BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 07/15/24**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE:**
	CURRENT EFFECTIVE DATE: 07/15/24
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 2ND QTR 2025	**ARCHIVE DATE:**

SAPHNELO™ (anifrolumab-fnia)

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Saphnelo (anifrolumab-fnia) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is physician specializing in the patient's diagnosis or is in consultation with a Rheumatologist or Nephrologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of moderate to severe systemic lupus erythematosus (SLE) who are receiving standard therapy confirmed by **ALL** of the following:

     - Documentation of positive for anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-double stranded DNA (anti-dsDNA) greater than or equal to 30 IU/mL
     - Moderate to severe disease activity defined as **ONE** of the following:

       a. SLEDAI-2K (SLE Disease Activity Index 2000) of 6 or greater
       b. British Isles Lupus Assessment Group (BILAG) A organ domain score ≥1 OR BILAG B organ domain score ≥2 for any organ

     - Saphnelo will be used in combination with standard therapy (e.g., azathioprine, corticosteroids, hydroxychloroquine, methotrexate, mycophenolate mofetil)

  4. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label or intolerance or is not a candidate for **TWO** of the following standard therapies (used as monotherapy or in combination):

     - Azathioprine
     - Hydroxychloroquine
     - Methotrexate
     - Mycophenolate mofetil
     - Systemic steroid (e.g., prednisone)

  5. Individual has failure (used for ≥ 6 consecutive months), contraindication per FDA label, intolerance or is not a candidate for Benlysta (belimumab)

  6. Individual does **NOT** have **ANY** of the following:

     - Severe active lupus nephritis (proteinuria greater than 6 g/dL over 24 hours, serum creatinine greater than 2.5 mg/dL, or on hemodialysis)
     - Severe active central nervous system lupus
     - Evidence of serious or chronic infections

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- Concurrent use of live or live-attenuated vaccines

7. Saphnelo will not be used in combination with other cyclophosphamide or other biologics (e.g., Benlysta, rituximab, etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Saphnelo (anifrolumab-fnia) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Rheumatologist or Nephrologist

2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:

   - Improvement in involved organ systems (such as mucocutaneous, musculoskeletal, immune)
   - Able to reduce corticosteroid dose by at least 25% over baseline
   - No new organ involvement or evidence of disease progression
   - Reduced flares or a prolonged time to flare

3. Individual has been adherent with the medication

4. Saphnelo will be used in combination with standard therapy (e.g., azathioprine, corticosteroids, hydroxychloroquine, methotrexate, mycophenolate mofetil)

5. Individual does **NOT** have **ANY** of the following:

   - Severe active lupus nephritis (proteinuria greater than 6 g/dL over 24 hours, serum creatinine greater than 2.5 mg/dL, or on hemodialysis)
   - Severe active central nervous system lupus
   - Evidence of serious or chronic infections
   - Concurrent use of live or live-attenuated vaccines

6. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use, including hypersensitivity (e.g., angioedema)

7. Saphnelo will not be used in combination with other cyclophosphamide or other biologics (e.g., Benlysta, rituximab, etc.)

Renewal duration: 12 months

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- Saphnelo (anifrolumab-fnia) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Description:

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown cause that can affect virtually every organ, the most common pattern is a mixture of constitutional complaints with skin, musculoskeletal, mild hematologic, and serologic involvement. Some patients will have predominately hematologic, renal, or central nervous system manifestations. The disease may be characterized by periods of remissions and of chronic or acute relapses and the symptoms may vary from mild to severe depending upon the type of organs involved. Renal involvement is clinically apparent in approximately 50 percent of SLE patients. Neuropsychiatric involvement of SLE consists of a broad range of neurologic and psychiatric manifestations including cognitive dysfunction, organic brain syndromes, delirium, psychosis, seizures, headache, and/or peripheral neuropathies. Other less common problems are movement disorders, cranial neuropathies, myelitis, and meningitis.

SLE treatment regimen medications include any of the following (alone or in combination): corticosteroids, immunosuppressives (including azathioprine, methotrexate, mycophenolate), antimalarials (hydroxychloroquine, chloroquine), and NSAIDs. Cyclophosphamide and biologics including Benlysta (belimumab), rituximab, and Saphnelo (anifrolumab-fnia) are reserved for moderate to severe or refractory disease.

Saphnelo (anifrolumab-fnia) is a type I interferon (IFN) receptor antagonist indicated for the treatment of adult patients with moderate to severe SLE, who are receiving standard therapy.

Limitations of Use: The efficacy of Saphnelo has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Use of Saphnelo is not recommended in these situations.

Type I IFNs play a role in the pathogenesis of SLE. Approximately 60-80% of adult patients with active SLE express elevated levels of type I IFN inducible genes. Anifrolumab is a human IgG1κ monoclonal

antibody that binds to subunit 1 of the type I interferon receptor (IFNAR) with high specificity and affinity. This binding inhibits type I IFN signaling, thereby blocking the biologic activity of type I IFNs.. Blockade of receptor mediated type I IFN signaling inhibits IFN responsive gene expression as well as downstream inflammatory and immunological processes.

Definitions:

SLEDAI-2K
The Systemic Lupus Erythematosus Disease Activity Index-2K (SLEDAI-2K) is a scoring systems for global disease activity. The SLEDAI-2K does not capture improving or worsening, and does not include severity within a specific organ system.
SLEDAI-2K Online Calculator | RheumCalc

British Isles Lupus Activity Group (BILAG) assessment:
- An organ-specific assessment consisting of 86-items based on a healthcare provider's intention to treat.
- The assessor scores organ manifestations on a 4-point scale, where 1 = improved, 2 = same, 3 = worse, and 4 = new within the last month.
- The areas assessed include general, mucocutaneous, neuropsychiatric, musculoskeletal, cardiorespiratory, vasculitis, renal and hematologic.
- Multiple manifestations and laboratory findings within an organ system are combined into a single score for that system (using a computer program), and the resulting score is classified as:
  - A = very active disease
  - B = moderate activity
  - C = mild stable disease
  - D = resolved activity
  - E = organ was never involved
- The ACR defined a clinically meaningful improvement in the BILAG score to be a ≥ 7-point reduction

Physicians Global Assessment (PGA):
- The PGA is a visual analog scale that is scored from 0 to 3
- In SLE, a score of:
  - 0 = absence of disease activity
  - 1 = mild lupus disease activity
  - 2 = moderate activity
  - 3 = severe activity
- An increase of ≥ 10%, or 0.3 points, is considered to be clinically meaningful disease activity worsening

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History:	**Date:**	**Activity:**
Pharmacy and Therapeutics Committee	05/16/24	Approved guideline (effective 07/15/24)
Clinical Pharmacist	05/14/24	Development

Coding:

HCPCS: J0491

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Resources:

Literature reviewed 05/16/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis*. 2019;78(6):736-745.

2. Saphnelo (anifrolumab-fnia) product information, revised by manufacturer AstraZeneca Pharmaceuticals LP. 12/2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2024.

3. Wallace DJ, Gladman DD. Clinical manifestations and diagnosis of systemic erythematosus in adults. In: UpToDate, Pisetsky DS, Case SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated June 16, 2023. Accessed May 13, 2024.

4. Wallace DJ. Overview of the management and prognosis of systemic lupus erythematosus in adults. In: UpToDate, Pisetsky DS, Rigby WFC, Case SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated April 16, 2024. Accessed May 13, 2024.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html