anifrolumab (Saphnelo™)

Policy # 00767
Original Effective Date: 12/13/2021
Current Effective Date: 12/13/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider anifrolumab (Saphnelo™)‡ for the treatment of systemic lupus erythematosus to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of anifrolumab (Saphnelo) will be considered when all of the following patient selection criteria are met:

- Initial
  - Patient has a diagnosis of active systemic lupus erythematosus (SLE); AND
  - Patient is ≥18 years of age; AND
  - Patient is autoantibody-positive (ANA [anti-nuclear antibody] or anti-double-stranded deoxyribonucleic acid [anti-dsDNA]); AND
  - Patient is receiving standard therapy (i.e., corticosteroids, antimalarials, non-steroidal anti-inflammatory drugs [NSAIDs], immunosuppressives); AND
  - Patient does NOT have severe active central nervous system lupus or severe active lupus nephritis; AND
  - Patient is NOT receiving other biologics (e.g., belimumab [Benlysta®]‡)
- Continuation
  - Patient has received an initial authorization for Saphnelo; AND
  - Patient has demonstrated a beneficial response to Saphnelo for the treatment of active SLE (e.g., reduction in flares, reduction in corticosteroid dose, decrease of anti-dsDNA titer, improvement in complement levels [i.e., C3, C4], or improvement in specific organ dysfunction); AND

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*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient is receiving standard therapy (i.e. corticosteroids, antimalarials, NSAIDs, immunosuppressives); AND
- Patient is NOT receiving other biologics (e.g., Benlysta).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of anifrolumab (Saphnelo) when the patient has not previously demonstrated a beneficial response to the drug to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of anifrolumab (Saphnelo) when patient selection criteria are not met (except those denoted to be **not medically necessary****) to be **investigational.***

Background/Overview

Saphnelo is a monoclonal antibody that blocks the type I interferon (IFN) and is indicated for the treatment of moderate to severe systemic lupus erythematosus (SLE) in adults receiving standard therapy. In appropriate patients, it should be administered as an intravenous infusion of 300 mg every 4 weeks.

SLE is a chronic inflammatory disease of unknown cause that can affect the mucocutaneous, gastrointestinal, hematologic, musculoskeletal, neurologic, psychiatric, pulmonary, renal, and reproductive systems. Immunological abnormalities are a prominent feature of the disease. For example, autoantibodies against dsDNA (i.e. anti-dsDNA) and Smith nuclear antigen (i.e. anti-SM) are highly specific for SLE. Increases in anti-dsDNA titers, erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP), and a decrease in serum complement levels often precede active SLE. Standard treatment options for SLE include prednisone, hydroxychloroquine, NSAIDs, and

immunosuppressive agents such as cyclophosphamide, methotrexate, azathioprine, and mycophenolate. Benlysta is another biologic agent that is indicated for patients with active SLE who are receiving standard therapy, but it has not been compared to Saphnelo in clinical trials.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Saphnelo was approved in July 2021 for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), who are receiving standard therapy.

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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Saphnelo were evaluated in three 52-week, multicenter, randomized, double-blind, placebo-controlled studies. Patients were diagnosed with SLE according to the American College of Rheumatology classification criteria. All patients were ≥18 years of age and had moderate to severe disease, with a SLE Disease Activity Index 2000 (SLEDAI-2K) score ≥6 points, organ level involvement based on British Isles Lupus Assessment Group (BILAG) assessment, and a Physician's Global Assessment (PGA) score ≥1, despite receiving standard SLE therapy consisting of either one or any combination of oral corticosteroids, antimalarials, and/or immunosuppressants at baseline. Patients continued to receive their existing SLE therapy at stable doses during the clinical trials, with the exception of oral corticosteroids where tapering was a component of the protocol. Patients who had severe active lupus nephritis and patients who had severe active central nervous system lupus were excluded. The use of other biologic agents and cyclophosphamide were not permitted during the trials. In each trial, patients received Saphnelo or placebo, administered by intravenous infusion, every 4 weeks. Efficacy was established based on

assessment of clinical response using the composite endpoints, the British Isles Lupus Assessment Group based Composite Lupus Assessment (BICLA) and the SLE Responder Index (SRI-4).

Trial 1 randomized 305 patients (1:1:1) who received Saphnelo 300 mg, Saphnelo 1000 mg, or placebo for up to 52 weeks. The primary endpoint was combined assessment of the SRI-4 and the sustained reduction in oral corticosteroids measured at Week 24. In the Saphnelo 300 mg group, 54.6% of patients met the primary endpoint compared to 25.8% of those in the placebo group. The corresponding. difference in response rates was 28.8% (95% CI 15.7, 41.9).

Trial 2 randomized 457 patients who received Saphnelo 150 mg, 300 mg, or placebo (1:2:2). The primary endpoint was improvement in disease activity evaluated at 52 weeks, measured by SRI-4. In the Saphnelo 300 mg group, 47.1% of patients were classified as responders compared to 30.2% in the placebo group. The corresponding difference in response rates was 17% (95% CI: 7.2, 26.8).

Trial 3 randomized 362 patients (1:1) to receive Saphnelo 300 mg or placebo. The primary endpoint was the improvement in disease activity evaluated at 52 weeks measured by the BICLA. In the Saphnelo group, 47.8% of patients were classified as responders compared to 31.5% in the placebo group. The corresponding difference in response rates was 16.3% (95% CI 6.3, 26.3, p=0.001).

References

1. Saphnelo [package insert]. AstraZeneca Pharmaceuticals. Wilmington, DE. Updated July 2021.

Policy History

Original Effective Date: 12/13/2021
Current Effective Date: 12/13/2021
11/04/2021 Medical Policy Committee review
11/10/2021 Medical Policy Implementation Committee approval. New policy.
12/21/2021 Coding update
Next Scheduled Review Date: 11/2022

Coding

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The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J3490, J3590 Add code effective 1/1/2022: C9086
ICD-10 Diagnosis	M32.0-M32.9

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

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A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.