



## PRIOR AUTHORIZATION POLICY

- POLICY:** Lupus – Benlysta Subcutaneous Prior Authorization Policy
- Benlysta® (belimumab subcutaneous injection – GlaxoSmithKline)

**REVIEW DATE:** 03/11/2026

### **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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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**

Benlysta subcutaneous, a B-lymphocyte stimulator-specific inhibitor, is indicated for the following uses:<sup>1</sup>

- **Lupus nephritis**, in patients  $\geq 5$  years of age with active disease who are receiving standard therapy.
- **Systemic lupus erythematosus (SLE)**, in patients  $\geq 5$  years of age with active disease who are receiving standard therapy.

Limitations of Use: Benlysta has not been studied and is not recommended in patients with severe, active central nervous system lupus.<sup>1</sup>

The efficacy of Benlysta for the treatment of SLE was studied in patients with a history of autoantibodies (anti-nuclear antibodies and/or anti-double-stranded DNA) and an exploratory analysis of the pivotal trial indicated Benlysta was beneficial in patients who were autoantibody positive.<sup>1</sup>

Of note, intravenous Benlysta is addressed in a separate policy.

## **Guidelines**

### *Lupus Nephritis*

Guidelines for the management of lupus nephritis from Kidney Disease: Improving Global Outcomes (KDIGO) [2024] include Benlysta or Lupkynis® (voclosporin capsules) in combination with other medications plus glucocorticoids as initial treatment options for patients with active Class III or IV ( $\pm$  Class V) biopsy-confirmed lupus nephritis (strong recommendation, moderate certainty of evidence).<sup>3</sup> 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.

Guidelines from American College of Rheumatology (ACR) [2024] for treatment of lupus nephritis in patients with active/new onset/flare of Class III/IV ( $\pm$  Class V) disease conditionally recommend triple combination regimens as first-line (continuous) therapy with glucocorticoids + one of the following options: mycophenolic acid analogs (MPAA) + Benlysta; or MPAA + calcineurin inhibitor (e.g. Lupkynis); or low-dose cyclophosphamide + Benlysta.<sup>5</sup> For patients with extra-renal manifestations, a triple combination regimen with Benlysta is preferred over other alternatives.

### *SLE*

The American College of Rheumatology (ACR) guidelines for treatment of SLE (2025) recommend hydroxychloroquine (HCQ) for all patients (unless contraindicated), minimization of glucocorticoid exposure, and early introduction of conventional and/or biologic immunosuppressive therapies.<sup>6</sup> Treatment strategies should be stratified based on organ-specific manifestations such as hematologic, neuropsychiatric, cutaneous/mucocutaneous, serositis, musculoskeletal, systemic vasculitis, and/or cardiopulmonary. The following ACR recommendations are specific to Benlysta and Saphnelo® (anifrolumab-fnia intravenous infusion): (1) Cutaneous lupus: For ongoing moderate to severe cutaneous lupus refractory to topical and antimalarial therapies, and/or oral glucocorticoid necessitating escalation of therapy, ACR conditionally recommends the addition of methotrexate (MTX), mycophenolic acid analog (MPAA), anifrolumab Saphnelo, and/or belimumab Benlysta ([level of evidence [(LOE)]: very low to moderate]). (2) SLE arthritis: For a patient with persistent or recurrent active SLE arthritis on HCQ, regardless of prior/current nonsteroidal anti-inflammatory drugs or short-term glucocorticoid therapy, ACR conditionally recommends initial therapy with MTX, MPAA, or azathioprine (AZA), with a low threshold to add or substitute with belimumab Benlysta or anifrolumab Saphnelo for inadequate response over initial biologic therapy (LOE: very low to low). (3) Systemic vasculitis: For vasculitis attributed to active SLE, ACR conditionally recommends initial therapy with pulse/high-dose glucocorticoid taper and conventional (e.g., intravenous cyclosporine, MPAA, AZA) or biologic (e.g., anti-CD 20 therapy, belimumab Benlysta, anifrolumab Saphnelo) immunosuppressive therapy over glucocorticoid monotherapy alone (LOE: very low to low). In addition, Benlysta is recommended as an option for treatment of certain hematologic manifestations.

