CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Lupus – Benlysta Intravenous Utilization Management Medical Policy
- Benlysta® (belimumab intravenous infusion – GlaxoSmithKline)

REVIEW DATE: 03/11/2026

OVERVIEW

Benlysta intravenous, a B-lymphocyte stimulator-specific inhibitor, is indicated for the following uses:[1]
- **Lupus nephritis**, in patients ≥ 5 years of age with active disease who are receiving standard therapy.
- **Systemic lupus erythematosus** (SLE), in patients ≥ 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.[1]

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

Of note, subcutaneous 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 (± 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.

Guidelines from American College of Rheumatology (ACR) [2024] for treatment of lupus nephritis in patients with active/new onset/flare of Class III/IV (± 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.[5] 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.[6] 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), MPAA, Saphnelo, and/or 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 Benlysta or 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-CD20 therapy, Benlysta, 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-CD20 agents, Benlysta, 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.[2] 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 medical benefit coverage of Benlysta intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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 intravenous as well as the monitoring required for adverse events and long-term efficacy, approval requires Benlysta intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Benlysta intravenous is recommended in those who meet one of the following:

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 Intravenous or Subcutaneous. 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).

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 10 mg/kg given as an intravenous infusion; AND

B) Doses are administered at Weeks 0, 2, and 4, with subsequent doses separated by at least 4 weeks.

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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 ≥ 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 Intravenous or Subcutaneous. 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).

Dosing. Approve the following dosing regimen (A and B):

A) The dose is up to 10 mg/kg given as an intravenous infusion; AND

B) Doses are administered at Weeks 0, 2, and 4, with subsequent doses separated by at least 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Benlysta intravenous is not recommended in the following situations:

1. **Concurrent Use with Other Biologics.** Benlysta intravenous has not been studied in combination with other biologics.[1] Safety and efficacy have not been established with these combinations. See APPENDIX for examples of other 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.[1]

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).[4] Numerous other agents are available with higher ACR responses and established efficacy for rheumatoid arthritis.

4. 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. 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 L, Askanase A, Bermas B, 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: 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
Update	**06/04/2024**: No criteria changes. **Overview**: The indication for systemic lupus erythematous was updated to remove "auto-antibody positive" and following statement was added, "The efficacy of Benlysta for the treatment of SLE was studied in patients with a history of autoantibodies (anti-nuclear antibody and/or anti-double-stranded DNA) and an exploratory analysis of the pivotal trial indicated Benlysta was beneficial in patients who were autoantibody positive."	--
Annual Revision	No criteria changes. Updated Appendix.	03/19/2025
Update	**06/27/2025**: Overview was updated with American College of Rheumatology (2024) guidelines for lupus nephritis.	--
Annual Revision	The requirement "as determined by the prescriber" was updated to "according to the prescriber" throughout the Policy. **Systemic Lupus Erythematosus (SLE):** 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*
Biologics		
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, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, 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
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	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
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
Ustekinumab Products (Stelara® IV, biosimilar; Stelara SC, biosimilar)	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; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO, AS, nr-axSpA, PsA
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
Entyvio® (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; 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.