Benlysta® (belimumab)
(Subcutaneous)

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I. Length of Authorization

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

***NOTE:** Approve Benlysta subcutaneous loading dose for 1 month, then maintenance dose can be approved for the remainder of 12 months

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 200 mg/mL single-dose syringe/autoinjector: 2 syringes/autoinjectors per week for 4 doses, then 1 syringe/autoinjector per week

B. Max Units (per dose and over time) [HCPCS Unit]:

Systemic Lupus Erythematosus (SLE)

- 200 mg weekly

Lupus Nephritis

- Loading dose: 400 mg weekly for 4 doses
- Maintenance dose: 200 mg weekly

III. Initial Approval Criteria

- **The use of samples and free goods do not qualify as an established clinical response.**

Coverage is provided in the following conditions:

- ONE of the following:
  - The requested agent is eligible for continuation of therapy AND ONE of the following:
    - Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days; **OR**

- The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed; **OR**

- The patient has a diagnosis of active systemic lupus erythematosus (SLE) disease WITHOUT active Lupus Nephritis AND BOTH of the following:
  - The requested agent is FDA approved for SLE; **AND**
  - BOTH of the following:
    - ONE of the following:
      - The patient has tried and had an inadequate response to hydroxychloroquine; **OR**
      - The patient has an intolerance or hypersensitivity to hydroxychloroquine; **OR**
      - The patient has an FDA labeled contraindication to hydroxychloroquine; **AND**
    - ONE of the following:
      - The patient has tried and had an inadequate response to corticosteroids OR immunosuppressives (i.e., azathioprine, methotrexate, oral cyclophosphamide, mycophenolate); **OR**
      - The patient has an intolerance or hypersensitivity to therapy with corticosteroids OR immunosuppressives (i.e., azathioprine, methotrexate, oral cyclophosphamide, mycophenolate); **OR**
      - The patient has an FDA labeled contraindication to ALL corticosteroids AND immunosuppressives (i.e., azathioprine, methotrexate, oral cyclophosphamide, mycophenolate); **OR**
- The patient has a diagnosis of active lupus nephritis (LN) AND BOTH of the following:
  - The requested agent is FDA approved for lupus nephritis; **AND**
  - The patient has Class III, IV, or V lupus nephritis confirmed via kidney biopsy; **OR**
- The patient has another FDA approved indication for the requested agent; **AND**

- If the patient has an FDA approved indication, then ONE of the following:
  - The patient's age is within FDA labeling for the requested indication for the requested agent and route of administration; **OR**
  - The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication and route of administration; **AND**
- ONE of the following:
  - The patient has a diagnosis of active systemic lupus erythematosus (SLE) disease WITHOUT active Lupus Nephritis AND BOTH of the following:
    - The patient is currently treated with standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, oral cyclophosphamide, mycophenolate); **AND**

        - The patient will continue standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, oral cyclophosphamide, mycophenolate) in combination with the requested agent; **OR**
    - The patient has a diagnosis of active lupus nephritis AND the patient will be using the requested agent with background immunosuppressive lupus nephritis therapy (e.g., corticosteroids with mycophenolate or for Benlysta corticosteroids with mycophenolate or IV cyclophosphamide); **OR**
    - The patient has another FDA approved indication for the requested agent; **AND**
- The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis; **AND**
- The patient does NOT have severe active central nervous system lupus; **AND**
- ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table**§**):
    - The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors); **OR**
    - The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following:
        - The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agents; **AND**
        - The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required); **AND**
- The patient does NOT have any FDA labeled contraindications to the requested agent

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria

Coverage can be renewed based on the following criteria:

- The patient has been previously approved for the requested agent through the plan's Prior Authorization process; **AND**
- ONE of the following:
    - The patient has a diagnosis of active systemic lupus erythematosus (SLE) disease WITHOUT active Lupus Nephritis AND ALL of the following:
        - The requested agent is FDA approved for SLE; **AND**
        - The patient will continue standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, oral cyclophosphamide, mycophenolate); **AND**
        - The patient has had clinical benefit with the requested agent; **OR**
    - The patient has a diagnosis of active lupus nephritis (LN) AND ALL of the following:

