Drug Coverage Policy

Effective Date……07/15/2026
Coverage Policy Number……IP0810
Policy Title…..Saphnelo Subcutaneous

Lupus – Saphnelo Subcutaneous for Individual and Family Plans

- Saphnelo® (anifrolumab-fnia subcutaneous injection – AstraZeneca)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Saphnelo subcutaneous, a type 1 interferon receptor antagonist, is indicated for the treatment of moderate to severe **systemic lupus erythematosus (SLE)** in adults who are receiving standard therapy.[1]

Limitations of Use: Saphnelo efficacy has not been evaluated and is not recommended in patients with severe active lupus nephritis or severe active central nervous system lupus.[1]

Of note, intravenous Saphnelo is not targeted in this policy.

Guidelines
American College of Rheumatology (ACR) guidelines for treatment of SLE (2025) recommend hydroxychloroquine (HCQ) for all patients (unless contraindicated), minimization of glucocorticoid exposure, and early introduction of conventional and/or biologic immunosuppressive therapies.[2] Treatment strategies should be stratified based on organ-specific manifestations such as hematologic, neuropsychiatric, cutaneous/mucocutaneous, serositis, musculoskeletal, systemic vasculitis, and/or cardiopulmonary. The following ACR recommendations are specific to Benlysta® (belimumab intravenous infusion and subcutaneous injection) and Saphnelo: (1) Cutaneous lupus: For ongoing moderate to severe cutaneous lupus refractory to topical and antimalarial therapies, and/or oral glucocorticoid necessitating escalation of therapy, ACR conditionally recommends the addition of methotrexate (MTX), mycophenolic acid analog (MPAA), Saphnelo and/or Benlysta [level of evidence (LOE): very low to moderate]. (2) SLE arthritis: For a patient with persistent or recurrent active SLE arthritis on HCQ, regardless of prior/current nonsteroidal anti-inflammatory drugs or short-term glucocorticoid therapy, ACR conditionally recommends initial therapy with MTX, MPAA, or azathioprine (AZA), with a low threshold to add or substitute with Benlysta or Saphnelo for inadequate response over initial biologic therapy (LOE: very low to low). (3) Systemic vasculitis: For vasculitis attributed to active SLE, ACR conditionally recommends initial therapy with pulse/high-dose glucocorticoid taper and conventional (e.g. intravenous cyclosporine, MPAA, AZA) or biologic (e.g., anti-CD 20 therapy, Benlysta, Saphnelo) immunosuppressive therapy over glucocorticoid monotherapy alone (LOE: very low to low). The guidelines do not express a preference between Benlysta and Saphnelo; selection should be individualized based on mechanism of action and patient-specific clinical characteristics.

European League Against Rheumatism (EULAR) guidelines for SLE (2023 update) also recommend HCQ for all patients, unless contraindicated.[3] Depending on the type and severity of organ involvement, glucocorticoids may be used but dosing should be minimized or withdrawn. In general, pharmacological interventions are directed by patient characteristics and the type/severity of organ involvement. The following EULAR recommendations are specific to Benlysta and Saphnelo: (1) In patients who do not respond to HCQ ± glucocorticoids, the addition of immunomodulating/immunosuppressive agents should be considered [e.g. MTX, AZA, MPAA, and/or biologic agents (e.g. Benlysta, Saphnelo)]. (2) For patients with active skin disease, treatment should include topical agents (e.g. glucocorticoids, calcineurin inhibitors), antimalarials (e.g. HCQ, chloroquine), and/or systemic glucocorticoids as needed, with MTX, MPAA, Saphnelo, or Benlysta considered as second-line.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Saphnelo subcutaneous. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Saphnelo subcutaneous as well as the monitoring required for adverse

