Corporate Medical Policy: Systemic Lupus Erythematosus (SLE) and Lupus Nephritis (LN) Targeted Therapies **"Notification"** **POLICY EFFECTIVE OCTOBER 1, 2026**

Restricted Product(s):

- anifrolumab-fnia (Saphnelo®) intravenous infusion or subcutaneous injection for administration by a healthcare professional
- anifrolumab-fnia (Saphnelo® Pen) subcutaneous injection for administration by a healthcare professional
- belimumab (Benlysta®) intravenous infusion and subcutaneous injection for administration by a healthcare professional
- obinutuzumab (Gazyva®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- Anifrolumab-fnia (Saphnelo®, Saphnelo® Pen)
  - For the treatment of adults with moderate to severe systemic lupus erythematosus (SLE) who are receiving standard therapy
  - Limitations of use: Efficacy has not been evaluated for severe active lupus nephritis or severe active central nervous system lupus
- Belimumab (Benlysta®)
  - For the treatment of patients 5 years of age and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy
  - For the treatment of patients 5 years of age and older with active lupus nephritis (LN) who are receiving standard therapy
  - Limitations of use: Efficacy has not been evaluated for severe active central nervous system lupus
- Obinutuzumab (Gazyva®)
  - For the treatment of adults with active lupus nephritis (LN) who are receiving standard therapy

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient has a clinical diagnosis of systemic lupus erythematosus (SLE) **[medical record documentation required]**; **AND**
2. If the request is for **anifrolumab-fnia (Saphnelo, Saphnelo Pen)**, then ALL of the following:
   a. The patient is 18 years of age or older; **AND**
   b. The patient has autoantibody-positive SLE (e.g., presence of anti-nuclear antibodies [ANA], double stranded DNA antibodies [anti-dsDNA], anti-Smith antibodies [anti-Sm], etc.) **[medical record documentation required]**; **AND**

c. The patient has active disease while on standard therapy for SLE (e.g., corticosteroids, anti-malarials [hydroxychloroquine, chloroquine], mycophenolic acid analogs, non-steroidal anti-inflammatory drugs [NSAIDs], non-biologic immunosuppressants [azathioprine, methotrexate, cyclosporine, oral cyclophosphamide]) alone or as combination therapy **[medical record documentation required]**; **AND**
d. ONE of the following:
    i. The patient will be receiving the requested agent in combination with hydroxychloroquine **[medical record documentation required]**; **OR**
    ii. The patient has an FDA labeled contraindication or clinical intolerance to hydroxychloroquine **[medical record documentation required]**; **AND**
e. ONE of the following:
    i. The patient has tried and had an inadequate response to belimumab (Benlysta) **[medical record documentation required]**; **OR**
    ii. The patient has an intolerance or hypersensitivity to belimumab (Benlysta) **[medical record documentation required]**; **OR**
    iii. The patient has an FDA labeled contraindication to belimumab (Benlysta) **[medical record documentation required]**; **OR**
    iv. The prescriber has submitted written clinical rationale to support that the use of belimumab (Benlysta) is not clinically appropriate for the patient **[medical record documentation required]**; **AND**
f. The patient does NOT have severe active lupus nephritis OR severe active central nervous system lupus; **AND**

3. If the request is for **belimumab (Benlysta)**, then ALL of the following:
    a. The patient is 5 years of age or older; **AND**
    b. ONE of the following:
        i. The patient has autoantibody-positive SLE (e.g., presence of anti-nuclear antibodies [ANA], anti-double stranded DNA antibodies [anti-dsDNA], anti-Smith antibodies [anti-Sm], etc.) **[medical record documentation required]**; **AND**
            1. The patient has active disease while on standard therapy for SLE (e.g., corticosteroids, anti-malarials [hydroxychloroquine, chloroquine], mycophenolic acid analogs, non-steroidal anti-inflammatory drugs [NSAIDs], non-biologic immunosuppressants [azathioprine, methotrexate, cyclosporine, oral cyclophosphamide]) alone or as combination therapy **[medical record documentation required]**; **OR**
        ii. The patient has biopsy-proven active Class III, IV, and/or Class V lupus nephritis (LN) **[medical record documentation required]**; **AND**
            1. The patient will be receiving the requested agent in combination with a standard immunosuppressive therapy regimen for active LN (e.g., azathioprine, cyclophosphamide, glucocorticoids, mycophenolic acid analogs, etc.) **[medical record documentation required]**; **AND**
    c. ONE of the following:
        i. The patient will be receiving the requested agent in combination with hydroxychloroquine **[medical record documentation required]**; **OR**

ii. The patient has an FDA labeled contraindication or clinical intolerance to hydroxychloroquine **[medical record documentation required]**; **AND**

d. The patient does NOT have severe active central nervous system lupus; **AND**

e. ONE of the following:

i. The patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:

