Effective Date: 10/27/2021
Last P&T Approval/Version: 10/27/2021
Next Review Due By: 11/2022
Policy Number: C21970-A

Saphnelo (anifrolumab-fnia)

PRODUCTS AFFECTED

Saphnelo (anifrolumab-fnia)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
moderate to severe systemic lupus erythematosus (SLE)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
1. Documented diagnosis of systemic lupus erythematosus
   AND
2. Prescriber attests that member is currently receiving standard of care therapy with at least ONE of the following: prednisone (or equivalent), hydroxychloroquine, azathioprine, mycophenolate mofetil, or methotrexate
   AND
3. Prescriber attests to no evidence of ANY of the following:
   (a) Concurrent use of another biologic [i.e., Actemra, Benlysta, Cimzia, Enbrel, Humira, Kineret,Orencia, Remicade, Rituxan, Simponi, Stelara,]

AND
(b) Active central nervous system (CNS) lupus [such as seizures, psychosis, organic brainsyndrome, cerebrovascular accident, cerebritis]
AND
(c) Active lupus nephritis

AND

4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted forreview [Contraindications to Saphnelo (anifrolumab-fnia) include: patients with a history of anaphylaxis with anifrolumab-fnia, use of live or live-attenuated vaccines, not recommended for use with other biologic therapies.
AND
5. IF THIS IS A PHARMACY BENEFIT REQUEST FOR A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Documentation of medication(s) tried, dates oftrial(s) and reason for treatment failure(s) is required.

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:
   1. Adherence to Saphnelo (anifrolumab-fnia) and standard of care therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required) as verified by Prescriber and member's medication fill history [REVIEWER: Review Rx fill history for compliance]
      AND
   2. Documentation of no intolerable adverse effects or drug toxicity
      AND
   3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (ie. A dose reduction of corticosteroid or immunosuppressant therapy, zero flares or a decrease in amount of significant clinical flares which required a systemic corticosteroid boost during treatment)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified a rheumatologist or physician who specializes in the treatment of in the management of patients with systemic autoimmune diseases [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY: 300mg every 4 weeks

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Saphnelo (anifrolumab-fnia). For information on site of care, see

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Medispan GPI-6 description

FDA-APPROVED USES: indicated for the treatment of adult patients with moderate to severe systemic lupus erythematosus (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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Systemic lupus erythematosus (SLE) is a chronic, occasionally life-threatening, multisystem immune-mediated disorder. Patients may present with a wide array of symptoms, signs, and laboratory findings and have a variable prognosis that depends upon the disease severity and type of organ involvement. Due to the variable disease course, effective management of SLE requires regular clinical and laboratory monitoring to assess disease activity; guide therapy to alleviate symptoms and reduce progressive organ damage; prevent and treat relapses; assess side effects related to drug therapy; encourage adherence with medications; and coordinate care with the patient's other providers.

The diagnosis of systemic lupus erythematosus (SLE) is based upon the judgment of an experienced clinician who recognizes characteristic constellations of symptoms and signs in the setting of supportive serologic studies after excluding alternative diagnoses. This is often challenging due to the great variability in the expression of SLE. Although the classification criteria were designed for research purposes, many clinicians refer to aspects of these criteria when making the diagnosis of SLE

1997 ACR criteria – The classification criteria that were developed by the American Rheumatism Association (ARA, now the ACR) for the classification of SLE were established by cluster analyses, primarily in academic centers and in White American patients. The patient is classified with SLE using the ACR criteria if four or more of the manifestations are present, either serially or simultaneously, during any interval of observations. A positive lupus erythematosus cell test,

used in older criteria, was replaced by the presence of antiphospholipid antibodies. When tested against other rheumatic diseases, these criteria have a sensitivity and specificity of approximately 96 percent.

