09-J5000-51

Original Effective Date: 03/15/26

Reviewed: 08/12/26

Revised: 10/01/26

Subject: Lupus

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions
Definitions	Related Guidelines	Other	References	Updates

DESCRIPTION:

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of an unknown cause that can affect multiple systems including the musculoskeletal, renal, pulmonary, gastrointestinal, and hematologic systems. The etiology of SLE is not completely understood; however, many of the clinical manifestations are mediated directly or indirectly by antibody formation and the creation of immune complexes.

Diagnosis of SLE is based on classification criteria developed by the American Rheumatism Association now the American College of Rheumatology [ACR]) that uses history, physical examination, and laboratory data for diagnosis. Several disease activity instruments are used in clinical trials. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is comprised of 24 clinical and laboratory manifestations of SLE that are scored based on presence or absence in the previous 10 days. Organ involvement is weighted, and the final score can range from 0-105. A SLEDAI score of 6 or more has been shown to be consistent with active disease requiring therapy. The SLEDAI was modified in the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) trial; this modification, known as SELENA-SLEDAI added clarity to some of the definition of activity in the individual items but did not change the basic scoring system. A clinically meaningful difference has been reported to be an improvement of 7 points or a worsening of 8 points. The British Isles Lupus Assessment Group (BILAG) is an organ specific, 86 question assessment based on the healthcare provider's intention to treat. The assessor scores organ manifestations as improve (=1), same (=2), worse (=3), or new (=4) over the last month.

All patients with SLE should be evaluated for lupus nephritis (LN) at the time of initial diagnosis and then at least annually or upon an SLE flare. Proteinuria is usually the first sign leading to an LN diagnosis; patients may also exhibit hypertension, hematuria, or a decrease in kidney function (i.e. decreased eGFR). A kidney biopsy is used to confirm a diagnosis and stage the disease according to the classification revised by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) in 2003, as follows:

- Class I – Minimal mesangial lupus nephritis
- Class II – Mesangial proliferative lupus nephritis
- Class III – Focal lupus nephritis (active and chronic; proliferative and sclerosing)

- Class IV – Diffuse lupus nephritis (active and chronic; proliferative and sclerosing; segmental and global)
- Class V – Membranous lupus nephritis
- Class VI – Advanced sclerosis lupus nephritis

Anifrolumab-fnia (Saphnelo)

Saphnelo is the first type I interferon (IFN) receptor agonist to be FDA-approved and the first drug for SLE since 2011, when GlaxoSmithKline's Benlysta (belimumab) was approved. While Benlysta inhibits B-cell stimulating factor, Saphnelo binds to subunit 1 of the type I IFN receptor, blocking the activity of type I IFNs involved in regulating the inflammatory pathways implicated in SLE.

Saphnelo's efficacy and safety data were evaluated in 3 trials: MUSE (Trial 1; NCT01438489), TULIP-1 (Trial 2; NCT02446912), and TULIP-2 (Trial 3; NCT02446899). All 3 studies were randomized, double-blind, placebo-controlled trials in patients ≥18 years of age diagnosed with SLE according to the American College of Rheumatology (ACR) classification criteria (SLEDAI-2K score of 6 or greater) and who were receiving standard therapy (at least one of the following: oral corticosteroids (OCSs), antimalarials, and immunosuppressants [methotrexate, azathioprine, or mycophenolate mofetil]). Patients with severe active lupus nephritis or severe active CNS lupus were excluded.

Results from the trials were inconsistent: although MUSE and TULIP-2 met the primary endpoints, TULIP-1 failed to do so. Table 1 provides a summary of the results.

Table 1

Response at 52 Weeks for Anifrolumab-fnia 300 mg vs Placebo in Randomized Trials		
	BICLA response	SRI(4) response
TULIP-2 phase III trial (n=362)	47.8% vs 31.5%* mean difference, 16.3 (95% CI, 6.3 to 26.3)	55.5% vs 37.3%*^ mean difference, 18.2 (95% CI, 8.1 to 28.3)
TULIP-1 phase III trial (n=364)	37% vs 27%^^ difference, 10.1 (95% CI, 0.6 to 19.7)	36% vs 40% difference, -4.2 (95% CI, -14.2 to 5.8)
MUSE phase IIB trial (n=201)	53.5% vs 25.7%* OR, 3.42 (90% CI, 2.06 to 5.68)	51.5% vs 25.5%* OR, 3.08 (90% CI, 1.86 to 5.09)
*significant result		
^result not adjusted for multiple comparisons		
^^statistical significance not formally assessed		
KEY: BICLA, British Isles Lupus Assessment Group-based Composite Lupus Assessment; SRI(4), SLE Responder Index-4		

