Clinical Policy: Belimumab (Benlysta)

Reference Number: PA.CP.PHAR.88
Effective Date: 01/2018
Last Review Date: 07/2024

Description
Belimumab (Benlysta®) is B-lymphocyte stimulator specific inhibitor.

FDA Approved Indication(s)
Benlysta is indicated for the treatment of:

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

Limitation(s) of use: The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Use of Benlysta is not recommended in these situations.

Policy/Criteria
It is the policy of PA Health & Wellness that Benlysta is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Systemic lupus erythematosus (must meet all):

1. Diagnosis of SLE;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 5 years;
4. Documentation confirms that member is positive for autoantibody (e.g., anti-nuclear antibody (ANA), anti-double-stranded DNA (anti-ds-DNA), anti-Smith antigen (anti-Sm), anti-ribonucleoprotein (anti-RNP), anti-Ro/SSA, anti-La/SSB antiphospholipid antibody);
5. Prescribed in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate);
6. Benlsyta is not prescribed concurrently with Lupkynis® or a biologic (e.g., rituximab, Saphnelo®);
7. Request meets one of the following (a or b):
   a. IV: Dose does not exceed 10 mg/kg per dose every 2 weeks for the first 3 doses and every 4 weeks thereafter;
   b. SC (i or ii):
      i. For pediatric members weighing ≥ 40 kg and adults: Dose does not exceed 200 mg once weekly;
      ii. For pediatric members weighing 15 kg to < 40kg: Dose does not exceed 200mg once every 2 weeks.

Approval duration: 12 months

B. Lupus Nephritis (must meet all)**:**
1. Diagnosis of LN with kidney biopsy that confirms one of the following (a, b, or c):
   a. LN Class III (focal);
   b. LN Class IV (diffuse segmental or global);
   c. LN Class V (membranous);
2. Prescribed by or in consultation with a nephrologist or rheumatologist;
3. Age ≥ 5 years;
4. Member has a confirmed diagnosis of systemic lupus erythematosus;
5. Prescribed in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate);
6. Benlsyta is not prescribed concurrently with Lupkynis® or a biologic (e.g., rituximab, Saphnelo®);
7. Request meets one of the following (a or b):
   a. IV: Dose does not exceed 10 mg/kg at 2-week intervals for the first 3 doses* and at 4-week intervals thereafter;
   b. SC (I or ii):
      i. For pediatric members weighing ≥ 40 kg and adults: Dose does not exceed 400 mg per week for the first 4 doses*, then 200 mg once weekly;
      ii. For pediatric members weighing 15 kg to < 40 kg: Dose does not exceed 200 mg per week for the first 4 doses*, then 200 mg once every 2 weeks.

**Loading doses not permitted if previously receiving Benlysta for treatment of SLE*

Approval duration: 12 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member meets one of the following (a or b):
   a. For SLE: member is responding positively to therapy;
   b. For LN: member is responding positively to therapy as evidenced by one of the following (i, ii, or iii):
      i. Reduced level of proteinuria measured by UPCR ≤ 0.5 mg/mg from baseline with low dose steroids (e.g., prednisone);
      ii. No reduction from baseline in eGFR of greater than 20% with low dose steroids (e.g., prednisone);
      iii. eGFR ≥ 60 ml/min/1.73 m^2 with low dose steroids (e.g., prednisone);
3. Prescribed in in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate);

4. Benlsyta is not prescribed concurrently with Lupkynis® or a biologic (e.g., rituximab, Saphnelo®);
5. If request is for a dose increase, request meets one of the following (a or b):
   a. IV: New dose does not exceed 10 mg/kg every 4 weeks;
   b. SC: New dose does not exceed(i or ii):
      i. For pediatric members weighing ≥ 40 kg and adults: 200 mg once weekly;
      ii. For pediatric members weighing 15 kg to < 40kg: 200 mg once every 2 weeks;

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Refer to PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

B. Autoantibody negative SLE.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ANA: anti-nuclear antibody
Anti-dsDNA: anti-double-stranded DNA
Anti-Sm: anti-Smith
DNA: deoxyribonucleic acid
FDA: Food and Drug Administration
LN: lupus nephritis
SC: subcutaneous
SLE: systemic lupus erythematosus

