PRIOR AUTHORIZATION POLICY

POLICY: Lupus – Lupkynis Prior Authorization Policy
- Lupkynis™ (voclosporin capsules – Aurinia)

REVIEW DATE: 03/13/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

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Depending on the type and severity of organ involvement, glucocorticoids can be used but dosing should be minimized or withdrawn.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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Lupkynis. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Lupkynis as well as the monitoring required for adverse events and long-term efficacy, approval requires Lupkynis to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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.

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational or unproven for ANY other use(s) 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. Fanouriakis A, Kostopoulou M, Andersen J, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis*. 2024;83(1):15-29.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Lupus Nephritis Work Group. KDIGO 2024 Clinical Practice Guideline for the management of LUPUS NEPHRITIS. *Kidney Int.* 2024;105(1S):S1-S69.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Lupus Nephritis:** For initial therapy, a requirement was added that the patient has biopsy-confirmed lupus nephritis. For initial therapy and a patient currently taking Lupkynis, the requirement that the patient is taking mycophenolate mofetil and a corticosteroid was changed to more generally require that the patient is taking an immunosuppressive regimen. Mycophenolate	03/08/2023

	mofetil or azathioprine with a systemic corticosteroid were added as examples of immunosuppressive regimens. The exception for a patient who is not a candidate for mycophenolate mofetil and a systemic corticosteroid due to inadequate efficacy or significant intolerance with these medications was removed from the policy.	
Selected Revision	**Lupus Nephritis:** For initial therapy, the requirement that the "Patient has autoantibody-positive systemic lupus erythematosus (SLE), defined as positive for antinuclear antibodies (ANA) and/or anti-double-stranded DNA (anti-dsDNA) antibody" was removed from the policy.	07/05/2023
Annual Revision	No criteria changes.	03/13/2024

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.