1. Inability to self-administer the medication; **AND**
2. Lack of caregiver or support system for assistance with administration of self-administered products; **OR**

ii. The prescriber has submitted written clinical rationale to support the use of the provider-administered formulation over a self-administered formulation **[medical record documentation required]**; **AND**

4. If the request is for **obinutuzumab (Gazyva)**, then ALL of the following:

a. The patient is 18 years of age or older; **AND**

b. The patient has biopsy-proven active Class III, IV, and/or Class V lupus nephritis (LN) **[medical record documentation required]**; **AND**

c. The patient will be receiving the requested agent in combination with a standard immunosuppressive therapy regimen for active LN (e.g., azathioprine, cyclophosphamide, glucocorticoids, mycophenolic acid analogs, etc.) **[medical record documentation required]**; **AND**

d. ONE of the following:

i. The patient will be receiving the requested agent in combination with hydroxychloroquine **[medical record documentation required]**; **OR**

ii. The patient has an FDA labeled contraindication or clinical intolerance to hydroxychloroquine **[medical record documentation required]**; **AND**

5. The patient will NOT be using the requested medication in combination with voclosporin (Lupkynis) or another biologic immunomodulator agent (e.g., belimumab [Benlysta], obinutuzumab [Gazyva], anifrolumab-fnia [Saphnelo, Saphnelo Pen], a rituximab product, etc.) for the same indication; **AND**
6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist, rheumatologist) or has consulted with a specialist in the area of the patient's diagnosis; **AND**
7. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
8. If the request is for Benlysta, Saphnelo, or Saphnelo Pen:

a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has experienced clinical benefit with the requested medication (e.g., disease remission, reduction in flares, reduction in corticosteroid dose, decrease of anti-dsDNA titer, improvement in organ-specific manifestations [e.g., hematologic, musculoskeletal, neuropsychiatric, vascular, etc.]) **[medical record documentation required]**; **AND**
4. For patients with a diagnosis of lupus nephritis:
    a. The request is for belimumab (Benlysta) or obinutuzumab (Gazyva); **AND**
    b. The patient has achieved stabilization or improvement in BOTH of the following **[medical record documentation required]**:
        i. Proteinuria (i.e., urine protein:creatinine ratio [UPCR] ≤0.7 g/g); **AND**
        ii. Kidney function (i.e., an estimated glomerular filtration rate [eGFR] ≥ 60 mL/min/1.73m^2 or no decrease in eGFR more than 20% from baseline); **AND**
5. ONE of the following **[medical record documentation required]**:
    a. The patient is currently being treated with and will continue receiving hydroxychloroquine; **OR**
    b. The patient has an FDA labeled contraindication or clinical intolerance to hydroxychloroquine; **AND**
6. If the request is for belimumab (Benlysta), ONE of the following:
    a. The patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:
        i. Inability to self-administer the medication; **AND**
        ii. Lack of caregiver or support system for assistance with administration of self-administered products; **OR**
    b. The prescriber has submitted written clinical rationale to support the use of the provider-administered formulation over a self-administered formulation **[medical record documentation required]**; **AND**
7. The patient will NOT be using the requested medication in combination with voclosporin (Lupkynis) or another biologic immunomodulator agent (e.g., belimumab [Benlysta], obinutuzumab [Gazyva], anifrolumab-fnia [Saphnelo, Saphnelo Pen], a rituximab product, etc.) for the same indication; **AND**
8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist, rheumatologist) or has consulted with a specialist in the area of the patient's diagnosis; **AND**
9. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
10. If the request is for Benlysta, Saphnelo, or Saphnelo Pen:

a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

Note: Obinutuzumab (Gazyva) may require authorization for oncology related indications; please refer to our Prior Review and Limitations Page https://www.bcbsnc.com/providers/prior-authorization/prescription-drugs/commercial-drug-search