(4) Thrombocytopenia: For chronic asymptomatic thrombocytopenia (< 30,000/microliters) attributed to SLE, ACR conditionally recommends initiation of glucocorticoid with an additional therapy (e.g., MPAA, AZA, calcineurin inhibitor, anti-CD 20 agents, belimumabBenlysta, and/or intravenous immunoglobulins) over observation or glucocorticoid monotherapy (LOE: very low).

The European League Against Rheumatism (EULAR) guidelines for SLE (2023 update) also recommend HCQ for all patients, unless contraindicated.<sup>2</sup> Depending on the type and severity of organ involvement, glucocorticoids may be used but dosing should be minimized or withdrawn. In general, pharmacological interventions are directed by patient characteristics and the type/severity of organ involvement. The following EULAR recommendations are specific to Benlysta and Saphnelo: (1) In patients who do not respond to HCQ ± glucocorticoids, the addition of immunomodulating/immunosuppressive agents should be considered (e.g. MTX, AZA, MPAA, and/or biologic agents [e.g. Benlysta, Saphnelo]). (2) For patients with active skin disease, treatment should include topical agents (e.g., glucocorticoids, calcineurin inhibitors), antimalarials (e.g., HCQ, chloroquine), and/or systemic glucocorticoids as needed, with MTX, MPAA, Saphnelo, or Benlysta considered as second-line.

## **POLICY STATEMENT**

Prior Authorization is recommended for prescription benefit coverage of Benlysta subcutaneous. 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 Benlysta subcutaneous as well as the monitoring required for adverse events and long-term efficacy, approval requires Benlysta subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

• **Benlysta® (belimumab subcutaneous injection – GlaxoSmithKline) 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 Indications**

**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, and iv):

**i.** Patient is ≥ 5 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: Examples of an immunosuppressive regimen include azathioprine, cyclophosphamide, leflunomide, methotrexate, mycophenolate mofetil, and/or a systemic corticosteroid.

**iv.** The medication is prescribed by or in consultation with a nephrologist or rheumatologist; OR

**B) Patient is Currently Receiving Benlysta Subcutaneous or Intravenous.** Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

**i.** The medication is being used concurrently with an immunosuppressive regimen; AND

Note: Examples of an immunosuppressive regimen include azathioprine, cyclophosphamide, leflunomide, methotrexate, mycophenolate mofetil, and/or a systemic corticosteroid.

**ii.** The medication is prescribed by or in consultation with a nephrologist or rheumatologist; AND

**iii.** According to the prescriber, patient has responded to Benlysta subcutaneous or intravenous.

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).

**2. Systemic Lupus Erythematosus.** 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, and iv):

**i.** Patient is  $\geq 5$  years of age; AND

**ii.** Patient has autoantibody-positive systemic lupus erythematosus (SLE), defined as positive for at least one of the following: antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA) antibodies, anti-Smith (anti-Sm) antibodies; AND

Note: Not all patients with SLE are positive for anti-dsDNA, but most will be positive for ANA.

**iii.** Patient meets ONE of the following (a or b):

**a)** The medication is being used concurrently with at least one other standard therapy for SLE; OR

Note: Examples of standard therapies for SLE include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).

**b)** According to the prescriber, patient is determined to be intolerant to standard therapy due to a significant toxicity; AND

**iv.** The medication is prescribed by or in consultation with a rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist; OR

**B) Patient is Currently Receiving Benlysta Subcutaneous or Intravenous.** Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

**i.** Patient meets ONE of the following (a or b):

**a)** The medication is being used concurrently with at least one other standard therapy for SLE; OR

Note: Examples of standard therapies for SLE include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).

- b)** According to the prescriber, patient is determined to be intolerant to standard therapy due to a significant toxicity; AND
- ii.** The medication is prescribed by or in consultation with a rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist; AND
- iii.** According to the prescriber, patient has responded to Benlysta subcutaneous or intravenous.

Note: Examples of a response include reduction in flares, reduction in corticosteroid dose, decrease of anti-dsDNA titer, improvement in complement levels (i.e., C3, C4), or improvement in specific organ dysfunction (e.g., musculoskeletal, blood, hematologic, vascular, others).