events and long-term efficacy, approval requires Saphnelo subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Saphnelo Subcutaneous is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Systemic Lupus Erythematosus.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has autoantibody-positive systemic lupus erythematosus (SLE), defined as positive for at least one of the following: antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA) antibodies, anti-Smith (anti-Sm) antibodies; AND
       Note: Not all patients with SLE are positive for anti-dsDNA, but most will be positive for ANA.
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** The medication is being used concurrently with at least one other standard therapy for SLE; OR
         Note: Examples of standard therapies for SLE include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).
       - **b)** According to the prescriber, patient is determined to be intolerant to standard therapy due to a significant toxicity; AND
     - **iv.** The medication is prescribed by or in consultation with a rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist; OR
   - **B)** Patient is Currently Receiving Saphnelo Intravenous or Subcutaneous. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient meets ONE of the following (a or b):
       - **a)** The medication is being used concurrently with at least one other standard therapy for SLE; OR
         Note: Examples of standard therapies for SLE include an antimalarial (e.g., hydroxychloroquine), systemic corticosteroid (e.g., prednisone), and other immunosuppressants (e.g., azathioprine, mycophenolate mofetil, methotrexate).
       - **b)** According to the prescriber, patient is determined to be intolerant to standard therapy due to a significant toxicity; AND
     - **ii.** According to the prescriber, patient has responded to Saphnelo; AND
       Note: Examples of a response include 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 (e.g., musculoskeletal, blood, hematologic, vascular, others).
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist, clinical immunologist, nephrologist, neurologist, or dermatologist.

Conditions Not Covered

Saphnelo Subcutaneous for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Other Biologics.** Saphnelo has not been studied in combination with other biologics.[1] Safety and efficacy have not been established with these combinations. See APPENDIX for examples of other biologics that should not be taken in combination with Saphnelo.

References

1. Saphnelo® intravenous and subcutaneous injection [prescribing information]. Wilmington DE: AstraZeneca; April 2026.
2. Sammaritano LR, Askanase A, Bermas BL, et al. 2025 American College of Rheumatology (ACR) Guideline for the Treatment of Systemic Lupus Erythematosus. *Arthritis Rheumatol*. Published online November 4, 2025.
3. Fanouriakis A, Kostopoulou M, Andersen J, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis*. 2024;83(1):15-29.

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Benlysta® (belimumab SC injection, IV infusion)	BLyS inhibitor	SLE, lupus nephritis
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, HS, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, JIA, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Simponi®, Simponi Aria® (golimumab SC injection, IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Kineret® (anakinra SC injection) **Tocilizumab Products** (Actemra® IV, biosimilars; Actemra SC, biosimilars)	Inhibition of IL-1 Inhibition of IL-6	RA
		SC formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection) **Siliq®** (brodalumab SC injection)	Inhibition of IL-6 Inhibition of IL-17	PJIA, RA
		PsO
Cosentyx® (secukinumab SC injection; IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, HS, nr-axSpA, PsO, PsA
Kineret® (anakinra SC injection)	Inhibition of IL-1	IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection) **Ustekinumab Products** (Stelara® IV, biosimilars; Stelara SC, biosimilars)	Inhibition of IL-17A/17F Inhibition of IL-12/23	AS, HS, nr-axSpA, PsO, PsA
		SC formulation: CD, PsO, PsA, UC
Siliq® (brodalumab SC injection)	Inhibition of IL-17	IV formulation: CD, UC

Ilumya® (tildrakizumab-asmn SC injection) **Omvoh®** (mirikizumab IV infusion, SC injection)	Inhibition of IL-23 Inhibition of IL-23	PsO CD, UC
Skyrizi® (risankizumab-rzaa SC injection, IV infusion)	Inhibition of IL-23	SC formulation: CD, PsO, PsA, UC
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	IV formulation: CD, UC
Tremfya® (guselkumab SC injection, IV infusion)	Inhibition of IL-23	SC formulation: CD, PsO, PsA, UC
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion, SC injection)	Integrin receptor antagonist	CD, UC
Orencia® (abatacept IV infusion, SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed antibody	RA

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; IV – Intravenous; BLyS – B-lymphocyte stimulator-specific inhibitor; SLE – Systemic lupus erythematosus; IFN – Interferon; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis.

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	06/04/2026	07/15/2026

The policy effective date is in force until updated or retired.