Medical Policy:
BENLYSTA® (belimumab)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.71	July 26, 2023	

Definitions

Benlysta is a human IgG1 lambda monoclonal antibody that inhibits the binding of soluble B lymphocyte stimulator protein (BLyS) to its B cell receptors.

Length of Authorization

Coverage will be provided for 12 months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time) [Medical Benefit]:

- Loading Dose (doses administered on days 1, 15 and 29):
  - 360 billable units per 29 days
- Maintenance Dose:
  - 120 billable units per 28 days

Guideline

I. INITIAL APPROVAL CRITERIA

1. **<u>Systemic Lupus Erythematosus (SLE)</u>**
    A. Patient is 5 years of age or older; **AND**
    B. Patient has autoantibody-positive SLE test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-double-stranded DNA [anti-dsDNA] antibody; **AND**
    C. Patient meets **ONE** of the following:
        i. The medication is being used concurrently with at least one other standard therapy; **OR**
        <u>Note:</u> Examples of standard therapies include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).
        ii. Patient is determined to be intolerant to standard therapy due to a significant toxicity, as determined by the prescriber; **AND**
    D. Patient must NOT have an active infection; **AND**
    E. Patient has NOT received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**
    F. Patient does NOT have any of the following exclusion criteria:
        i. Severe active central nervous system lupus
        ii. Individuals who are on other biologics
2. **<u>Lupus Nephritis</u>**
    A. Patient is ≥ 5 years of age; **AND**
    B. Patient has autoantibody-positive SLE, defined as positive for antinuclear antibodies (ANA) and/or anti-double-stranded DNA (anti-dsDNA) antibody; **AND**
    C. Patient meets **ONE** of the following:
        i. The medication is being used concurrently with at least one other standard therapy; **OR**
        <u>Note</u>: Examples of standard therapies include corticosteroids AND mycophenolate mofetil OR corticosteroids with cyclophosphamide for induction followed by azathioprine for maintenance.
        ii. Patient is determined to be intolerant to standard therapy due to a significant toxicity, as determined by the prescriber; **AND**
    D. Patient must NOT have an active infection; **AND**
    E. Patient has NOT received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**
    F. Patient does NOT have any of the following exclusion criteria:
        i. Severe active central nervous system lupus
        ii. Individuals who are on other biologics

II. RENEWAL CRITERIA

Authorizations can be renewed based on the following criteria:

1. Patient continues to meet the criteria identified in section I; **AND**
2. Adequate documentation of disease stability and/or improvement as determined by the prescriber; **AND**
   Note: FOR SLE- 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).
   Note: For Lupus Nephritis - 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).
3. Absence of unacceptable toxicity from the drug.
   Note: Examples of unacceptable toxicity include the following: depression, suicidal thoughts, serious infections, signs or symptoms of progressive multifocal leukoencephalopathy (PML), malignancy, severe hypersensitivity reaction, etc.

Dosing/Administration

Indication	Dose
Systemic lupus erythematosus (SLE)	• ≥5 years for IV and ≥18 years for SC • IV: Loading Dose: 10 mg/kg intravenously (by a healthcare provider) every 2 weeks x 3 doses (days 1, 15 and 29) Maintenance Dose: 10 mg/kg intravenously (by a healthcare provider) every 4 weeks • SC: 200 mg once weekly
Lupus Nephritis	• ≥5 years for IV and ≥18 years for SC • IV: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter • SC: 400-mg dose (two 200-mg injections) once weekly for the first 4 doses, then 200 mg once weekly thereafter

Applicable Procedure Codes

Code	Description
J0490	Injection, belimumab, 10 mg; 1 billable unit = 10 mg

Applicable NDCs

Code	Description
49401-0101-xx	Benlysta 120 mg/5 mL SDV for injection
49401-0102-xx	Benlysta 400 mg/20 mL SDV for injection

ICD-10 Diagnoses

Code	Description
M32.10	Systemic lupus erythematosus organ or system involvement unspecified
M32.11	Endocarditis in systemic lupus erythematosus
M32.12	Pericarditis in systemic lupus erythematosus
M32.13	Lung involvement in systemic lupus erythematosus
M32.14	Glomerular disease in systemic lupus erythematosus

