Reference number(s)
2502-A

Standard Medicare Part B Management Benlysta

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Benlysta	belimumab

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, the member has no exclusions to the prescribed therapy, and the drug or biological is usually not self-administered. The criteria outlined in this policy is only applicable to drugs not usually self-administered and are furnished incident to a physician's service. Requests for drugs on a region's self-administered drug list are not covered. Members enrolled in Medicare Part D may seek coverage under their Medicare Part D plan.

FDA-Approved Indications[1]

Benlysta is indicated for the treatment of:

- Patients 5 years of age and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy
- Patients 5 years of age and older with active lupus nephritis who are receiving standard therapy

Limitations of Use

The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system (CNS) lupus. Use of Benlysta is not recommended in this situation.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

© 2026 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Documentation

The following documentation must be available, upon request, for all submissions:

Initial requests

Medical records (e.g., chart notes, laboratory reports) documenting the presence of autoantibodies relevant to SLE (e.g., antinuclear antibodies [ANA] by immunofluorescence [IFA] 1:80 or higher, anti-double-stranded DNA [anti-ds DNA], anti-Smith [anti-Sm], antiphospholipid antibodies, low complement proteins), or kidney biopsy supporting diagnosis (where applicable).

Continuation requests

Medical records (e.g., chart notes, laboratory reports) documenting disease stability or improvement.

Exclusions

Coverage will not be provided for members with any of the following exclusions:

- Severe active central nervous system (CNS) lupus (including seizures that are attributed to CNS lupus, psychosis, organic brain syndrome, cerebritis, or CNS vasculitis requiring therapeutic intervention before initiation of belimumab) in a member initiating therapy with Benlysta.
- Member is using Benlysta in combination with other biologics.

Coverage Criteria

Systemic Lupus Erythematosus (SLE)[1-3]

Authorization of 12 months may be granted for treatment of active SLE when both of the following criteria are met:

- Prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., ANA by IFA 1:80 or higher], anti-ds DNA, anti-Sm, antiphospholipid antibodies, low complement proteins).
- The member meets either of the following criteria:
    - The member is receiving standard treatment for SLE with any of the following (alone or in combination):
        - Glucocorticoids (e.g., prednisone, methylprednisolone, dexamethasone)
        - Antimalarials (e.g., hydroxychloroquine)
        - Immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate, cyclosporine, cyclophosphamide)
    - The member has a clinical reason to avoid treatment with a standard treatment regimen.

Active Lupus Nephritis[1-4]

© 2026 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Authorization of 12 months may be granted for treatment of active lupus nephritis when both of the following criteria are met:

- The member meets either of the following:
  - Lupus nephritis is confirmed on kidney biopsy
  - If a kidney biopsy is not feasible or if the member is not a candidate for kidney biopsy, prior to initiating therapy, the member is positive for autoantibodies relevant to SLE (e.g., ANA by IFA 1:80 or higher, anti-ds DNA, anti-Sm, antiphospholipid antibodies, low complement proteins)
- Member is receiving standard therapy regimen (e.g., cyclophosphamide, mycophenolate mofetil, azathioprine, hydroxychloroquine, corticosteroids) or has a clinical reason to avoid treatment with a standard therapy regimen.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication listed in the coverage criteria.
- The member is receiving benefit from therapy. Benefit is defined as disease stability or improvement.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Benlysta.
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
  - Clinical Pharmacology
- EULAR recommendations for the management of systemic lupus erythematosus with kidney involvement: 2025 update
- 2019 European League Against Rheumatism/American College of Rheumatology (ACR) classification criteria for systemic lupus erythematosus
- Kidney Disease: Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guideline for the Management of Glomerular Diseases
- The British Society for Rheumatology guideline for the management of systemic lupus erythematosus
- Derivation and Validation of Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for Systemic Lupus Erythematosus

© 2026 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

- 2025 American College of Rheumatology (ACR) Guideline for the treatment of systemic lupus erythematosus.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Benlysta are covered.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

The content of the exclusions can be found in the prescribing information.

