



## PRIOR AUTHORIZATION POLICY

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

**REVIEW DATE:** 03/13/2024; selected revision 06/05/2024

### **INSTRUCTIONS FOR USE**

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### **CIGNA NATIONAL FORMULARY COVERAGE:**

#### **OVERVIEW**

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

- **Lupus nephritis**, in adults 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.

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.

Of note, intravenous Benlysta is not targeted in this policy.

#### **Guidelines**

Guidelines for the management of lupus nephritis from Kidney Disease: Improving Global Outcomes (KDIGO) [2024] recommendations include Benlysta or Lupkynis in combination with other medications plus glucocorticoids as initial treatment options

for patients with active Class III or IV 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.

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Depending on the type and severity of organ involvement, glucocorticoids can be used but dosing should be minimized or withdrawn when possible.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

## **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<sup>®</sup> (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 ≥ 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: 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.

**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. Patient has responded to Benlysta subcutaneous or intravenous, as determined by the prescriber.  
Note: Examples of a response include improvement in organ dysfunction, reduction in flares, reduction in corticosteroid dose, decrease of anti-dsDNA titer, and improvement in complement levels (i.e., C3, C4).

**2. Systemic Lupus Erythematosus (SLE).** Approve for the duration noted if the patient meets ONE of the following (A or B):

**A) Initial Therapy.** Approve for 4 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 antinuclear antibodies (ANA) and/or anti-double-stranded DNA (anti-dsDNA) antibody; 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; OR  
Note: Examples of standard therapies include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).
  - b) Patient is determined to be intolerant to standard therapy due to a significant toxicity, as determined by the prescriber; AND
- iv. The medication is prescribed by or in consultation with a rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist.

**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; OR

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

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

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 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 Other Biologics.** Benlysta has not been studied and is not recommended 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>5</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; May 2024.
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.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/08/2023
Selected Revision	<b>Lupus Nephritis:</b> For initial therapy, a requirement was added that the patient has biopsy-confirmed lupus nephritis. For initial therapy and a patient currently taking Benlysta, the requirement that the patient is taking with standard therapy was changed to more generally require that the patient is taking an immunosuppressive regimen. Leflunomide, methotrexate, and/or systemic corticosteroids were added to existing concurrent medication examples. The exception for a patient who is intolerant to standard therapy due to significant toxicity as determined by the prescriber was removed from the Policy.	04/26/2023
Selected Revision	<b>Lupus Nephritis:</b> 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
Selected Revision	<b>Systemic Lupus Erythematosus:</b> For initial therapy, the age requirement was updated to $\geq 5$ years of age. Previously, the requirement was $\geq 18$ years of age.	06/05/2024

## APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
<b>Biologics</b>		
<b>Benlysta</b> ® (belimumab SC injection, IV infusion)	BlyS inhibitor	SLE, lupus nephritis
<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
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
<b>Simponi</b> ®, <b>Simponi</b> ® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
<b>Actemra</b> ® (tocilizumab IV infusion, tocilizumab SC injection)	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^, RA
<b>Stelara</b> ® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC

		IV formulation: CD, UC
<b>Siliq</b> <sup>™</sup> (brodalumab SC injection)	Inhibition of IL-17	PsO
<b>Cosentyx</b> <sup>®</sup> (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
<b>Taltz</b> <sup>®</sup> (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
<b>Ilumya</b> <sup>™</sup> (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
<b>Skyrizi</b> <sup>®</sup> (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsA, PsO
<b>Tremfya</b> <sup>™</sup> (guselkumab SC injection)	Inhibition of IL-23	PsO
<b>Entyvio</b> <sup>™</sup> (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.

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