        - The requested agent is FDA approved for lupus nephritis; **AND**
        - The patient will continue background lupus nephritis therapy (e.g., corticosteroids with mycophenolate or for Benlysta corticosteroids with mycophenolate or IV cyclophosphamide); **AND**
        - The patient has had clinical benefit with the requested agent; **OR**
    - The patient has another FDA approved indication for the requested agent AND has had clinical benefit with the requested agent; **AND**
- The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis; **AND**
- The patient does NOT have severe active central nervous system lupus; **AND**
- ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table**§**):
    - The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors); **OR**
    - The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following:
        - The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agents; **AND**
        - The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required); **AND**
- The patient does NOT have any FDA labeled contraindications to the requested agent

§ Agents NOT to be used Concomitantly	
Contraindicated as Concomitant Therapy	
Abrilada (adalimumab-afzb)	Omvoh (mirikizumab-mrkz)
Actemra (tocilizumab)	Opzelura (ruxolitinib)
Adalimumab	Orencia (abatacept)
Adbry (tralokinumab-ldrm)	Otezla (apremilast)
Amjevita (adalimumab-atto)	Remicade (infliximab)
Arcalyst (rilonacept)	Renflexis (infliximab-abda)
Avsola (infliximab-axxq)	Riabni (rituximab-arrx)
Benlysta (belimumab)	Rinvoq (upadacitinib)
Bimzelx (bimekizumab-bkzx)	Rituxan (rituximab)
Cibinqo (abrocitinib)	Rituxan Hycela (rituximab/hyaluronidase human)
Cimzia (certolizumab)	Ruxience (rituximab-pvvr)
Cinqair (reslizumab)	Siliq (brodalumab)
Cosentyx (secukinumab)	Simponi (golimumab)
Cyltezo (adalimumab-adbm)	Simponi ARIA (golimumab)
Dupixent (dupilumab)	Skyrizi (risankizumab-rzaa)
Enbrel (etanercept)	Sotyktu (deucravacitinib)
Entyvio (vedolizumab)	Stelara (ustekinumab)
Fasenra (benralizumab)	Taltz (ixekizumab)
Hadlima (adalimumab-bwwd)	Tezspire (tezepelumab-ekko)
Hulio (adalimumab-fkjp)	Tremfya (guselkumab)

§ Agents NOT to be used Concomitantly	
Contraindicated as Concomitant Therapy	
Humira (adalimumab) Hyrimoz (adalimumab-adaz) Idacio (adalimumab-aacf) Ilaris (canakinumab) Ilumya (tildrakizumab-asmn) Inflectra (infliximab-dyyb) Infliximab Kevzara (sarilumab) Kineret (anakinra) Litfulo (ritlecitinib) Nucala (mepolizumab) Olumiant (baricitinib)	Truxima (rituximab-abbs) Tysabri (natalizumab) Velsipity (etrasimod) Wezlana (ustekinumab-auub) Xeljanz (tofacitinib) Xeljanz XR (tofacitinib extended release) Xolair (omalizumab) Yuflyma (adalimumab-aaty) Yusimry (adalimumab-aqvh) Zeposia (ozanimod) Zymfentra (infliximab-dyyb)

V. Dosage/Administration

Indication	Dose
Systemic Lupus Erythematosus (SLE)	200 mg subcutaneously* once weekly • For ADULT patients transitioning from intravenous therapy, administer the first subcutaneous dose 1 to 4 weeks after the last IV dose.
Lupus Nephritis	400 mg (two 200 mg injections) subcutaneously* once weekly for 4 doses, then 200 mg once weekly thereafter • ADULT patients may transition from intravenous therapy to subcutaneous therapy any time after the patient completes the first 2 intravenous doses. Administer the first subcutaneous dose of 200 mg 1 to 2 weeks after the last IV dose.
******May be self-administered*	

VI. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologic (applicable to the subcutaneous formulation only)

NDC:

