PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 03/08/2023; selected revision 07/05/2023

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. 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 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]

Safety and efficacy have not been established in combination with cyclophosphamide, and this combination is not recommended. The recommended starting dose is 23.7 mg twice daily taken on an empty stomach, used in combination with mycophenolate mofetil and corticosteroids. Dose modifications are required based on estimated glomerular filtration rate (eGFR). Lupkynis is not recommended if baseline eGFR is ≤ 45 mL/min/1.73 m^2 unless the benefit exceeds the risk. If therapeutic benefit is not apparent by Week 24, consider discontinuation of Lupkynis.

Guidelines

Guidelines for lupus nephritis from the European League Against Rheumatism-European Renal Association-European Dialysis and Transplant Association (2019) recommend treatment based on disease classification.[2] Patient survival, long-term preservation of kidney function, and prevention of organ damage are among the goals of treatment. Patients with systemic lupus erythematosus with evidence of kidney involvement are recommended for kidney biopsy. First-line initial therapy for patients with Class III or IV disease (± Class V) includes mycophenolate mofetil or

intravenous cyclophosphamide, in combination with glucocorticoids. In pure Class V disease, the first-line choice is mycophenolate mofetil + glucocorticoids. Following a response to initial therapy, mycophenolate mofetil or azathioprine (± low-dose glucocorticoids) are the drugs of choice for subsequent immunosuppressive treatment. Mycophenolate mofetil in combination with a calcineurin inhibitor (especially tacrolimus) is among the alternative therapies for those with nephrotic-range proteinuria or for Class V nephritis. Guidelines from Kidney Disease: Improving Global Outcomes (KDIGO)[2021] mention Lupkynis as a novel calcineurin inhibitor; however, a recommendation as to its place in therapy is not listed.[3] With approval of Lupkynis, multi-targeted therapy (e.g., glucocorticoid + mycophenolate mofetil + a calcineurin inhibitor) will be reassessed for a recommendation from KDIGO.

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.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/09/2022
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 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.	03/08/2023
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

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.