In pooled analyses of the TULIP-1 and TULIP-2 trials, anifrolumab (n=360) compared with placebo (n=366) was associated with a significantly lower annualized flare rate (0.51 vs 0.67; rate ratio, 0.75; 95% CI, 0.6 to 0.95), prolonged time to first flare (median time, 140 vs 119 days; HR 0.7; 95% CI, 0.55 to 0.89) and fewer patients with flares (33.6% vs 42.9%; difference, -9.3; 95% CI, -16.3 to -2.3). A flare was 1 or more new British Isles Lupus Assessment Group (BILAG)-2004 A or 2 or more new BILAG-2004 B domain scores compared with prior visit. Among patients who were receiving prednisone or equivalent 10 mg/day or more at baseline, a reduction to 7.5 mg/day or less was achieved by significantly more patients with anifrolumab compared with placebo in TULIP-2 (51.5% vs 30.2%; difference, 21.2 percentage points;

95% CI, 6.8 to 35.7) and MUSE (56.4% vs 26.6%), but not in TULIP-1 (41% vs 32%; difference, 8.9; 95% CI, -4.1 to 21.9).

In pooled results of all 3 trials, anifrolumab was associated with higher incidences of bronchitis (11% vs 5.2%) and herpes zoster (6.1% vs 1.3%).

Belimumab (Benlysta®) Injection

Belimumab (Benlysta) is a human monoclonal antibody that inhibits B lymphocyte stimulator protein (BLyS). In March 2011, belimumab was approved the US Food and Drug Administration (FDA) for the treatment of active, autoantibody positive systemic lupus erythematosus (SLE). Belimumab was originally approved as an intravenous injection, but a subcutaneous formulation was was approved in 2017. Belimumab should be used as an adjunct to standard therapy. SLE is a chronic inflammatory disease of unknown cause that can affect multiple systems including the musculoskeletal, renal, pulmonary, gastrointestinal, and hematologic systems. The etiology of SLE is not completely understood; however, many of the clinical manifestations are mediated directly or indirectly by antibody formation and the creation of immune complexes.

Voclosporin (Lupkynis)

Voclosporin (Lupkynis), a calcineurin inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in January 2021 for the treatment of adult patients with active lupus nephritis. Voclosporin inhibits the activation of T cells and can decrease the production of proinflammatory cytokines. It is structurally similar to cyclosporine A, differing in only one amino acid, which increases its potency and rate of elimination. Prior to approval of voclosporin, belimumab was the only approved drug for treatment of LN

The safety and efficacy of voclosporin were evaluated in a randomized controlled trial of patients with systemic lupus erythematosus and biopsy confirmed lupus nephritis (N=357; median age 31 years, 88% women). Patients were randomized to treatment with voclosporin (23.7 mg twice daily with adjustments as needed) in combination with mycophenolate mofetil (2 g/day target dose) and corticosteroids (IV methylprednisolone induction with oral taper to target prednisone dose of 2.5 mg/day) or placebo in combination with mycophenolate mofetil and corticosteroids. The primary endpoint was patients who achieved a complete renal response, defined as urine protein to creatinine ratio of 0.5 mg/mg or less AND estimated GFR (eGFR) of at least 60 mL/min/1.73 m(2), no decrease in baseline eGFR of greater than 20%, OR no treatment- or disease-related eGFR associated event (e.g., blood creatinine increased, creatinine renal clearance decreased, glomerular filtration rate decreased, serum creatinine increased, renal impairment, renal failure, or renal failure acute). Patients must not have received more than 10 mg prednisone for 3 or greater consecutive days or for 7 or greater days in total during weeks 44 through 52 to be considered a responder. Patients who received rescue medication or withdrew from the study were considered non-responders.