2012 SLICC criteria – In 2012, the SLICC proposed classification criteria that were developed to address inherent weaknesses of the 1997 ACR classification criteria. Classification as having SLE by the SLICC criteria requires either that a patient satisfy at least 4 of 17 criteria, including at least 1 of the 11 clinical criteria and one of the six immunologic criteria, or that the patient has biopsy-proven nephritis compatible with SLE in the presence of ANA or anti-double-stranded DNA (anti-dsDNA) antibodies. Despite the improved sensitivity compared with the ACR criteria, the SLICC criteria might delay the diagnosis of SLE in a significant number of patients, and some patients might not be classified at all. These situations were demonstrated in a study in which patients with SLE from two large cohorts were grouped according to whether the SLICC criteria were met before, at the same time as, or after the ACR criteria, and the groups were then compared [57]. Among the patients diagnosed later with the SLICC criteria, in the majority of cases, the delay was due to the fact that the combination of malar rash and photosensitivity both fall within the acute cutaneous SLE category and thus only count as one criterion.

2019 EULAR/ACR criteria – The European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria for SLE were developed to improve detection of early- or new-onset SLE as well as improve the sensitivity and specificity compared with previous criteria. The classification for SLE requires the presence of a positive antinuclear antibodies (ANA) as an entry criterion. Additive criteria consist of seven clinical (ie, constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal) and three immunologic (ie, antiphospholipid antibodies, complement proteins, SLE-specific antibodies) categories, each of which are weighted from 2 to 10. Patients are classified as having SLE with a score of 10 or more points. In the validation cohort, which included patients with early disease, the EULAR/ACR criteria had a sensitivity of 96.1 percent and a specificity of 93.4 percent, compared with the 96.7 percent sensitivity and 83.7 percent specificity of the Systemic Lupus International Collaborating Clinics (SLICC) criteria and the 82.8 percent sensitivity and 93.4 percent specificity of the ACR criteria.

The goals of therapy for patients with systemic lupus erythematosus (SLE) are to ensure long-term survival, achieve the lowest possible disease activity, prevent organ damage, minimize drug toxicity, improve quality of life, and educate patients about their role in disease management. Treatment of SLE is individualized based upon patient preferences, clinical manifestations, disease activity and severity, and comorbidities. Patients require monitoring at regular intervals by a rheumatologist or other provider to optimize both nonpharmacologic and pharmacologic therapies and achieve treatment goals. Patients often have multiorgan system involvement and may require multidisciplinary care.

Saphnelo (anifrolumab-fnia)

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. Generally, IFNs signal for the immune system to be activated when there is an infection; however, in SLE, these signals are occurring unnecessarily, which leads to inflammation throughout the body. Saphnelo is thought to dampen these signals and decrease inflammation and systemic manifestations of SLE. Most adults (up to 80%) and children (90%) with SLE have

increased type I IFN signaling, which is associated with increased disease activity and severity.

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 and who were receiving standard therapy (at least one of the following: oral corticosteroids (OCSs), antimalarials, and immunosuppressants [methotrexate, azathioprine, or mycophenolate mofetil]).

MUSE (Trial 1; NCT01438489)-

Methods: Patients (n = 305) were randomized to receive intravenous anifrolumab (300 mg or 1,000 mg) or placebo, in addition to standard therapy, every 4 weeks for 48 weeks. Randomization was stratified by SLE Disease Activity Index 2000 score (<10 or ≥10), oral corticosteroid dosage (<10 or ≥10 mg/day), and type I IFN gene signature test status (high or low) based on a 4-gene expression assay. The primary end point was the percentage of patients achieving an SLE Responder Index (SRI[4]) response at week 24 with sustained reduction of oral corticosteroids (<10 mg/day and less than or equal to the dose at week 1 from week 12 through 24). Other end points (including SRI[4], British Isles Lupus Assessment Group [BILAG]-based Composite Lupus Assessment [BICLA], modified SRI[6], and major clinical response) were assessed at week 52. The primary end point was analyzed in the modified intent-to-treat (ITT) population and type I IFN-high subpopulation. The study result was considered positive if the primary end point was met in either of the 2 study populations. The Type I error rate was controlled at 0.10 (2-sided), within each of the 2 study populations for the primary end point analysis.

