VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Benlysta® (belimumab subcutaneous injection – Human Genome Sciences, Inc./GlaxoSmithKline)

TAC APPROVAL DATE: 05/08/2019

OVERVIEW

Benlysta SC is a B-lymphocyte stimulator (BLyS)-specific inhibitor.[1] It is indicated for the treatment of active, autoantibody-positive, systemic lupus erythematosus (SLE) in adults who are receiving standard therapy. Benlysta SC has not been studied and is not recommended in those with severe active lupus nephritis, severe active central nervous system (CNS) lupus, or in combination with other biologics or intravenous (IV) cyclophosphamide. In some of the clinical trials with Benlysta IV, Black patients had a lower response rate for the primary endpoint relative to Black patients receiving placebo; therefore, caution is recommended when considering Benlysta SC in Black patients. Benlysta SC is given as a 200 mg SC injection once weekly (QW) in the abdomen or thigh. Patients transitioning from Benlysta intravenous (IV) should receive the first SC dose 1 to 4 weeks after the last IV dose. Benlysta SC has not been evaluated and is not available in a syringe for pediatric use. However, Benlysta IV is indicated in patients ≥ 5 years of age.

Disease Overview

SLE is a chronic autoimmune disease that triggers inflammation in different parts of the body.[2] The disease may affect many different organs with a wide variety of symptoms, including skin rashes, fevers, and joint pain/swelling. Fatigue can be extreme and is the symptom that most often affects quality of life. Inflammation at various sites can lead to complications, including serious kidney damage, CNS symptoms (e.g., headache, hallucinations, seizure, stroke), vasculitis, pericarditis, and CV disease.[3] Levels of BLyS are elevated in SLE, with higher levels correlating with increased SLE disease activity. Benlysta blocks the binding of soluble BLyS to its receptors on B cells, thus inhibiting the survival of B cells and reducing the differentiation of B cells into immunoglobulin-producing plasma cells.[1]

Guidelines

Guidelines from the European League Against Rheumatism (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. Guidelines for lupus nephritis from the American College of Rheumatology (ACR) [2012] do not address Benlysta's place in therapy.[5]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Benlysta SC. Because of the specialized skills required for evaluation and diagnosis of patients treated with Benlysta SC as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Benlysta SC 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 SC is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Systemic Lupus Erythematosus (SLE).** Approve Benlysta SC for the duration noted if the patient meets one of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following criteria (i, ii, iii, and iv):
     - **i.** The patient is an adult ≥ 18 years of age; AND
     - **ii.** The patient has autoantibody-positive SLE (i.e., positive for antinuclear antibodies [ANA] and/or anti-double-stranded DNA antibody [anti-dsDNA]);
       NOTE: Not all patients with SLE are positive for anti-dsDNA, but most will be positive for ANA; AND
     - **iii.** The agent is being used concurrently with at least one other standard therapy (i.e., antimalarials [e.g., hydroxychloroquine], a systemic corticosteroid [e.g., prednisone], and/or other immunosuppressants [e.g., azathioprine, mycophenolate mofetil, methotrexate]) unless the patient is determined to be intolerant due to a significant toxicity, as determined by the prescribing physician; AND
     - **iv.** The agent is prescribed by or in consultation with rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist.
   - **B)** Patient is Currently Receiving Benlysta Subcutaneous or Intravenous: Approve for 3 years if the patient meets ALL of the following criteria (i, ii, and iii):
     - **i.** The agent is being used concurrently with at least one other standard therapy (i.e., antimalarials [e.g., hydroxychloroquine], a systemic corticosteroid [e.g., prednisone], and/or other immunosuppressants [e.g., azathioprine, mycophenolate mofetil, methotrexate]) unless the patient is determined to be intolerant due to a significant toxicity, as determined by the prescribing physician; AND
     - **ii.** The agent is prescribed by or in consultation with rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist; AND
     - **iii.** The patient has responded to Benlysta subcutaneous or intravenous (e.g., 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]), as determined by the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Benlysta SC has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Use with Other Biologics (e.g., Rituxan® [rituximab injection]) or with Cyclophosphamide Intravenous (IV).** Benlysta SC has not been studied and is not recommended in combination with other biologics or intravenous (IV) cyclophosphamide in patients with SLE.[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 (RA).** A Phase II dose-ranging study evaluating patients with RA showed only small ACR 20 responses with Benlysta (e.g., ACR 20 response at Week 24 was 28% with Benlysta 10 mg/kg).[6] Numerous other agents are available with higher ACR responses and established efficacy for RA.

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; April 2019.
2. Lupus detailed fact sheet. The Centers for Disease Control and Prevention Web site. Web site last reviewed on October 17, 2018. Accessed on May 2, 2019. Available at: https://www.cdc.gov/lupus/facts/detailed.html.
3. Lupus. Mayo Clinic Web site. Updated October 2017. Accessed on May 2, 2019. Available at: http://www.mayoclinic.org/diseases-conditions/lupus/basics/complications/CON-20019676.
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 Mar 29. [Epub ahead of print].
5. 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.
6. 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.
7. Stohl W, Schwarting A, Okada M, et al. Efficacy and safety of subcutaneous belimumab in systemic lupus erythematosus: A randomized, double-blind, placebo-controlled, 52-week study. *Arthritis Rheumatol.* 2017;69(5):1016-1027.
8. ACR classification criteria. Updated in 1997. Accessed on May 2, 2019. Available at: https://www.rheumatology.org/Portals/0/Files/1997%20Update%20of%201982%20Revised.pdf.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	08/16/2017
Selected revision	Add criteria to approve Benlysta SC if the patient is intolerant due to toxicity of conventional SLE therapies. Expand list of prescribers who must be consulted prior to approval to include a clinical immunologist, nephrologist, neurologist, and dermatologist. Expand examples of a response to include a decrease in anti-dsDNA titer, improvement in complement levels, and improvement in specific organ dysfunction.	09/13/2017
Annual revision	No changes to the criteria. In Conditions Not Recommended for Approval, update the list of biologics that should not be taken in combination with Benlysta SC.	07/18/2018
Early annual revision	**Systemic Lupus Erythematosus:** For patients continuing on therapy with Benlysta, the requirement that the patient is ≥ 18 years of age was removed from the policy. This age criterion now only applies to those initiating therapy with Benlysta SC.	05/09/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.

APPENDIX

Biologic or Targeted Synthetic DMARD	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita™ (adalimumab-atto for SC injection)	Inhibition of TNF
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Truxima® (rituximab-abbs IV injection)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Skyrizi™ (risankizumab SC injection)	Inhibition of IL-23
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23
Tremfya® (guselkumab for SC injection)	Inhibition of IL-23
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist
Otezla® (apremilast tablets)	Inhibition of PDE4
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways

SC – Subcutaneous; TNF – Tumor necrosis factor; IL – Interleukin; IV – Intravenous; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.