Treatment with voclosporin resulted in significantly higher proportion of patients achieving a complete renal response at both 24 weeks (32.4% vs 19.7%; OR 2.2, 95% CI 1.3 to 3.7) and 52 weeks (40.8% vs 22.5%; OR 2.7, 95% CI 1.6 to 4.3) compared to placebo in combination with mycophenolate mofetil and corticosteroids. The most common adverse reactions reported in clinical trials ≥10% included: decreased GFR, hypertension, diarrhea, headache, anemia, cough, and urinary tract infection. Decreases in GFR were mostly observed during the first 3 months of treatment with voclosporin and resolved with dosing modification (71%) or discontinuation (14%). Overall, hypertension was reported in 66 patients receiving voclosporin, but serious hypertension was limited to just 7 patients. Voclosporin does not appear to exhibit the cardiovascular and metabolic adverse effects seen in other CNIs, such as tacrolimus.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline 09-J5000-54, Drug Waste Reduction.

Site of Care: If belimumab (Benlysta) or anifrolumab-fnia (Saphnelo) are administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46, Site of Care Policy for Select Non-Oncology medications.

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary. This statement applies to belimumab (Benlysta) for subcutaneous administration and voclosporin (Lupkynis) only.

Anifrolumab-fnia (Saphnelo)

Initiation of anifrolumab-fnia (Saphnelo) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with systemic lupus erythematosus (SLE)
2. Member's disease is active as evidenced by Safety of Estrogens in Lupus Erythematosus National Assessment modification of the SLE Disease Activity Index (SELENA-SLEDAI) score of 6 or greater while on current regimen.
   NOTE: SELENA-SLEDAI scoring system can be located at www.rheumatology.org
3. Member is currently receiving standard of care SLE treatment including one or more of the following
   a. Corticosteroids (e.g., prednisone)
   b. Aspirin
   c. Non-steroidal anti-inflammatory drug (NSAID)
   d. Anti-malarials (e.g., hydroxychloroquine, chloroquine)
   e. Non-biologic immunosuppressants (e.g., azathioprine, methotrexate, cyclosporine, oral cyclophosphamide)
4. There is no evidence of active central nervous system lupus (e.g., psychosis, seizures, cerebrovascular accident) within the past 60 days
5. **ONE** of the following:
   a. Member has tried and had an inadequate response to belimumab (Benlysta) after at least a 6 month duration of therapy – documentation from the medical record or paid claims must be provided
   b. Member had persistent intolerable adverse effects with or hypersensitivity to belimumab (Benlysta) – the specific adverse effect or hypersensitivity must be specified
   c. Member has a contraindication to treatment with belimumab (Benlysta)
6. Anifrolumab is not administered concomitantly with belimumab (Benlysta) or other biologic DMARD therapies (e.g., abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), etanercept-szzs (Erelzi), golimumab (Simponi, Simponi Aria), and infliximab (Remicade)
7. Dose does not exceed
   a. IV: 300 mg once every 4 weeks
   b. SC: 120 mg once every week

Approval duration: 1 year

Continuation of anifrolumab-fnia (Saphnelo) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of SLE **OR** the member has previously met all indication-specific criteria
2. Member is receiving a beneficial response to treatment
3. Anifrolumab is not administered concomitantly with belimumab (Benlysta) or other biologic DMARD therapies (e.g., abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), etanercept-szzs (Erelzi), golimumab (Simponi, Simponi Aria), and infliximab (Remicade)
4. Dose does not exceed:
    a. IV: 300 mg once every 4 weeks
    b. SC: 120 mg once every week

Approval duration: 1 year

Belimumab (Benlysta®) Injection

Initiation of belimumab (Benlysta®) meets the definition of medical necessity when used for members diagnosed with **ANY** of the following conditions when ALL associated criteria are met:

1. Systemic lupus erythematosus (SLE)
    a. Member's disease is active as evidenced by Safety of Estrogens in Lupus Erythematosus National Assessment modification of the SLE Disease Activity Index (SELENA-SLEDAI) score of 6 or greater while on current regimen.
    NOTE: SELENA-SLEDAI scoring system can be located at www.rheumatology.org
    b. Member has a diagnosis of systemic lupus erythematosus (SLE) as confirmed by laboratory testing demonstrated the presence of autoantibodies [e.g., antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA) antibodies, anti-Smith (anti-Sm) antibodies, anti-Ro/SSA antibodies, anti-La/SSB antibodies]
    c. Member is currently receiving standard of care SLE treatment including one or more of the following
        i. Corticosteroids (e.g., prednisone)
        ii. Aspirin
        iii. Non-steroidal anti-inflammatory drug (NSAID)
        iv. Anti-malarials (e.g., hydroxychloroquine, chloroquine)
        v. Non-biologic immunosuppressants (e.g., azathioprine, methotrexate, cyclosporine, oral cyclophosphamide)
    d. There is no evidence of active central nervous system lupus (e.g., psychosis, seizures, cerebrovascular accident) within the past 60 days
    e. Belimumab is not used in combination with other biologic DMARD therapies (e.g., abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), etanercept-szzs (Ereizi), golimumab (Simponi, Simponi Aria), and infliximab (Remicade))
    f. Member is 5 years of age or older

g. The dose does not exceed **EITHER** of the following
    i. IV injection:
        1. First 6 weeks: 10 mg/kg every 2 weeks for 3 doses
        2. Thereafter: 10 mg/kg every 4 weeks
    ii. SC injection: 200 mg once weekly

2. Lupus Nephritis
    a. Member has biopsy-proven lupus nephritis (LN) of International Society of Nephrology/Renal Pathology Society (ISN/RPS) class III (focal lupus nephritis) or IV (diffuse lupus nephritis) with or without coexisting class V (membranous lupus nephritis), or pure class V lupus nephritis – documentation of biopsy results must be provided
    b. Belimumab will be used in combination with standard lupus nephritis therapy which must include BOTH of the following:
        i. A corticosteroid (includes any tapering doses of corticosteroids)
        ii. ANY of the following non-biologic immunosuppressants:
            - azathioprine
            - cyclophosphamide
            - leflunomide
            - mycophenolate mofetil or mycophenolate sodium
        iii.
    c. Belimumab is not used in combination with anifrolumab-fnia (Saphnelo), obinutuzumab (Gazyva), rituximab, or voclosporin (Lupkynis)
    d. Belimumab is is prescribed by, or in consultation with, a nephrologist or rheumatologist
    e. Member is 5 years of age or older
    f. The dose does not exceed **EITHER** of the following
        i. IV injection:
            1. First 6 weeks: 10 mg/kg every 2 weeks for 3 doses
            2. Thereafter: 10 mg/kg every 4 weeks
        ii. SC injection:
            1. First 4 weeks: 400 mg once weekly for 4 doses
            2. Thereafter: 200 mg once weekly

3. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets one of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. Dose does not exceed maximum FDA-approved dose and frequency

Approval duration: 1 year

Continuation of belimumab (Benlysta®) meets the definition of **medical necessity** when **ALL** of the following criteria are met:

1. Authorization or reauthorization for belimumab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of SLE, LN, or other FDA-approved or NCCN supported diagnosis, **OR** the member previously met **ALL** indication-specific initiation criteria
2. Member has demonstrated a beneficial response with belimumab therapy for the treatment of active systemic lupus erythematosus, lupus nephritis, or other FDA-approved or NCCN supported diagnosis
3. Belimumab is not used in combination with another biologic DMARD therapy (e.g., abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), certolizumab (Cimzia), etanercept (Enbrel), etanercept-szzs (Ereizi), golimumab (Simponi, Simponi Aria), and infliximab (Remicade))
4. If for lupus nephritis, belimumab is not used in combination with anifrolumab-fnia (Saphnelo), obinutuzumab (Gazyva), rituximab, or voclosporin (Lupkynis)
5. The dose does not exceed **EITHER** of the following:
    a. IV injection:10 mg/kg every 4 weeks
    b. SC injection: 200 mg once weekly