M32.15	Tubulo-interstitial nephropathy in systemic lupus erythematosus
M32.19	Other organ or system involvement in systemic lupus erythematosus
M32.8	Other forms of systemic lupus erythematosus
M32.9	Systemic lupus erythematosus, unspecified

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & Connecticare	7/26/2023	Annual Review: No criteria changes
EmblemHealth & Connecticare	4/25/2023	SLE: Removed from initial Criteria: SELENA-SLEDAI score ≥6 for IV and ≥8 for SC
EmblemHealth & Connecticare	9/12/2022	-Addition of Lupus Nephritis to criteria to align with FDA label. SLE Criteria: -Revision of wording for age limits under SLE criteria (change from "Adult greater than 5" to "Patient is 5 years of age or greater" -Addition of "The medication is being used concurrently with at least one other standard therapy; OR Patient is determined to be intolerant to standard therapy due to a significant toxicity, as determined by the prescriber" to SLE criteria -Removal of 1.Patient has one of the following: a.Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 6-12 b British Isles Lupus Assessment Group (BILAG) A organ domain score ≥1 c.BILAG B organ domain score ≥2 ADDED SELENA-SLEDAI score ≥6 for IV and ≥8 for SC - Removal of Patient has failed to respond adequately to at least two (2) standard therapies (anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives (excluding intravenous cyclophosphamide)
EmblemHealth & ConnectiCare	4/01/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	8/12/2019	Updated age-range from 18 to 5 years of age and older for IV

References

1. Benlysta [package insert]. Rockville, MD; Human Genome Sciences/GlaxoSmithKline; July 2017. Accessed September 2022.
2. Boyce EG, Fusco BE. Belimumab: review of use in systemic lupus erythematosus. Clin Ther. 2012 May;34(5):1006-22. doi: 10.1016/j.clinthera.2012.02.028. Epub 2012 Mar 30.
3. Navarra SV, Guzmán RM, Gallacher AE, et al. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. Lancet. 2011 Feb;377(9767):721-31. doi: 10.1016/SO140-6736(10)61354-2. Epub 2011 Feb 4.

4. Furie R, Petri M, Zamani O, et al. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. Arthritis Rheum. 2011 Dec;63(12):3918-30. doi: 10.1002/art.30613.
5. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012 Aug;64(8):2677-86. doi: 10.1002/art.34473.
6. Furie R, Stohl W, Ginzler EM, et al. Biologic activity and safety of belimumab, a neutralizing anti-B-lymphocyte stimulator (BLyS) monoclonal antibody: a phase I trial in patients with systemic lupus erythematosus. Arthritis Res Ther. 2008;10(5):R109. doi: 10.1186/ar2506. Epub 2008 Sep 11.
7. Kim SS, Kirou KA, Erkan D. Belimumab in systemic lupus erythematosus: an update for clinicians. Ther Adv Chronic Dis. 2012 Jan;3(1):11-23. doi: 10.1177/2040622311424806.
8. Calvo-Alén J1, Silva-Fernández L, Úcar-Angulo E, et al. SER consensus statement on the use of biologic therapy for systemic lupus erythematosus. Reumatol Clin. 2013 Sep-Oct;9(5):281-96.
9. Gordon C, Amissah-Arthur MB, Gayed M, et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. Rheumatol 2017 Oct 6. doi: 10.1093/rheumatology/kex286.
10. NICE. Belimumab for treating active autoantibody-positive systemic lupus erythematosus: Technology Appraisal Guidance [TAG397]. https://www.nice.org.uk/guidance/ta397/ Accessed November 2017.
11. Wisconsin Physician Service Insurance Corp. Local Coverage Determination (LCD): Drugs and Biologics (Non-chemotherapy) (L34741). Centers for Medicare & Medicare Services. Updated on 10/17/2017 with effective dates 11/1/2017. Accessed November 2017.