

Date Effective: 9/2017
Reviewed: 9/2017, 12/2018, 11/2019, 9/2020, 01/2021, 4/2021, 01/2022, 9/2022, 01/2023, 12/2023, 01/2024, 08/2024, 03/2025, 02/2026
Pharmacy Scope (SQ): Medicaid
Medical Scope (IV): Medicaid, Commercial, Medicare

## **BENLYSTA (belimumab)** **Intravenous**

### **POLICY**

#### **Summary of Evidence**

Clinical trials evaluating the efficacy and safety of Benlysta in patients with SLE have demonstrated its effectiveness as an adjunctive therapy. Key findings from pivotal trials, such as BLISS-52 and BLISS-76, have shown that Benlysta, in combination with standard therapy, significantly improves disease activity and reduces the risk of severe lupus flares compared to placebo. Benlysta met its primary endpoints in these trials, demonstrating a higher response rate, reduced disease activity, and a decreased requirement for corticosteroids. Adverse events associated with Benlysta are generally mild to moderate in severity and include infusion reactions, infections, and nausea.

#### ***Initial Criteria:***

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

#### **Systemic Lupus Erythematosus (SLE)**

- Member is 5 years of age or older\*; **AND**
- Member has documented diagnosis of active SLE **AND**
- Member has one of the following:
  - Safety of Estrogen in Lupus National Assessment -Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 6-12; **OR**
  - British Isles Lupus Assessment Group (BILAG) B organ domain score  $\geq 2$ ; **AND**
- Member has failed to respond adequately to at least two (2) standard therapies such as anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, or immunosuppressives (excluding intravenous cyclophosphamide); **AND**
- Used in combination with standard therapy (e.g. anti-malarials, corticosteroids, nonsteroidal anti-inflammatory drugs, immunosuppressives); **AND**
- Member must not have an active infection; **AND**
- Member has not received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**
- Will not be used in combination with Lupkynis (voclosporin) or Saphnelo (anifrolumab); **AND**
- Member does not have any of the following exclusion criteria:
  - Severe active central nervous system lupus
  - Individuals who are on other biologics

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## Lupus Nephritis

- Member is 5 years of age or older\*\*; **AND**
- Member has active lupus nephritis Class III, IV, or V as confirmed by renal biopsy; **AND**
- Member 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 is provided: urine protein:creatinine ratio (uPCR), estimated glomerular filtration rate (eGFR), or urine protein; **AND**
- Used in combination with standard therapy (e.g., anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives); **AND**
- Member must not have an active infection; **AND**
- Member has not received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**
- Will not be used in combination with Lupkynis (voclosporin) or Saphnelo (anifrolumab); **AND**
- Member does not have any of the following exclusion criteria:
  - Severe active central nervous system lupus
  - Individuals who are on other biologics; **AND**

\*Benlysta 200mg/ml auto-injector for subcutaneous injection (not prefilled syringe) is ~~only~~ indicated for the treatment of SLE in members that are 5 years of age and older that weigh at least 15kg.

\*\*Benlysta 200mg/mL subcutaneous injection (auto-injector and prefilled syringe) is indicated for the treatment of SLE and lupus nephritis in members 18 years of age and older.

### *Continuation of Therapy Criteria:*

- Meets all initial criteria and is tolerating treatment; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: depression, suicidal thoughts, serious infections, signs or symptoms of progressive multifocal leukoencephalopathy (PML), malignancy, severe hypersensitivity reactions/anaphylaxis, serious infusion reactions, etc.; **AND**

### **SLE:**

- Adequate documentation of disease stability and/or improvement as indicated by one or more of the following when compared to pre-treatment baseline:
  - Improvement in the SELENA-SLEDAI score of  $\geq 4$  points; **OR**
  - No new BILAG-A organ domain score or 2 new BILAG-B organ domain scores; **OR**
  - No worsening ( $<30$ -point point increase) in Physician's Global Assessment (PGA) score; **OR**
  - Seroconverted (negative) or had a 20% reduction in autoantibody level; **OR**

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**Lupus Nephritis:**

- Adequate documentation of disease stability and/or improvement as indicated by one or more of the following when compared to pre-treatment baseline:
  - Urine protein:creatinine ratio (uPCR); **OR**
  - Estimated glomerular filtration rate (eGFR); **OR**
- Urine protein

**Coverage Durations:**

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

**Policy Rationale:**

Benlysta was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Benlysta according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

**Pharmacy Quantity Limit and Dosing:**

Benlysta 200mg/ml subcutaneous injection has a quantity limit of 4 injections per 28 days (daily dose of 0.143), with a post-limit loading dose for of 8 injections per 28 days (daily dose of 0.286) for a diagnosis of Lupus Nephritis only.

Benlysta 200mg/ml auto-injector for subcutaneous injection (not prefilled syringe) is indicated for the treatment of SLE in patients that are 5 years of age and older and weigh at least 15kg. Benlysta 200mg/mL subcutaneous injection (auto-injector and prefilled syringe) is indicated for the treatment of SLE and lupus nephritis in patients 18 years of age and older.

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Indication	Dose (subcutaneous)
SLE	<p><b><u>Patients 5 years of age and older (Auto-injector only):</u></b></p> <p><u>15 kg to &lt;40 kg: 200 mg once every 2 weeks.</u></p> <p><u>≥ 40 kg: 200 mg once weekly</u></p> <p><b><u>Adults (Auto-injector or prefilled syringe):</u></b></p> <p><u>200 mg once weekly</u></p>
Lupus Nephritis	<p><b><u>Adults (Auto-injector or prefilled syringe):</u></b></p> <p>Loading dose: 400mg once weekly for 4 doses</p> <p>Maintenance dose: 200mg once weekly</p>

**Medical Quantity Limit and Dosing:**

Indication	Dose	Maximum dose (1 billable unit = 10 mg)
<b>SLE or Lupus Nephritis</b>	<u>Loading Dose:</u> 10 mg/kg intravenously (by a healthcare provider) every 2 weeks x 3 doses (days 1, 15 and 29)	<u>Loading Dose (on days 1, 15 and 29):</u>  360 billable units per 29 days
	<u>Maintenance Dose:</u> 10 mg/kg intravenously (by a healthcare provider) every 4 weeks	<u>Maintenance Dose:</u>  120 billable units per 28 days

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J0490	Injection, belimumab, 10mg

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## References:

1. Benlysta [package insert]. Rockville, MD; Human Genome Sciences/GlaxoSmithKline; June 2025. Accessed January 2026.
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. 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 SepOct;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 March 2019.
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.

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13. Wisconsin Physician Service Insurance Corp. Local Coverage Determination (LCD): Drugs and Biologics (Non-chemotherapy) (L34741). Centers for Medicare & Medicare Services. Updated on 05/24/2018 with effective dates 06/01/2018. Accessed March 2019.