Results: The primary end point was met by more patients treated with anifrolumab (34.3% of 99 for 300 mg and 28.8% of 104 for 1,000 mg) than placebo (17.6% of 102) (P = 0.014 for 300 mg and P = 0.063 for 1,000 mg, versus placebo), with greater effect size in patients with a high IFN signature at baseline (13.2% in placebo-treated patients versus 36.0% [P = 0.004] and 28.2% [P = 0.029]) in patients treated with anifrolumab 300 mg and 1,000 mg, respectively. At week 52, patients treated with anifrolumab achieved greater responses in SRI(4) (40.2% versus 62.6% [P < 0.001] and 53.8% [P = 0.043] with placebo, anifrolumab 300 mg, and anifrolumab 1,000 mg, respectively), BICLA (25.7% versus 53.5% [P < 0.001] and 41.2% [P = 0.018], respectively), modified SRI(6) (28.4% versus 49.5% [P = 0.002] and 44.7% [P = 0.015], respectively), major clinical response (BILAG 2004 C or better in all organ domains from week 24 through week 52) (6.9% versus 19.2% [P = 0.012] and 17.3% [P = 0.025], respectively), and several other global and organ-specific end points. Herpes zoster was more frequent in the anifrolumab-treated patients (2.0% with placebo treatment versus 5.1% and 9.5% with anifrolumab 300 mg and 1,000 mg, respectively), as were cases reported as influenza (2.0% versus 6.1% and 7.6%, respectively), in the anifrolumab treatment groups. Incidence of serious adverse events was similar between groups (18.8% versus 16.2% and 17.1%, respectively).

TULIP-1 (Trial 2; NCT02446912),
TULIP-2 (Trial 3; NCT02446899)

Methods: TULIP-1 and TULIP-2 were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab (300 mg every 4 weeks for 48 weeks). For patients receiving baseline glucocorticoid ≥10 mg/day, attempted taper to ≤7.5 mg/day prednisone or equivalent from Weeks 8-40 was required and defined as sustained reduction when maintained through Week 52. Flares were defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B scores versus the previous visit.

Flare assessments were compared for patients receiving anifrolumab versus placebo.

Results: Compared with placebo (n = 366), anifrolumab (n = 360) was associated with lower annualized flare rates (rate ratio 0.75, 95% confidence interval [CI] 0.60-0.95), prolonged time to first flare (hazard ratio 0.70, 95% CI 0.55-0.89), and fewer patients with ≥1 flare (difference -9.3%, 95% CI -16.3 to -2.3), as well as flares in organ domains commonly active at baseline (musculoskeletal, mucocutaneous). Fewer BILAG-based Composite Lupus Assessment respondershad ≥1 flare with anifrolumab (21.1%, 36/171) versus placebo (30.4%, 34/112). Of patients who achieved sustained glucocorticoid reductions from ≥10 mg/day at baseline, more remained flare free with anifrolumab (40.0%, 76/190) versus placebo (17.3%, 32/185). TULIP-1 (Trial 2; NCT02446912) did not meet its primary endpoint on the SRI-4 composite measure.

Prior to the unblinding of the TULIP-1 data, the primary endpoint of TULIP-2 was changed from SRI-4 to BICLA response. Combined data from all 3 trials demonstrated benefits in overall disease activity, skin and joints manifestations, and the ability to taper down steroid doses; however, these endpoints were not formally assessed for statistical significance

Safety

Combined data from all 3 clinical trials found adverse reactions were reported in 87% of patients receiving Saphnelo versus 79% of patients receiving placebo. Common adverse reactions included upper respiratory infection (43%), bronchitis (11%), infusion-related reactions (9.4%), herpes zoster (6.1%), and cough (5%).

