PRIOR AUTHORIZATION POLICY

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

DATE REVIEWED: 05/27/2020

OVERVIEW

Benlysta subcutaneous (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.

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).[2] 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.[3]

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, 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. The patient meets ONE of the following (a or b):

a) The agent 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) The patient is determined to be intolerant standard therapy due to a significant toxicity, as determined by the prescriber; 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 patient meets ONE of the following (a or b):

a) The agent 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) The patient is determined to be intolerant due to a significant toxicity, as determined by the prescriber; 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, 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

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 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).[4] 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; 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 for Products*
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.