

PRIOR AUTHORIZATION POLICY

POLICY: Lupus – Benlysta Intravenous Prior Authorization Policy

- Benlysta® (belimumab intravenous infusion – GlaxoSmithKline)

REVIEW DATE: 03/13/2024

OVERVIEW

Benlysta intravenous, a B-lymphocyte stimulator (BLyS)-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.

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 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.

Of note, subcutaneous 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).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.

European League Against Rheumatism (EULAR) guidelines for SLE (2023 update) 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Depending on the type and severity of organ involvement, glucocorticoids can be used but dosing should be minimized or withdrawn when possible. Methotrexate, azathioprine, mycophenolate, and/or biologic agents (Benlysta, Saphnelo® [anifrolumab-fnia intravenous infusion]) should be considered in patients who do not respond to hydroxychloroquine \pm glucocorticoids. EULAR also states biologic agents (Benlysta, Saphnelo) should be considered as second-line therapy for the treatment of patients with active skin disease. Patient with active proliferative lupus nephritis should also consider combination therapy with biologic agents (Benlysta, Lupkynis™ [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 intravenous. 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.
 - 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.** 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 ≥ 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 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; 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 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 and is not recommended in combination with other biologics.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 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 RA.
- 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; 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.

APPENDIX

* 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.