis* **No** criteria changes	6/15/2024

The policy effective date is in force until updated or retired.

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		

Benlysta® (belimumab SC injection, IV infusion)	BLyS inhibitor	SLE, lupus nephritis
Saphnelo™ (anifrolumab-fnia IV infusion)	IFN receptor antagonist	SLE
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsA, PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; IV – Intravenous; BLyS – B-lymphocyte stimulator-specific inhibitor; SLE – Systemic lupus erythematosus; IFN – Interferon; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis.