Medical Policy Bulletin
Title:
Anifrolumab-fnia (Saphnelo™)
Policy #:
MA08.140c

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

INITIAL THERAPY

Anifrolumab (Saphnelo), administered by intravenous infusion, is considered medically necessary and, therefore, covered for the treatment of adult individuals with moderate to severe systemic lupus erythematosus (SLE) who are receiving standard therapy* and **do not** have severe active lupus nephritis or severe active central nervous system lupus.

*Standard therapy for SLE with the use of anifrolumab (Saphnelo) includes, but is not limited to, oral corticosteroids, antimalarials (e.g., hydroxychloroquine, chloroquine), and/or immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate mofetil/mycophenolic acid) but excluding other biologic agents (including B-cell targeted therapies) and cyclophosphamide.

CONTINUATION THERAPY

Continuation of anifrolumab (Saphnelo) is considered medically necessary and, therefore, covered when all of the following criteria are met:

- All criteria under Initial Therapy as stated above are met.
- There is documented improvement or stabilization in disease activity due to anifrolumab (Saphnelo) treatment based on scoring instruments in SLE-associated disease area and severity (e.g., Systemic Lupus Erythematosus Disease Activity INDEX 2000 [SLEDAI-2K], British Isles Lupus Assessment Group [BILAG], and the Physician's Global Assessment [PGA] scores). It is expected that the same objective measurement scale will be used for both baseline and response to treatment.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for anifrolumab (Saphnelo) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

There is no Medicare coverage determination addressing this service; therefore, the Company policy is applicable.

Certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when anifrolumab (Saphnelo) is covered under a member's medical benefit (Part B benefit). It does not address instances when anifrolumab (Saphnelo) is covered under a member's pharmacy benefit (Part D benefit).

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, anifrolumab (Saphnelo) is covered under the Evidence of Coverage of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

TESTS TO EVALUATE DISEASE SEVERITY

SLE lacks a gold standard for measuring disease activity. SRI-4 and BILAG are both composite measures used in the Saphnelo clinical trials.

BILAG Score (BICLA is driven by the BILAG score)

- The BILAG score is based on 97 items representing nine organ systems reflecting disease activity over the previous 4 weeks.
- Each item is rated on a scale: 0 = not present, 1 = improving, 2 = same, 3 = worse, 4 = new.
- Each organ system is then assigned a disease activity score:
    - A = severe, very active disease
    - B = moderate disease
    - C = mild disease
    - D = no current disease activity
    - E = no current or previous disease activity

BICLA

- Must have improvement in all baseline BILAG As and Bs with no worsening in other organ systems.
- No worsening in SLEDAI-2K.
- No worsening in PGA.
- No use of restricted medications.
- No discontinuation of the investigational product.

SLEDAI-2K Score (SRI-4 is driven by the SLEDAI-2K score)

- The SLEDAI-2K score is based on the presence of 24 descriptors in nine organ systems over the preceding 30 days.

- Each descriptor has a weighted score and is recorded as either present or absent (e.g., alopecia is a descriptor worth 2 points).
- A total SLEDAI-2K score is between 0 and 105, with higher scores representing greater disease activity.

SRI-4

- Must have at least a 4-point reduction of SLEDAI-2K score from baseline.
- No new BILAG-A and no more than 2 new BILAG B
- No worsening PGA.
- No use of restricted medications.
- No discontinuation of the investigational product.

SYSTEMIC LUPUS ERTHEMATOSIS (SLE)

Per the American College of Rheumatology (ACR) classification criteria for SLE disease severity:
Moderate disease – Patients with moderate disease severity may be described as having significant but non–organ-threatening disease (e.g., constitutional, cutaneous, musculoskeletal, or hematologic.
Severe disease – A patient with organ-threatening manifestations (e.g., kidney and central nervous system [CNS] involvement). For example, such a patient may develop kidney function impairment and significant proteinuria due to lupus nephritis. Laboratory evaluation may reveal a low C3, C4, elevated anti-double-stranded DNA (dsDNA) antibodies, and elevated acute phase reactants.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Anifrolumab-fnia (Saphnelo) was approved by the FDA on July 30, 2021, for the treatment of adult individuals with moderate to severe SLE who are receiving standard therapy. The recommended dosage is 300 mg intravenous infusion every 4 weeks.

The efficacy of anifrolumab (Saphnelo) has not been evaluated in individuals with severe active lupus nephritis (LN) or severe active central nervous system lupus. Use of anifrolumab (Saphnelo) is not recommended in these situations. Anifrolumab (Saphnelo) has not been studied in combination with other biologic therapies, including B-cell targeted therapies. Therefore, use of anifrolumab (Saphnelo) is not recommended for use in combination with biologic therapies.

PEDIATRIC USE
The safety and efficacy of anifrolumab (Saphnelo) in pediatric individuals less than 18 years of age have not been established.

