Saphnelo® (Anifrolumab-Fnia) (for Ohio Only)

Policy Number: CSOH2025D0109.C
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➲ Instructions for Use

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Related Policies

None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Saphnelo (anifrolumab-fnia) is proven and medically necessary for the treatment of moderate to severe systemic lupus erythematosus (SLE) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderate to severe systemic lupus erythematosus, without severe active central nervous system lupus or severe active lupus nephritis; **and**
  - Currently receiving at least **one** standard of care treatment for active systemic lupus erythematosus (e.g., antimalarials, corticosteroids, or immunosuppressants) that is not a biologic; **and**
  - History of failure, contraindication, or intolerance to Benlysta intravenous (IV) or subcutaneous (SQ); **and**
  - Patient is not receiving Saphnelo in combination with a biologic agent or Benlysta; **and**
  - Saphnelo is dosed according to U.S. Food and Drug Administration (FDA) labeled dosing for SLE; **and**
  - Prescribed by or in consultation with a rheumatologist; **and**
  - Initial authorization is for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received Saphnelo injection for intravenous infusion; **and**
  - Documentation of positive clinical response; **and**
  - Patient is without severe active central nervous system lupus or severe active lupus nephritis; **and**
  - Currently receiving at least **one** standard of care treatment for active systemic lupus erythematosus (e.g., antimalarials, corticosteroids, or immunosuppressants) that is not a biologic; **and**
  - Patient is not receiving Saphnelo in combination with a biologic agent or Benlysta; **and**
  - Saphnelo is dosed according to U.S. FDA labeled dosing for SLE; **and**
  - Prescribed by or in consultation with a rheumatologist; **and**
  - Authorization is for no more than 12 months

Saphnelo is unproven and not medically necessary for:

- Severe active lupus nephritis
- Severe active central nervous system (CNS) lupus
- Use in combination with other biologics

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0491	Injection, anifrolumab-fnia, 1 mg

Diagnosis Code	Description
M32.10	Systemic lupus erythematosus, organ or system involvement unspecified
M32.11	Endocarditis in systemic lupus erythematosus
M32.12	Pericarditis in systemic lupus erythematosus
M32.13	Lung involvement in systemic lupus erythematosus
M32.14	Glomerular disease in systemic lupus erythematosus
M32.15	Tubulo-interstitial nephropathy in systemic lupus erythematosus
M32.19	Other organ or system involvement in systemic lupus erythematosus
M32.8	Other forms of systemic lupus erythematosus
M32.9	Systemic lupus erythematosus, unspecified

Background

Saphnelo is a human IgG1$_{K}$ 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. Saphnelo also induces the internalization of IFNAR1, thereby reducing the levels of cell surface IFNAR1 available for receptor assembly. Blockade of receptor mediated type I IFN signaling inhibits IFN responsive gene expression as well as downstream inflammatory and immunological processes. Inhibition of type I IFN blocks plasma cell differentiation and normalizes peripheral T-cell subsets. 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.

Clinical Evidence

Furie et al. evaluated the efficacy and safety of anifrolumab, a type I interferon (IFN) receptor antagonist, in a phase IIb, randomized, double-blind, placebo-controlled study of adults with moderate-to-severe systemic lupus erythematosus (SLE). 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 two study populations. The Type I error rate was controlled at 0.10 (2-sided), within each of the two study populations for the primary end point analysis. 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). Researchers concluded that anifrolumab substantially reduced disease activity compared with placebo across multiple clinical end points in the patients with moderate-to-severe SLE.

Pooled data from the phase 3 TULIP-1 and TULIP-2 trials in patients with moderate to severe SLE were analyzed by Furie et al. to determine anifrolumab's effect on flares, including those arising with glucocorticoid taper. 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. 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 responders had ≥ 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). The authors concluded that analyses of pooled TULIP-1 and TULIP-2 data support that anifrolumab reduces flares while permitting glucocorticoid taper in patients with SLE.

Anifrolumab did not have a significant effect on the primary end point in a previous phase 3 trial. The current phase 3 trial used a secondary end point from that trial as the primary end point. Morand et al. randomly assigned patients in a 1:1 ratio to receive intravenous anifrolumab (300 mg) or placebo every 4 weeks for 48 weeks. The primary end point of this trial was a response at week 52 defined with the use of the British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA). A BICLA response requires reduction in any moderate-to-severe baseline disease activity and no worsening in any of nine organ systems in the BILAG index, no worsening on the Systemic Lupus Erythematosus Disease Activity Index, no increase of 0.3 points or more in the score on the Physician Global Assessment of disease activity (on a scale from 0 [no disease activity] to 3 [severe disease]), no discontinuation of the trial intervention, and no use of medications restricted by the protocol. Secondary end points included a BICLA response in patients with a high interferon gene signature at baseline; reductions in the glucocorticoid dose, in the severity of skin disease, and in counts of swollen and tender joints; and the annualized flare rate. A total of 362 patients received the randomized intervention: 180 received anifrolumab and 182 received placebo. The percentage of patients who had a BICLA response was 47.8% in the anifrolumab group and 31.5% in the placebo group (difference, 16.3 percentage points; 95% confidence interval, 6.3 to 26.3; p = 0.001). Among patients with a high interferon gene signature, the percentage with a response was 48.0% in the anifrolumab group and 30.7% in the placebo group; among patients with a low interferon gene signature, the percentage was 46.7% and 35.5%, respectively. Secondary end points with respect to the glucocorticoid dose and the severity of skin disease, but not counts of swollen and tender joints and the annualized flare rate, also showed a significant benefit with anifrolumab. Herpes zoster and bronchitis occurred in 7.2% and 12.2% of the patients, respectively, who received anifrolumab. There was one death from pneumonia in the anifrolumab group. Researchers concluded that administration of anifrolumab resulted in a higher percentage of patients with a response (as defined by a composite end point) at week 52 than did placebo, in contrast to the findings of a similar phase 3 trial involving patients with SLE that had a different primary end point. The frequency of herpes zoster was higher with anifrolumab than with placebo.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Saphnelo is a type I interferon (IFN) receptor antagonist 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.
- Saphnelo is not recommended for use with other biologic therapies.

References

1. Saphnelo® [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP. August 2024.
2. Furie R, Khamashta M, Merrill JT, et al. Anifrolumab, an Anti-Interferon-α Receptor Monoclonal Antibody, in Moderate-to-Severe Systemic Lupus Erythematosus. Arthritis Rheumatol. 2017;69(2):376-386.
3. Furie R, Morand EF, Askanase AD, et al. Anifrolumab reduces flare rates in patients with moderate to severe systemic lupus erythematosus. *Lupus.* 2021;30(8):1254-1263.
4. Morand EF, Furie R, Tanaka Y, et al. Trial of Anifrolumab in Active Systemic Lupus Erythematosus. *N Engl J Med*. 2020;382(3):211-221.
5. Benlysta [package insert]. Rockville, MD: Human Genome Sciences, Inc.; June 2024.

Policy History/Revision Information

Date	Summary of Changes
08/01/2025	**Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CSOH2024D0109.B

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.