PRIOR AUTHORIZATION POLICY

POLICY: Lupus – Benlysta Intravenous Prior Authorization Policy
- Benlysta® (belimumab intravenous infusion – Human Genome Sciences/GlaxoSmithKline)

REVIEW DATE: 02/09/2022; selected revision 08/24/2022

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, autoantibody-positive, systemic disease in those who are receiving standard therapy.

Benlysta intravenous has not been studied and is not recommended in those with severe active central nervous system lupus, or in combination with other biologics. In some of the clinical trials involving Benlysta, Black patients had a lower response rate for the primary endpoint relative to Black patients receiving placebo; therefore, caution is recommended when considering Benlysta in Black patients. Of note, there is also a subcutaneous formulation of Benlysta with a similar indication except use is limited to adults ≥ 18 years.

Guidelines

Benlysta is addressed in the following guidelines:

- **Lupus Nephritis:** Guidelines for lupus nephritis are available from the European League Against Rheumatism (EULAR) and European Renal Association/European Dialysis and Transplant Association (ERA-EDTA) [2019].[2] Benlysta may be considered as add-on treatment for non-responding/refractory lupus nephritis, to facilitate glucocorticoid sparing, control extra-renal lupus activity, and decrease the risk for extra-renal flares. Guidelines from KDIGO (Kidney Disease: Improving Global Outcomes) [2021] list Benlysta among the therapies recommended for second-line treatment of lupus nephritis.[3] The guidelines note that optimal use of Benlysta will become clearer as its use increases.
- **SLE:** Guidelines from the EULAR (2019) recommend consideration of add-on therapy with Benlysta for patients who have an inadequate response to standard of care (e.g., combinations of hydroxychloroquine and glucocorticoids with or without immunosuppressive agents).[4] EULAR defines an inadequate response as residual disease activity not allowing tapering of glucocorticoids and/or frequent relapses.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Benlysta intravenous. Approvals are authorized 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, initial 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 criteria:

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 conditions (i, ii, iii, and iv):
     - **i.** Patient is ≥ 5 years of age; AND
     - **ii.** Patient has autoantibody-positive SLE, defined as positive for antinuclear antibodies (ANA) and/or anti-double-stranded DNA (anti-dsDNA) antibody; AND
     - **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 azathioprine, mycophenolate mofetil, cyclophosphamide.
       - **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 nephrologist or rheumatologist.
   - **B)** Patient is Currently Receiving Benlysta Intravenous or Subcutaneous. Approve for 1 year if the patient meets ALL of the following criteria (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 azathioprine, mycophenolate mofetil, cyclophosphamide.
       - **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 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.** 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 conditions (i, ii, iii, and iv):
     - **i.** Patient is ≥ 5 years of age; AND
     - **ii.** Patient has autoantibody-positive 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 criteria (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 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).[5] 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]. Rockville, MD: Human Genmome Sciences/GlaxoSmithKline; July 2022.
2. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res (Hoboken).* 2012;64(6):797-808.
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. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis*. 2019;78(6):736-745.

5. 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.
6. Lupkynis™ capsules [prescribing information]. Rockville, MD: Aurinia; January 2021.

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Lupus Nephritis:** This newly approved condition was added to the policy. For initial therapy the patient must be ≥ 18 years of age. Criteria approve for 6 months for initial therapy (1 year for continuation), if the medication is being used concurrently with at least one other standard therapy unless intolerant. For continuation, the patient must also have demonstrated a response to initial therapy. For all approvals, Benlysta must be prescribed by or in consultation with a specialist. **Conditions Not Recommended for Approval:** Concurrent use with cyclophosphamide was removed from the Conditions Not Recommended for Coverage (no longer supported in the labeling).	01/20/2021
Annual Revision	**Conditions Not Recommended for Approval:** Concurrent use with Lupkynis (voclosporin capsules) was added as a condition not recommended for approval.	02/09/2022
Selected Revision	**Lupus Nephritis:** To align with the updated labeling, the age of approval was changed from ≥ 18 years of age to ≥ 5 years of age.	08/24/2022

APPENDIX

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; 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; IV – Intravenous, 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.