Approval duration: 1 year

<u>Voclosporin (Lupkynis)</u>

Initiation of voclosporin (Lupkynis) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Indication for use is lupus nephritis (LN)
2. Member has biopsy-proven lupus nephritis (LN) of International Society of Nephrology/Renal Pathology Society (ISN/RPS) class III (focal lupus nephritis) or IV (diffuse lupus nephritis) with or without coexisting class V (membranous lupus nephritis), or pure class V lupus nephritis – documentation of biopsy results must be provided
3. Voclosporin will be used in combination with standard lupus nephritis therapy which must include BOTH of the following:
    a. A corticosteroid (includes any tapering doses of corticosteroids)
    b. ANY of the following non-biologic immunosuppressants:
        i. azathioprine
        ii. cyclophosphamide
        iii. leflunomide
        iv. mycophenolate mofetil or mycophenolate sodium
4. Voclosporin is not used in combination with anifrolumab-fnia (Saphnelo), belimumab (Benlysta), rituximab, or obinutuzumab (Gazyva)
5. Voclosporin is prescribed by, or in consultation with, a nephrologist or rheumatologist
6. Member is 18 years of age or older
7. Dose does not exceed 23.7 mg twice daily

Approval duration:1 year

Continuation of voclosporin (Lupkynis) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of active lupus nephritis, **OR** the member has previously met all indication-specific criteria
2. Member has achieved a beneficial response to treatment with voclosporin
3. Voclosporin is not used in combination with anifrolumab-fnia (Saphnelo), belimumab (Benlysta), rituximab, or obinutuzumab (Gazyva)
4. Voclosporin is prescribed by or in consultation with a nephrologist or rheumatologist
5. Member is 18 years of age or older
6. Dose does not exceed 23.7 mg twice daily

Approval duration:1 year

DOSAGE/ADMINISTRATION:

FDA-approved

Anifrolumab-fnia (Saphnelo)

- 300 mg as an intravenous infusion over a 30-minute period every 4 weeks

Belimumab (Benlysta®) Injection

- Intravenous Administration
    - 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter. Reconstitute, dilute, and administer as an intravenous infusion over a period of 1 hour.
    - Consider administering premedication for prophylaxis against infusion reactions and hypersensitivity reactions.
- Subcutaneous Administration (18 years of age and older)
    - 200 mg once weekly.

Voclosporin (Lupkynis)

- 23.7 mg orally, twice a day.

Dose Adjustments

Anifrolumab-fnia (Saphnelo)

- None

Belimumab (Benlysta®) Injection

- None

Voclosporin (Lupkynis)

- If eGFR <60 mL/min/1.73 m2 and reduced from baseline by >20% and <30%, reduce the dose by 7.9 mg twice a day. Re-assess eGFR within two weeks; if eGFR is still reduced from baseline by >20%, reduce the dose again by 7.9 mg twice a day.

- If eGFR <60 mL/min/1.73 m2 and reduced from baseline by ≥30%, discontinue LUPKYNIS. Re-assess eGFR within two weeks; consider re-initiating LUPKYNIS at a lower dose (7.9 mg twice a day) only if eGFR has returned to ≥80% of baseline.
- For patients that had a decrease in dose due to eGFR, consider increasing the dose by 7.9 mg twice a day for each eGFR measurement that is ≥80% of baseline; do not exceed the starting dose.
- Patients with severe renal impairment: the recommended dose is 15.8 mg twice daily
- Patients with mild and moderate hepatic impairment: the recommended dose is 15.8 mg twice daily

Drug Availability

Anifrolumab-fnia (Saphnelo)

- Injection for IV infusion: 300 mg/2 mL (150 mg/mL) in a single-dose vial
- Injection for subcutaneous injection: 120 mg/0.8 mL in a single-dose prefilled syringe or single-dose autoinjector (SAPHNELO PEN)

Belimumab (Benlysta®) Injection

- IV infusion: 120 mg or 400 mg lyophilized powder in single-dose vials for reconstitution and dilution prior to intravenous infusion
- Subcutaneous injection: 200 mg/mL single-dose prefilled autoinjector or single-dose prefilled syringe

Voclosporin (Lupkynis)

- Capsules: 7.9 mg

PRECAUTIONS:

Boxed Warning

Anifrolumab-fnia (Saphnelo)

- None

Belimumab (Benlysta®) Injection

- None

Voclosporin (Lupkynis)

- Increased risk for developing malignancies and serious infections that may lead to hospitalization or death

Contraindications

Anifrolumab-fnia (Saphnelo)

- History of anaphylaxis with anifrolumab-fnia

Belimumab (Benlysta®) Injection

- Belimumab is contraindicated in persons who experienced a previous anaphylactic reaction when administered belimumab.