- Benlysta 200 mg/mL single-dose prefilled syringe/autoinjector: 49401-0088-xx

VII. References

1. Benlysta [package insert]. Philadelphia, PA; GlaxoSmithKline LLC; February 2023. Accessed August 2023.
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. Rheumatology (Oxford). 2018 Jan 1;57(1):e1-e45. doi: 10.1093/rheumatology/kex286.
10. NICE. Belimumab for treating active autoantibody-positive systemic lupus erythematosus: Technology Appraisal Guidance [TA397]. https://www.nice.org.uk/guidance/ta397. Published: 22 June 2016. Accessed March 2021.
11. American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis Rheum.1999;42(9):1785–1796.
12. Lam NC, Ghetu MV, Bieniek ML. Systemic Lupus Erythematosus: Primary Care Approach to Diagnosis and Management. Am Fam Physician. 2016 Aug 15;94(4):284-94.
13. Wallace DJ, Stohl W, Furie RA, et al. A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of Belimumab in Patients With Active Systemic Lupus Erythematosus. Arthritis Rheum, 61 (9), 1168-78, 2009 Sept 15. doi: 10.1002/art.24699
14. D'Cruz D, Maksimowicz-McKinnon K, Oates J, et al. Efficacy and safety of belimumab in patients of black race with systemic lupus erythematosus: results from the EMBRACE study. 10.1136/lupus-2019-lsm.199
15. Brunner HI, Abud-Mendoza C, Viola DI, et al. Efficacy and Safety of Intravenous Belimumab in Children with Systemic Lupus Erythematosus [abstract]. *Arthritis Rheumatol.* 2018; 70 (suppl 10). https://acrabstracts.org/abstract/efficacy-and-safety-of-intravenous-belimumab-in-children-with-systemic-lupus-erythematosus/.
16. Stohl W, Schwarting A, Okada M, et al. Efficacy and Safety of Subcutaneous Belimumab in Systemic Lupus Erythematosus: A Fifty-Two-Week Randomized, Double-Blind, Placebo-Controlled Study. Arthritis Rheumatol, 69 (5), 1016-1027; May 2017. DOI: 10.1002/art.40049.

17. 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: 736–745.
18. Furie R, Rovin BH, Houssiau F, et al. Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis. N Engl J Med 2020; 383:1117-1128. DOI: 10.1056/NEJMoa2001180.
19. 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. doi:10.1002/acr.21664.
20. Bertsias GK, Tektonidou M, Amoura Z, et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. Ann Rheum Dis. 2012;71(11):1771-1782. doi:10.1136/annrheumdis-2012-201940.
21. NICE. Belimumab for treating active autoantibody-positive systemic lupus erythematosus: Technology appraisal guidance [TA752]. https://www.nice.org.uk/guidance/ta752. Published: 15 December 2021. Accessed March 2023.
22. Aringer M, Costenbader K, Daikh D, et al. 2019 European League against Rheumatism/American College of rheumatology classification criteria for systemic lupus erythematosus. Arthritis Rheumatol 2019;71:1400–12.
23. Fanouriakis A, Tziolos N, Bertsias G, et al. Update on the diagnosis and management of systemic lupus erythematosus. Ann Rheum Dis 2021; 80:14-25. doi:10.1136/annrheumdis-2020-218272
24. Lam NC, Brown JA, Sharma R. Systemic Lupus Erythematosus: Diagnosis and Treatment. Am Fam Physician. 2023 Apr 107(4):383-395.
25. Yee CS, Cresswell L, Farewell V, Rahman A, Teh LS, Griffiths B et al. Numerical scoring for the BILAG-2004 index. Rheumatology (Oxford) 2010; 49(9):1665-9.
26. Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002; 29(2):288-91.
27. Chessa E, Piga M, Floris A, Devilliers H, Cauli A, Arnaud L. Use of Physician Global Assessment in systemic lupus erythematosus: a systematic review of its psychometric properties. Rheumatology (Oxford). 2020 Dec 1;59(12):3622-3632. doi: 10.1093/rheumatology/keaa383.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 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

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC