Washington State Health Care Authority

# Neuromuscular Agents – Lupus Agents

## Medical policy no. 99.40.20-1 Effective Date: 6/1/2024

***Note:*** *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

*To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx*

### Medical necessity

| Drug | Medical Necessity |
|---|---|
| Belimumab (Benlysta)<br>Voclosporin (Lupkynis) | **Neuromuscular Agents- Lupus Agents** may be considered medically necessary in patients who meet the criteria described in the clinical policy below.<br><br>If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health. |

### Clinical policy:

| Clinical Criteria | |
|---|---|
| **Lupus Nephritis**<br>Belimumab (Benlysta)<br>Voclosporin (Lupkynis) | Belimumab (Benlysta) may be approved when all the following criteria are met:<br>1. Patient is 5-17 years old and will be receiving IV infusions; **OR**<br>2. Patient is 18 years of age or older and will be receiving either IV infusions or subcutaneous injections; **AND**<br>3. Prescribed by, or in consultation with a rheumatologist or nephrologist; **AND**<br>4. Diagnosis of active class III or IV lupus nephritis with or without class V lupus nephritis confirmed by renal biopsy; **AND**<br>5. Patient will continue receiving standard of care treatment for lupus nephritis (e.g., corticosteroids and immunosuppressants); **AND**<br>6. Baseline assessments of the following measurements are completed:<br>a. Urinary protein to creatinine ratio; **OR**<br>b. Estimated Glomerular Filtration Rate (eGFR); **AND**<br>7. Will not be used in combination with voclosporin |

| | |
|---|---|
| | Voclosporin (Lupkynis) may be approved when all the following criteria are met:<br>8. Criteria 3,4 and 6 is met; **AND**<br>9. Patient is 18 years of age or older; **AND**<br>10. Laboratory results showing estimated glomerular filtration rate (eGFR) > 45 mL/min/$m^2$**; AND**<br>11. Patient will continue taking mycophenolate and a corticosteroid; **AND**<br>12. Will not be used in combination with tacrolimus, cyclophosphamide or belimumab; **AND**<br>13. Treatment with belimumab used for lupus nephritis for a minimum of at least six months has been ineffective, contraindicated, or not tolerated.<br><br>If ALL criteria are met, the request will be authorized for **12 months.** |
| | **Criteria (Reauthorization)**<br>Belimumab (Benlysta) or Voclosporin (Lupkynis) may be approved when all the following criteria are met:<br><br>1. Criteria 5 **OR** 10 is met; **AND**<br>2. Criteria 7 **OR** 12 is met; **AND**<br>3. Documentation is submitted showing reassessment of baseline measurements demonstrating disease stability or a positive clinical response.<br><br>If ALL criteria are met, the request will be authorized for **12 months.** |
| **Systemic Lupus Erythematosus (SLE)**<br>Belimumab (Benlysta) | Belimumab (Benlysta) may be approved when all the following criteria are met:<br>1. Patient is 5-17 years old and will be receiving IV infusions; **OR**<br>2. Patient is 18 years of age or older and will be receiving either IV infusions or subcutaneous injections; **AND**<br>3. Prescribed by, or in consultation with rheumatologist or nephrologist; **AND**<br>4. Diagnosis of SLE; **AND**<br>5. Laboratory results showing active disease and autoantibody-positive tests (e.g., anti-nuclear antibody [ANA] or anti-double stranded DNA [anti-dsDNA]); **AND**<br>6. Baseline assessments using one of the following functional assessment tools are completed:<br>a. SLE Index Score (SIS); **OR**<br>b. British Isles Lupus Assessment Group (BILAG); **OR**<br>c. Systemic Lupus Activity Measure (SLAM); **OR**<br>d. Systemic Lupus Erythematosus Disease Activity Score (SLEDAI); **OR** |

| | |
|---|---|
| | e. Physicians Global Assessment (PGA); **OR**<br>f. Systemic Lupus International Collaborating Clinic (SLICC) Damage Index; **OR**<br>g. Urinary protein to creatinine ratio; **OR**<br>h. Estimated Glomerular Filtration Rate (eGFR); **AND**<br>7. Patient will continue receiving standard hydroxychloroquine therapy for SLE with at least ONE of the following medications:<br>a. An NSAID<br>b. A corticosteroid (e.g., prednisone, methylprednisolone)<br>c. An immunosuppressant (e.g., azathioprine, mycophenolate, cyclophosphamide<br><br>If ALL criteria are met, the request will be authorized for **12 months.** |
| | **Criteria (Reauthorization)**<br>Belimumab (Benlysta) may be approved when all the following criteria are met:<br><br>1. Criteria 7 is met; **AND**<br>2. Documentation is submitted showing reassessment of baseline measurements demonstrating disease stability or a positive clinical response.<br><br>If ALL criteria are met, the request will be authorized for **12 months.** |

## Dosage and quantity limits

| Drug | Indication | FDA Approved Dosing | Dosage Form and Quantity Limit |
|---|---|---|---|
| **Benlysta** | Lupus Nephritis | IV: 10 mg/kg IV over 1 hour every 2 weeks for the first 3 doses and every 4 weeks thereafter<br><br>SubQ: 400 mg (two 200-mg) injections subQ once weekly for 4 doses, then 200 mg subQ once weekly thereafter | • 120 mg vial<br>• 400 mg vial<br>• 200 mg/mL auto-injector: 8 syringes for first four doses then 4 syringes/28 days |
| **Benlysta** | SLE | IV: 10 mg/kg IV over 1 hour every 2 weeks for the first 3 doses and every 4 weeks thereafter<br><br>SubQ: 200 mg subQ once weekly | • 120 mg vial<br>• 400 mg vial<br>• 200 mg/mL auto-injector: 4 syringes/28 days |
| **Lupkynis** | Lupus Nephritis | 23.7 mg orally twice daily | • 7.9 mg capsules: 6 capsules per day |

## Coding:

| HCPCS Code | Description |
|---|---|
| J0490 | Injection, belimumab, 10 mg |

## Background:

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease which can affect multiple organs or organ systems in the body and is the most common form of lupus. It is characterized by fatigue, skin rashes, fevers, and pain or swelling in the joints. The 2019 European Alliance of Associations for Rheumatology (EULAR) Update recommends management of SLE using hydroxychloroquine, glucocorticoids, immunosuppressive therapies and cyclophosphamide with add-on belimumab for patients do not have an adequate response.

Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE). About half of the patients with SLE will develop LN with between 10-30% of those patients will progress to kidney failure. Per the American College of Rheumatology (ACR), treatment for LN should be based off the International Society of Nephrology/Renal Pathology Society (ISN/RPS) LN classification. Class I and II do not usually require immunosuppressive treatment whereas Class III and IV without or without Class V require aggressive therapy with glucocorticoids and immunosuppressive agents.

Belimumab (Benlysta) is a B-lymphocyte stimulator specific inhibitor indicated for the treatment of patient aged 5 years and older with active, autoantibody-positive, systemic SLE who are receiving standard therapy and adult patients with LN who are receiving standard therapy. The safety and efficacy of belimumab was evaluated in two randomized, double-blind, placebo-controlled, phase III studies involving patients aged 18 and older with SLE (BLISS52 and BLISS-76 study). The design of these studies was based on the results of a phase II study which identified that patients who were autoantibody-positive had a better response to belimumab. As a result, BLISS-52 and BLISS-76 limited the study population to only include autoantibody-positive SLE patients. Patients were on a standard of care SLE treatment regimen comprising of at least one of the following: corticosteroids, antimalarials, nonsteroidal anti-inflammatory drugs (NSAIDS), and/or immunosuppressives (azathioprine, methotrexate, or mycophenolate). Patients with severe active lupus nephritis and severe central nervous system (CNS) lupus were excluded. Patients using other biologics including B-cell targeted therapies such as rituximab or intravenous cyclophosphamide in the previous six months were also excluded. BLISS-52 (N=865) and BLISS-76 (N=826) had similar designs except for duration. BLISS-76 was 76 weeks in duration and BLISS-52 was 52 weeks in length. Eligible patients had active SLE disease which was defined as a Safety of Estrogen in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI) score >6. Patients were randomly assigned to receive belimumab 1 mg/kg, 10 mg/kg, or placebo in addition to standard of care. The study medication was administered on Days 0, 14, 28, and then every 28 days for 48 weeks in BLISS-52 and 72 weeks in BLISS-76. In both BLISS-52 and BLISS-76, the proportion of SLE patients achieving a SLE Responder Index-4 (SRI-4) response was significantly higher in the belimumab 10 mg/kg group than placebo while the effect on SRI-4 was not consistently significantly different for the belimumab 1 mg/kg group.

The safety and efficacy of Benlysta in patients with lupus nephritis was evaluated in a 104 week, randomized, double-blind, placebo-controlled trial that included 448 patients with active proliferative and/or membranous

lupus nephritis. Patients had to be at least 18 years of age and have an ANA positive SLE that fulfilled the ACR classification criteria. Patients were required to have a urine protein to creatinine ratio of 1 or more and biopsy-proven lupus nephritis ISN/RPS class III, IV, or V. Induction therapy had to be initiated within 60 days before randomization and therapies had to include either induction with glucocorticoids in combination with MMF or IV cyclophosphamide, followed by MMF or AZA for maintenance therapy. The primary efficacy endpoint was Primary Efficacy Renal Response (PERR) at week 104, defined as a response at Week 100 confirmed by a repeat measurement at week 104 of the following parameters: urine protein: creatinine ratio (uPCR) ≤0.7 g/g and estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m2 or no decrease in eGFR of >20% from pre-flare value. The major secondary endpoints included Complete Renal Response (CRR) (defined as a response at week 100 confirmed by a repeat measurement at week 104 of the following parameters: uPCR 10% from pre-flare value); PERR at week 52; and time to renal-related event or death (renal-related event defined as first event of end-stage renal disease, doubling of serum creatinine, renal worsening [defined by quantified increase in proteinuria and/or impaired renal function], or receipt of renal disease-related prohibited therapy due to inadequate lupus nephritis control or renal flare management).

The safety and efficacy of Lupkynis were investigated in a 52-week, randomized, double-blind, placebo-controlled trial in patients with a diagnosis of systemic lupus erythematosus and with International Society of Nephrology/Renal Pathology Society (ISN/RPS) biopsy proven active Class III or IV LN (alone or in combination with Class V LN) or Class V LN. A total of 357 patients with LN were randomized in a 1:1 ratio to receive either Lupkynis 23.7 mg twice daily or placebo. Patients in both arms received background treatment with MMF and corticosteroids. The primary efficacy endpoint was the proportion of patients achieving complete renal response at week 52. To be considered a responder, the patient must not have received more than 10 mg prednisone for ≥3 consecutive days or for ≥7 days in total during weeks 44 through 52. Patients who received rescue medication or withdrew from the study were considered non-responders. A higher proportion of patients in the Lupkynis arm than the placebo arm achieved complete renal response at week 52 (Lupkynis 40.8% vs placebo 22.5%, p <0.001). A higher proportion of patients in the Lupkynis arm than the placebo arm achieved complete renal response at week 24 (32.4% vs. 19.7%; odds ratio: 2.2; 95% CI: 1.3, 3.7). Time to UPCR of ≤0.5 mg/mg was shorter in the Lupkynis arm than the placebo arm (median time of 169 days vs. 372 days; hazard ratio: 2.0; 95% CI: 1.5, 2.7).

## References:


1. Benlysta Prescribing Information. GlaxoSmithKline LLC. February 2023.
2. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Annals of the Rheumatic Diseases 2019;78:736-745.
3. Lupkynis prescribing information. Aurinia Pharmaceuticals, Inc. January 2021.
4. 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 (BLISS-SC). Arthritis Rheumatol. 2017 May; 69 (5): 1016-1027.


## History

| Approved Date | Effective Date | Version | Action and Summary of Changes |
|---|---|---|---|
| 12/13/2023 | 06/01/2024 | 99.40.20-1 | Approved by DUR Board<br>New policy created |