Medical Policy:

Benlysta® (belimumab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.71	February 27, 2025	

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):

- 400 billable units per 29 days

Maintenance Dose:

- 120 billable units per 28 days

Guideline

I. INITIAL APPROVAL CRITERIA

1. **Systemic Lupus Erythematosus (SLE)**

A. Patient is 5 years of age or older; **AND**

B. Patient must NOT have an active infection; **AND**

C. Patient has NOT received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**

D. Patient does NOT have any of the following exclusion criteria:

i. Severe active central nervous system lupus; **AND**

ii. Individuals who are on rituximab, anifrolumab, or IV cyclophosphamide*; **AND**

E. Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody *test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA*); **AND**

F. Patient has failed to respond adequately to at least two (2) standard therapies such as anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives (excluding intravenous cyclophosphamide); **AND**

G. Patient has one of the following:

i. Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 6-12; **OR**

ii. ≥2 British Isles Lupus Assessment Group (BILAG) B organ domain scores

2. **Lupus Nephritis**

A. Patient is ≥ 5 years of age; **AND**

B. Patient must NOT have an active infection; **AND**

C. Patient has NOT received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**

D. Patient does NOT have any of the following exclusion criteria:

i. Severe active central nervous system lupus; **AND**

ii. Individuals who are on rituximab OR anifrolumab, **AND**

E. Patient has active lupus nephritis Class III, IV, or V as confirmed by renal biopsy; **AND**

F. Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody test *(e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-doublestranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA)*; **AND**

G. Patient has failed to respond adequately to standard therapies including corticosteroids **AND** either cyclophosphamide or mycophenolate mofetil; **AND**

H. Baseline measurement of one or more of the following: urine protein:creatinine ratio (uPCR), estimated glomerular filtration rate (eGFR), or urine protein

***Systemic Lupus Erythematosus Diagnostic Criteria**
Patient must have at least 4 out of 11 diagnostic SLE features: 1. Malar rash 2. Discoid rash 3. Photosensitivity

4. Oral ulcers
5. Nonerosive arthritis (involving 2 or more peripheral joints)
6. Pleuritis/pericarditis
   - Pleuritis - history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion
   - Pericarditis - documented by electrocardiogram or rubbing heard by a physician or evidence of pericardial effusion
7. Renal disorder
   - Persistent proteinuria > 0.5 grams/day or > 3+ on urine dipstick
   - Cellular casts (red cell, hemoglobin, granular, tubular, or mixed)
8. Seizures/psychosis
9. Hematologic disorder
   - Hemolytic anemia with reticulocytosis
   - Leukopenia < 4,000/mm3 on ≥ 2 occasions
   - Lymphopenia < 1,500/mm3 on ≥ 2 occasions
   - Thrombocytopenia < 100,000/mm3 in the absence of offending drugs
10. Immunologic disorder
    - Presence of anti-Sm or antiphospholipid antibodies
    - Presence of anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA
11. Positive anti-nuclear antibody [ANA] greater than laboratory reference range

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**
   A. **FOR SLE-** Improvement in the SELENA_SLEDAI score of ≥ 4 points; **OR** no new BILAG-A organ domain score; **OR** 2 new BILAG-B organ domain scores; **OR** no worsening (< 0.30-point increase) in physicians Global Assessment (GA) score **OR** Seroconverted (negative)

   For Lupus Nephritis - Urine protein-creatinine ration (uPCR), **OR** Estimated glomerular filtration rate (eGFR); **OR** Urine protein

   B. 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 • 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
Lupus Nephritis	• ≥5 years for IV • IV: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals 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	2/27/2025	Updated billable units for max loading dose from 360 to 400. Removed voclosporin from initial criteria and replaced with anifrolumab, or IV cyclophosphamide.
EmblemHealth & Connecticare	4/1/2025	Annual Review: Initial Criteria: Systemic Lupus Erythematosus (SLE): Removed the following wording: “Patient has autoantibody-positive SLE test (e.g., antinuclear antibody [ANA] greater than laboratory reference range and/or antidouble-stranded DNA [anti-dsDNA] antibody; AND Patient meets ONE of the following: 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; AND” Updated the following statement to remove “other biologics” and replace with “voclosporin or rituximab” as follows: “Individuals who are on voclosporin or rituximab. Added: “Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA); AND Patient has failed to respond adequately to at least two (2) standard therapies such as anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives (excluding intravenous cyclophosphamide); AND Patient has one of the following:Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 6-12 ≥2 British Isles Lupus Assessment Group (BILAG) B organ domain scores Lupus Nephritis. Removed the following wording: “Patient has autoantibodypositive SLE, defined as positive for antinuclear antibodies (ANA) and/or antidouble-stranded DNA (anti-dsDNA) antibody; AND Patient meets ONE of the Proprietary information of EmblemHealth/ConnectiCare, Inc. © 2024 EmblemHealth & Affiliates Page 5 of 6 following: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; AND" Updated the following statement to remove "other biologics" and replace with "voclosporin or rituximab" as follows:Individuals who are on other biologics voclosporin or rituximab. Added: "Patient has active lupus nephritis Class III, IV, or V as confirmed by renal biopsy; AND Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or antidoublestranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA); AND Patient has failed to respond adequately to standard therapies including corticosteroids AND either cyclophosphamide or mycophenolate mofetil; AND Baseline measurement of one or more of the following: urine protein:creatinine ratio (uPCR), estimated glomerular filtration rate (eGFR), or urine protein" Renewal Criteria: FOR SLE- Removed the following: " Examples of a response include reduction in flares, reduction in corticosteroid dose, decrease of antidsDNA titer, improvement in complement levels (i.e., C3, C4), improvement in specific organ dysfunction (e.g., musculoskeletal, blood, hematologic, vascular, others), " Updated with: "Improvement in the SELENA_SLEDAI score of > 4 points; OR no new BILAG-A organ domain score; OR 2 new BILAG-B organ domain scores; OR no worsening (< 0.30-point increase) in physicians Global Assessment (GA) score OR Seroconverted (negative)" For Lupus Nephritis – Removed the following: "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)" replaced with: ". Urine protein-creatinine ration (uPCR), OR Estimated glomerular filtration rate (eGFR); OR Urine protein" Added SLE diagnostic criteria chart, updated dosing chart
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

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