Voclosporin (Lupkynis)

- Patients concomitantly using strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)
- Known serious or severe hypersensitivity reaction

Precautions/Warnings

Anifrolumab-fnia (Saphnelo)

- Serious infections
- Hypersensitivity
- Malignancy
- Immunization: Avoid use of live or live-attenuated vaccines
- Not recommended for use with other biologic therapies

Belimumab (Benlysta®) Injection

- Mortality: more deaths were reported with belimumab than with placebo during the controlled phase of clinical trials.
- Serious infections: serious and sometimes fatal infections have been reported in persons receiving immunosuppressive agents, including belimumab. Use with caution in persons with chronic infections. Consider interrupting belimumab therapy if a member develops a new infection while on treatment.
- Progressive Multifocal Leukoencephalopathy (PML): Persons with new-onset or deteriorating neurological signs and symptoms should be evaluated for PML by an appropriate specialist. If PML is confirmed, considered discontinuing immunosuppressant therapy, including belimumab.
- Hypersensitivity reactions: serious and fata reactions have been reported. Belimumab should be administered by a healthcare provider prepared to manage anaphylaxis. Monitor members during and for an appropriate period of time after belimumab administration.
- Depression: depression and suicidality have been reported in belimumab studies. Members should be instructed to contact their healthcare provider f they experience new or worsening depression, suicidal thoughts, or other mood changes.
- Immunization: live vaccines should not be given concurrently with belimumab.

Voclosporin (Lupkynis)

- Nephrotoxicity (acute and/or chronic): May occur due to concomitant nephrotoxic drugs. Monitor renal function; consider dosage reduction
- Hypertension: May require antihypertensive therapy; monitor relevant drug interactions
- Neurotoxicity: Including risk of posterior reversible encephalopathy syndrome (PRES); monitor for neurologic abnormalities; reduce dosage or discontinue
- Hyperkalemia: Risk may be increased with other agents associated with hyperkalemia; monitor serum potassium levels.
- QT Prolongation: Consider obtaining electrocardiograms and monitoring electrolytes in patients at high risk.

- Immunizations: Avoid live vaccines.
- Pure Red Cell Aplasia: Consider discontinuation

BILLING/CODING INFORMATION:

HCPCS Coding

J0490	Injection, belimumab, 10 mg
J0491	Injection, anifrolumab-fnia, 1 mg
J8499	Prescription drug, oral, non chemotherapeutic, nos (voclosporin only)

ICD-10 Diagnosis Codes That Support Medical Necessity

M32.10-M32.19	Systemic lupus erythematosus with organ or system involvement
M32.8	Other forms of systemic lupus erythematosus
M32.9	Systemic lupus erythematosus, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Systemic lupus erythematosus is a systemic autoimmune disease than can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage.

RELATED GUIDELINES:

Obinutuzumab (Gazyva), 09-J2000-07

OTHER:

None

REFERENCES:

1. AstraZeneca. Saphnelo (anifrolumab) injection. 2021 [cited 10/8/21]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d6203302-2128-41a7-b0b4-0e6c0704d4dc/.
2. Aurinia Pharma. Lupkynis (voclosporin) capsule. 2025 [cited 11/26/25]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9f489295-1156-52c7-5fd0-5c4c52f9b813.
3. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 9/1/24]. Available from: http://www.clinicalpharmacology.com/.
4. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 9/1/24]. Available from: http://clinicaltrials.gov/.
5. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 9/1/24].
6. Human Genome Sciences. Benlysta (belimumab) injection. 2019 [cited 10/28/22]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2fa3c528-1777-4628-8a55-a69dae2381a3
7. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 9/1/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/12/26.

GUIDELINE UPDATE INFORMATION:

03/15/26	New Medical Coverage Guideline: Merging MCGs 09-J4000-07, Anifrolumab-fnia (Saphnelo), 09-J1000-35, Belimumab (Benlysta®) Injection, 09-J3000-96, Voclosporin (Lupkynis)
04/15/26	Revision to guidelines consisting of updating the position statement for Lupkynis to remove requirements for antibodies and increased initial approval duration to 1 year across all products.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.
07/01/26	Revision: Updated Site of Care statement to the Position Statement.
10/01/26	Revision to guidelines consisting of updating the position statement and dosing to reflect new subcutaneous formulation of Saphnelo.