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
glucocorticoids (e.g., prednisone)	Varies	Varies
antimalarial agents (e.g., hydroxychloroquine, chloroquine)	Varies	Varies
non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): previous anaphylaxis to belimumab
- Boxed warning(s): none reported

Appendix D: Autoantibody Positive Versus Negative SLE
Only one of the five Benlysta pivotal trials included patients with autoantibody negative SLE; no significant differences between any of the Benlysta groups and the placebo group were observed. However, on further analysis Benlysta appeared to offer benefit to a subgroup of autoantibody positive patients. Benlysta's efficacy was confirmed in the remaining four trials which included only autoantibody positive patients. Because of the apparent lack of efficacy in autoantibody negative patients, Benlysta coverage will not be authorized for patients with autoantibody negative SLE.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

SLE, Lupus Nephritis	• IV:
	  ○ 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter
	• SC:
	  ○ For SLE:
	  ▪ Pediatric patients weighing ≥ 40kg and adults: 200 mg once weekly
	  ▪ Pediatric patients weighing 15kg to < 40kg: 200 mg once every 2 weeks
	  ○ For LN:
	  ▪ Pediatric patients weighing ≥ 40kg and adults: 400 mg once weekly for 4 doses, then 200 mg once weekly
	  ▪ Pediatric patients weighing 15 kg to < 40 kg: 200 mg once weekly for 4 doses, then 200 mg once every 2 weeks
	• Transition from IV to SC therapy*:
	  ○ For SLE: May transition from IV to SC therapy any time; administer first SC dose 1 to 4 weeks after the last IV dose
	  ○ For LN: May transition from IV to SC therapy after completing at least 2 IV doses; administer first SC dose 1 to 2 weeks after the last IV dose
		IV: 10 mg/kg/dose
		SC: 200 mg/week

VI. Product Availability

- Single-dose vial: 120 mg and 400 mg lyophilized powder for reconstitution
- Single-dose prefilled autoinjector/syringe: 200 mg/mL

VII. References

1. Benlysta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; June 2025. Available at http://www.benlysta.com. Accessed July 25, 2025.

2. 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(1S):S1-S69. 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;0:1–10. doi:10.1136/annrheumdis-2019-215089.
3. 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.
4. Fanouriakis A, Kostopoulou M, Andersen J, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis. 2024;83(1):1529.
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; 64:2677.
6. Weening J, Vivette D, Schwartz M, et al. The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. JASN February 2004, 15(2)241-250.
7. 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.* 2018;57:e1-e45. doi:10.1093/rheumatology/kex286.
8. Furie R, Rovin B, Houssiau F, et al. Two-year randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med*. 2020;3838(12):1117-1128. doi: 10.1056/NEJMoa2001180.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0490	Injection, belimumab, 10 mg

Reviews, Revisions, and Approvals	Date
added prescriber requirement, removed requirement to confirm lack of chronic infection treatment, expanded list of accepted autoantibodies; references reviewed and updated.	05/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019
3Q 2020 annual review: labeled age updated from adults down to age 5 and older; antiphospholipid antibody added to examples of SLE antibodies; added that concurrent standard therapy be continued in the continued approval section; references reviewed and updated.	08/2020
Added criteria to reflect new indication for lupus nephritis in adults	04/2021
2Q 2022 annual review: references reviewed and updated.	04/2022

Reviews, Revisions, and Approvals	Date
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023
2Q 2024 annual review: added exclusion for concurrent treatment with Lupkynis or a biologic for all indications; references reviewed and updated.	04/2024
2Q 2025 annual review: RT4: updated SLE dosing for SC to reflect expanded indication to patients 5+ years old; revised FDA Approved Indication(s) section to remove "autoantibody positive" from SLE indication per updated FDA labeling (no change to criteria); clarified SLE SC dosing for weight ≥ 40 kg applies to pediatric members; references reviewed and updated.	04/2025
RT4: updated LN criteria and section V dosage/administration to reflect newly approved SC autoinjector dosing for pediatric patients; modified initial approval duration from 6 months to 12 months as this is a maintenance medication for a chronic condition.	07/2025