## CONDITIONS NOT COVERED

• **Benlysta® (belimumab subcutaneous injection – GlaxoSmithKline) is(are) considered not medically necessary 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 Other Biologics.** Benlysta has not been studied in combination with other biologics.<sup>1</sup> Safety and efficacy have not been established with these combinations. See [APPENDIX](#) for examples of biologics that should not be taken in combination with Benlysta.
- 2. Concurrent Use with Lupkynis (voclosporin capsules).** Lupkynis has not been studied in combination with biologics such as Benlysta.<sup>1</sup>
- 3. Rheumatoid Arthritis.** A Phase II dose-ranging study evaluating patients with rheumatoid arthritis showed only small American College of Rheumatology (ACR) 20 responses with Benlysta (e.g., ACR 20 response at Week 24 was 28% with Benlysta 10 mg/kg).<sup>4</sup> Numerous other agents are available with higher ACR responses and established efficacy for rheumatoid arthritis.

## REFERENCES

1. Benlysta® injection [prescribing information]. Durham, NC: GlaxoSmithKline; June 2025.
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. Stohl W, Merrill JT, McKay JD, et al. Efficacy and safety of belimumab in patients with rheumatoid arthritis: a Phase II, randomized, double-blind, placebo-controlled, dose-ranging study. *J Rheumatol.* 2013;40(5):579-589.
5. Sammaritano LR, Askanase A, Bermas BL, et al. 2024 American College of Rheumatology (ACR) guidelines for the screening, treatment, and management of lupus nephritis. Published: May 7, 2025. Available at: <https://rheumatology.org/lupus-guideline>. Accessed on: February 24, 2026.
6. Sammaritano LR, Askanase A, Bermas BL, et al. 2025 American College of Rheumatology (ACR) guideline for the treatment of systemic lupus erythematosus. *Arthritis Rheumatol.* Published online November 4, 2025.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/13/2024
Selected Revision	<b>Systemic Lupus Erythematosus:</b> For initial therapy, the age requirement was updated to ≥ 5 years of age. Previously, the requirement was ≥ 18 years of age.	06/05/2024
Annual Revision	Updated Appendix.	03/19/2025
Selected Revision	<b>Lupus Nephritis:</b> For initial therapy, the age requirement was updated to ≥ 5 years of age. Previously, the requirement was ≥ 18 years of age.	07/02/2025
Annual Revision	The requirement “as determined by the prescriber” was updated to “according to the prescriber” throughout the Policy.  <b>Systemic Lupus Erythematosus (SLE):</b> The initial approval duration was changed from 4 to 6 months. The requirement for autoantibody-positive SLE was updated to include anti-Smith antibodies. The term “standard therapy” was clarified to “standard therapy for SLE”.	03/11/2026

## APPENDIX

	Mechanism of Action	Examples of Indications*
<b>Biologics</b>		
<b>Saphnelo®</b> (anifrolumab-fnia IV infusion)	IFN receptor antagonist	SLE
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
<b>Zymfentra®</b> (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
<b>Simponi®, Simponi Aria®</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
<b>Tocilizumab Products</b> (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
<b>Kevzara®</b> (sarilumab SC injection)	Inhibition of IL-6	RA
<b>Orencia®</b> (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
<b>Rituximab IV Products</b> (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
<b>Kineret®</b> (anakinra SC injection)	Inhibition of IL-1	JIA <sup>^</sup> , RA
<b>Omvo®</b> (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
<b>Ustekinumab Products</b> (Stelara® IV, biosimilar; Stelara SC, biosimilar)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
<b>Siliq®</b> (brodalumab SC injection)	Inhibition of IL-17	PsO

<b>Cosentyx</b> <sup>®</sup> (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
<b>Taltz</b> <sup>®</sup> (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
<b>Bimzelx</b> <sup>®</sup> (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO, AS, nr-axSpA, PsA
<b>Ilumya</b> <sup>®</sup> (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
<b>Skyrizi</b> <sup>®</sup> (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
<b>Tremfya</b> <sup>®</sup> (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
<b>Entyvio</b> <sup>®</sup> (vedolizumab IV infusion, vedolizumab SC injection)	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; IV – Intravenous; IFN – Interferon; SLE – Systemic lupus erythematosus; SC – Subcutaneous; 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.

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