Due to Saphnelo's mechanism of action in inhibiting the IFN pathway, infections such as herpes zoster are expected to some degree. Overall, 28 patients treated with Saphnelo developed herpes zoster, with 2 patients requiring hospitalization. Shingrix (zoster vaccine recombinant, adjuvanted) was approved in late July 2021 for the prevention of shingles in adults ≥18 years of age who are or will be at increased risk of shingles due to immunodeficiency or immunosuppression caused by a disease or therapy; however, the CDC's Advisory Committee on Immunization Practices (ACIP) has not yet endorsed this recommendation. Therefore, Shingrix could be considered in eligible patients prior to initiating Saphnelo to mitigate the risk of herpes zoster.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Saphnelo (anifrolumab-fnia) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Saphnelo (anifrolumab-fnia) include: patients with a history of anaphylaxis with anifrolumab-fnia

OTHER SPECIAL CONSIDERATIONS: The recommended dosage of SAPHNELO is 300 mg, administered as an intravenous infusion over a 30-minute period, every 4 weeks. If a planned infusion is missed, administer SAPHNELO as soon as possible. Maintain a minimum interval of 14 days between infusion

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3590 (NOC)	Unclassified biologics

AVAILABLE DOSAGE FORMS:
Saphnelo SOLN 300MG/2M
NDC- 00310304000

REFERENCES

1. Saphnelo (anifrolumab) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2021.
2. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012 Aug;64(8):2677-86. doi: 10.1002/art.34473
3. Aringer, M., Costenbader, K., Daikh, D., Brinks, R., Mosca, M., & Ramsey-Goldman, R. et al. (2019). 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Annals Of The Rheumatic Diseases, 78(9), 1151-1159. doi: 10.1136/annrheumdis-2018-214819
4. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997 Sep;40(9):1725. doi: 10.1002/art.1780400928. PMID: 9324032.
5. Petri M, Magder L. Classification criteria for systemic lupus erythematosus: a review. Lupus. 2004;13(11):829-37. doi: 10.1191/0961203304lu2019oa. PMID: 15580978.
6. Hannon CW, McCourt C, Lima HC, Chen S, Bennett C. Interventions for cutaneous disease in systemic lupus erythematosus. Cochrane Database Syst Rev. 2021 Mar 9;3:CD007478. doi: 10.1002/14651858.CD007478.pub2.
7. Casey KA, Smith MA, Sinibaldi D, Seto NL, Playford MP, Wang X, Carlucci PM, Wang L, Illei G, Yu B, Wang S, Remaley AT, Mehta NN, Kaplan MJ, White WI. Modulation of Cardiometabolic Disease Markers by Type I Interferon Inhibition in Systemic Lupus Erythematosus. Arthritis Rheumatol. 2021 Mar;73(3):459-471. doi: 10.1002/art.41518. Epub 2021 Feb 15.
8. Furie R, Khamashta M, Merrill JT, Werth VP, Kalunian K, Brohawn P, Illei GG, Drappa J, Wang L, Yoo S; CD1013 Study Investigators. Anifrolumab, an Anti-Interferon-α Receptor Monoclonal Antibody, in Moderate-to-Severe Systemic Lupus Erythematosus. Arthritis Rheumatol. 2017 Feb;69(2):376-386. doi: 10.1002/art.39962.
9. Furie R, Morand EF, Askanase AD, Vital EM, Merrill JT, Kalyani RN, Abreu G, Pineda L, Tummala R. Anifrolumab reduces flare rates in patients with moderate to severe systemic lupus erythematosus. Lupus. 2021 Jul;30(8):1254-1263. doi: 10.1177/09612033211014267. Epub 2021 May 12.
10. Furie R, Morand EF, Bruce IN, Isenberg D, van Vollenhoven R, Abreu G, Pineda L, Tummala R. What Does It Mean to Be a British Isles Lupus Assessment Group-Based Composite Lupus Assessment Responder? Post Hoc Analysis of Two Phase III Trials. Arthritis Rheumatol. 2021 Apr 28. doi: 10.1002/art.41778. [Epub ahead of print]