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
anifrolumab-fnia (Saphnelo®, Saphnelo® Pen) intravenous (IV) infusion, subcutaneous (SC) injection	Moderate to severe SLE in adults on standard therapy	IV: 300 mg every 4 weeks SC: 120 mg every week	J0491	6,240
belimumab (Benlysta®) intravenous (IV) infusion, subcutaneous (SC) injection	Active SLE in patients ≥ 5 years old on standard therapy Active LN in patients ≥ 5 years old on standard therapy	IV: 10 mg/kg at 2-week intervals for the first 3 doses, then at 4-week intervals thereafter SC: **Active SLE**: • 5 to < 18 years old (autoinjector only): ○ 15 to < 40 kg: 200 mg once every 2 weeks ○ ≥ 40 kg: 200 mg once weekly • ≥ 18 years old: 200 mg once weekly **Active LN**: • 5 to < 18 years old (autoinjector only):	IV: J0490 SC: C9399** J3490** J3590**	IV: Initial: 1,500 Continuation: 1,300 SC: Initial: 11,200 Continuation: 10,400

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		○ 15 to < 40 kg: 200 mg once weekly for 4 doses, then 200 mg once every 2 weeks ○ ≥40 kg: 400 mg (two 200 mg injections) once weekly for 4 doses, then 200 mg once weekly • ≥18 years old: 400 mg (two 200 mg injections) once weekly for 4 doses, then 200 mg once weekly		
obinutuzumab (Gazyva®) intravenous (IV) infusion	Active LN in adults on standard therapy	IV: 1,000 mg at the initial infusion (1st dose), then on week 2 (2nd dose), week 24 (3rd dose), week 26 (4th dose), and every 6 months thereafter (beginning 6 months after 4th dose)	J9301	Initial: 500 Continuation: 200

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

***Site of Care Medical Necessity Criteria [NOTE: Not applicable for obinutuzumab (Gazyva) requests]**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**

   c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
   d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
   e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
   f. Re-initiation of therapy, defined as ONE of the following:
      i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
      ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
   g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. 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(9):1400-1412.
2. Fanouriakis A, Kostopoulou M, Anders HJ, et al. EULAR recommendations for the management of systemic lupus erythematosus with kidney involvement: 2025 update. *Ann Rheum Dis*. 2026;85(1):75-90.
3. 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(1 suppl):S1-S69.
4. Mikdashi J, Nived O. Measuring disease activity in adults with systemic lupus erythematosus: the challenges of administrative burden and responsiveness to patient concerns in clinical research. *Arthritis Res Ther*. 2015;17(1):183.
5. Sammaritano LR, Askanase A, Bermas BL, et al. 2024 American College of Rheumatology guideline for the screening, treatment, and management of lupus nephritis. *Arthritis Care Res*. 2025;77(5):565-585.
6. Sammaritano LR, Askanase A, Bermas BL, et al. 2025 American College of Rheumatology guideline for the treatment of systemic lupus erythematosus. *Arthritis Care Res*. 2026;78(7):815-839.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

October 2026: Original medical policy criteria issued. Consolidated “Belimumab (Benlysta)”, “Anifrolumab-fnia (Saphnelo, Saphnelo Pen)”, and “Obinutuzumab (Gazyva)” medical policies into the following “Systemic Lupus Erythematosus (SLE) and Lupus Nephritis (LN) Targeted Therapies” medical policy. Reformatted SLE clinical diagnostic criteria to remove reference to ACR classification criteria and adjusted autoantibody positive verbiage to include different antibodies as examples. Restructured and adjusted LN continuation criteria to require stabilization or improvement in both proteinuria and kidney function with associated laboratory parameters. Added Lupkynis and listed other examples of biologic immunomodulators not to be used in combination for the same indication within initial and continuation criteria for SLE and LN. For Benlysta and Saphnelo/Saphnelo Pen, added requirement for combination use with hydroxychloroquine within initial and continuation criteria, adjusted list of standard SLE therapy examples to include mycophenolic acid analogs, and added specialist requirement within initial and continuation criteria. For Benlysta, reformatted criteria for age and for active LN requiring standard immunosuppressive therapy, and added requirement that the patient does not have severe active CNS lupus per FDA label; for self-administration requirements within initial and continuation criteria, removed age specific references and option for patients with LN who have not yet received two IV doses to align with updated FDA label. For Benlysta subcutaneous formulations, added HCPCS codes C9399, J3490, and J3590 to dosing reference table for clarity. For Gazyva, removed autoantibody positive requirement, adjusted LN class verbiage, and reformatted hydroxychloroquine combination use requirement for consistency with no change to intent; within continuation criteria, applied general clinical benefit requirements and adjusted requirement for current treatment with a standard immunosuppressive LN therapy to current treatment with hydroxychloroquine. **Policy notification given 8/3/2026 for effective date 10/1/2026**.
*Further historical criteria changes and updates for Corporate Medical Policies for each individual drug are available upon request from Medical Policy and/or Corporate Pharmacy.