PRIOR AUTHORIZATION POLICY

POLICY: Lupus – Benlysta Subcutaneous Prior Authorization Policy
- Benlysta® (belimumab subcutaneous injection – Human Genome Sciences/GlaxoSmithKline)

REVIEW DATE: 01/20/2021

OVERVIEW

Benlysta subcutaneous, a B-lymphocyte stimulator (BLyS)-specific inhibitor, is indicated for the following uses:[1]

- **Lupus nephritis**, in adults with active disease who are receiving standard therapy.
- **Systemic lupus erythematosus** (SLE), in patients ≥ 18 years of age with active, autoantibody-positive, systemic disease in those who are receiving standard therapy.

Benlysta subcutaneous 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 an intravenous formulation of Benlysta with a similar indication except use is expanded to those ≥ 5 years of age.

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].[3] 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.
- **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).[2] 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 subcutaneous. 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, initial approval requires Benlysta subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated. Approvals are authorized for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Benlysta subcutaneous is recommended in those who meet 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 ≥ 18 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 Subcutaneous or Intravenous. 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 ≥ 18 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 Subcutaneous or Intravenous. 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 subcutaneous is not recommended in the following situations:

1. **Concurrent Use with Other Biologics.** Benlysta 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. **Rheumatoid Arthritis.** A Phase II dose-ranging study evaluating patients with rheumatoid arthritis showed only small 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.

3. 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 Science Inc./GlaxoSmithKline; January 2020.
2. 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..
3. 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.
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

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	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: PJIA, PSA, RA
		IV formulation: PJIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Ilaris (canakinumab SC injection**)**	Inhibition of IL-1β	SJIA
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA, SJIA^
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	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)	Inhibition of IL-17A	AS, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, 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; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn's disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; ^ Off-label use of SJIA supported in guidelines.