09-J4000-07

Original Effective Date: 11/15/21

Reviewed: 09/11/24

Revised: 05/15/25

Subject: Anifrolumab-fnia (Saphnelo)

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:

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. 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.

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%).

POSITION STATEMENT:

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 300 mg every 4 weeks

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 300 mg every 4 weeks

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

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

Dose Adjustments

- None

Drug Availability

- 300 mg/2 mL (150 mg/mL) in a single-dose vial

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- History of anaphylaxis with anifrolumab-fnia

Precautions/Warnings

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

BILLING/CODING INFORMATION:

HCPCS Coding

J0491	Injection, anifrolumab-fnia, 1 mg

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.

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:

None

RELATED GUIDELINES:

None

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. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 9/1/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 9/1/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 9/1/24].
5. 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 04/09/25.

GUIDELINE UPDATE INFORMATION:

11/15/21	New Medical Coverage Guideline.
01/01/22	Revision: Added HCPCS code C9086.
04/01/22	Revision: Added HCPCS code J0491 and deleted codes C9086 and J3590.
10/15/23	Review and revision guideline consisting of updating position statement, coding, and references.
10/15/24	Review and revision guideline consisting of updating position statement and references.
05/15/25	Revision to guideline consisting of updating position statement