The British Society for Rheumatology report that ANAs are present in about 95% of SLE patients. If the test for ANAs is negative, there is a low clinical probability of a member having SLE. The presence of anti-dsDNA antibodies, low complement levels or anti-Smith (Sm) antibodies are highly predictive of a diagnosis of SLE in patients with relevant clinical features. Anti-Ro/La and anti-RNP antibodies are less-specific markers of SLE as they are found in other autoimmune rheumatic disorders as well as SLE.

The SLICC group devised evidence-based classification criteria for lupus. These criteria introduced a requirement for at least one clinical and one immunological criterion and two others from an expanded list of items compared with the ACR criteria. They also allowed biopsy-proven lupus nephritis in the presence of ANA or anti-dsDNA antibodies to be classified as lupus, without the need for other criteria. These classification criteria may be used to aid diagnosis.

The EULAR/ACR classification criteria for SLE require ANA antibodies ≥ 1:80 on HEp-2 cells or an equivalent positive test and a classification threshold score of ≥ 10. The classification criteria should not be used as diagnostic criteria. Testing by immunofluorescence on HEp-2 cells or a solid-phase ANA screening immunoassay with at least equivalent performance is highly recommended.

According to the 2023 update of the EULAR recommendations for the management of systemic lupus erythematosus, the goal of treatment should be remission or low disease activity and prevention of flares in all organs. Hydroxychloroquine is recommended for all patients, unless contraindicated. Glucocorticoids (GC), if needed, can be used at doses and route of administration that depend on the type and severity of organ involvement and should be reduced to maintenance dose of less than or equal to 5 mg/day (prednisone equivalent). In patients not responding to hydroxychloroquine (alone or in combination with GC) or patients unable to reduce GC below doses acceptable for chronic use, addition of immunomodulating/immunosuppressive agents such as methotrexate, azathioprine, or mycophenolate and/or biological agents (e.g., belimumab or anifrolumab) should be considered. In patients with organ-threatening or life-threatening disease, cyclophosphamide should be considered.

According to the 2025 ACR guideline for lupus nephritis, it is strongly recommended to initiate and continue hydroxychloroquine to manage and prevent extra-renal manifestations, unless contraindicated.

© 2026 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

References

1. Benlysta [package insert]. Philadelphia, PA: GlaxoSmithKline LLC; June 2025.
2. Fanouriakis A, Kostopoulou M, Alunno A, et al. EULAR recommendations for the management of systemic lupus erythematosus with kidney involvement: 2025 update. Ann Rheum Dis. January 2026;85(1):75-90. URL: https://ard.eular.org/article/S0003-4976%2825%2904412-7/fulltext. Accessed March 14, 2026.
3. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78:1151-1159.
4. Rovin BH, Adler SG, Barratt J, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Lupus nephritis Work Group. KDIGO 2024 Clinical Practice Guideline for the Management of Lupus Nephritis. Kidney Int. 2024; 105(15):S1-S69.
5. Gordon C, Amissah-Arthru MB, Gayed M, et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. Rheumatology (Oxford). 2018; 57(1):e1-e45.
6. Petri M, Orbai A-M, Alarcon GS, et al. Derivation and Validation of Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheum. 2012; 64:2677-2686. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3409311/. Accessed January 16, 2026.
7. Sammaritano LR, Askanase A, Bermas BL, et al. 2025 American College of Rheumatology (ACR) Guideline for the treatment of systemic lupus erythematosus. Arthritis Care Res. November 2025. URL: https://rheumatology.org/lupus-guideline. Accessed March 14, 2026.
8. Self-Administered Drug Exclusion List: and Biologicals Excluded from Coverage- Medical Policy Article (A52527) Version R57. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
9. Self-Administered Drug Exclusion List: (A52571). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
10. Self-Administered Drug Exclusion List: (A53032). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
11. Self-Administered Drug Exclusion List: (A53033). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
12. Self-Administered Drug Exclusion List: Medical Policy Article (A53021). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
13. Self-Administered Drug Exclusion List: (SAD List) (A52800). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
14. Self-Administered Drug Exclusion List: (A53127). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.
15. Self-Administered Drug Exclusion List: (A53066). Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed January 16, 2026.

© 2026 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.