Description

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect most organs of the body. The skin and the musculoskeletal system are organs that are frequently affected in individuals with SLE. The disease is characterized by intermittent flares. These flares can cause increased organ damage as well as decrease the quality of life for the individual with SLE. Standard therapies used to treat SLE can include antimalarial drugs (e.g., hydroxychloroquine, chloroquine), glucocorticoids, nonsteroidal anti-inflammatory drugs (NSAIDs), and immunosuppressants (e.g., azathioprine, methotrexate). The medications used to treat SLE and the flares can also cause organ damage that is separate from the damage caused by the disease itself. One of the goals of providers of care for individuals with SLE is to taper off glucocorticoids to the lowest dose that will prevent flares since the corticosteroids can cause organ damage and other undesirable side effects.

Anifrolumab (Saphnelo) is a human immunoglobulin (Ig) G1 kappa monoclonal antibody that binds to subunit 1 of the type I interferon (IFN) receptor (IFNAR) with high specificity and affinity. This binding inhibits type I IFN signaling, thereby blocking the biologic activity of type I IFNs. Anifrolumab (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 normalized peripheral T-cell subsets.

PEER-REVIEWED LITERATURE

Summary

The safety and efficacy of anifrolumab (Saphnelo) was evaluated in a phase IIb, randomized, double-blind, parallel group, placebo-controlled clinical trial (Furie et al., 2017) including 305 individuals with moderate-to-severe SLE. Ninety-nine individuals received anifrolumab (Saphnelo) 300 mg, 104 individuals received anifrolumab (Saphnelo) 1000 mg, and 102 individuals received placebo. All participants received the study drug by intravenous infusion (IV) every 4 weeks and continued to receive standard therapy. The length of the study was 48 weeks. Tapering of the individuals' oral corticosteroid (OC) dose was encouraged but was left to the discretion of the investigator at the site. The primary endpoint was the percentage of individuals achieving an SLE Responder Index (SRI) response at week 24 as well as maintaining a reduction of their OC dose to less than 10 mg/d and less than or equal to the dose at week 1 from weeks 12 through 24. The primary endpoint was reached by 34.3 percent of the 99 individuals receiving the 300-mg dose (*P*=0.014) and 28.8 percent of the individuals receiving the 1000-mg dose (*P*=0.063), but only 17.6 percent of individuals receiving placebo.

The safety and efficacy of anifrolumab (Saphnelo) was evaluated in a phase III, randomized, double-blind, parallel group, placebo-controlled clinical trial (Furie et al., 2019) including 457 individuals with moderate-to-severe SLE. One hundred eighty individuals received anifrolumab (Saphnelo) 300 mg, 93 individuals received anifrolumab (Saphnelo) 150 mg, and 184 individuals received placebo. All participants received the study drug by IV every 4 weeks and continued to receive standard therapy. The length of the study was 48 weeks. There were standard mandatory attempts at tapering of the participants' OCs if the individual was receiving a dose equivalent to 10 mg/d or more of prednisone at baseline starting at week 8 through week 40. The primary endpoint was the difference between the percentage of individuals achieving a SRI-4 response at week 52 with anifrolumab (Saphnelo) 300 mg versus placebo. Some of the secondary endpoints included the percentage of individuals who were able to taper and maintain their OC dose to 7.5 mg/d or less from week 40 through to week 52; the percentage of individuals with a cutaneous lupus erythematosus disease area and severity index (CLASI) activity score of 1 or more at baseline who were able to achieve a 50 percent or more decrease in their CLASI score by the 12th week; the percentage of individuals who reached SRI-4 by week 24; and the annualized flare rate total through the 52nd week. The primary endpoint was not achieved as only 35 percent of the anifrolumab (Saphnelo) 300 mg group and 40 percent of the placebo group achieved a SRI-4 response by week 52. However, 41 percent of the anifrolumab (Saphnelo) 300-mg group versus 32 percent of the placebo group were able to decrease and maintain their OC dose to 7.5 mg/d or less and the percentage of individuals who achieved at least 50 percent reduction of their CLASI score by the 12th week was 42 percent in the anifrolumab (Saphnelo) 300 mg group versus 25 percent in the placebo group. The annualized flare rates were also not significant at 0.60 for the anifrolumab (Saphnelo) group versus 0.72 for the placebo group.

The safety and efficacy of anifrolumab (Saphnelo) was evaluated in another phase III, randomized, double-blind, parallel group, placebo-controlled clinical trial (Morand et al., 2020) using a different primary endpoint. For this study, the primary endpoint was the difference in the proportion of individuals in a group receiving the study drug versus a group receiving placebo in response at week 52 in their British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) responses. The BICLA response was assessed by all of the following: a decrease in all severe or moderately severe disease activity from the individual's baseline to reassessment, no worsening in other organ systems or disease activity, no discontinuation of the trial protocols, and no use of restricted drugs beyond levels allowed in the trial's protocols. The secondary endpoints were a BICLA response in individuals who were identified as having a high IFN gene signature at baseline, decrease in OC dosage, decrease by 50 percent or more in the CLASI score by week 12, decrease by 50 percent or more in the swollen/tender joints count by week 52, and the annualized flare rate. Individuals with moderate to severe SLE were randomly assigned to receive anifrolumab (Saphnelo) 300 mg (180 individuals) or placebo (182 individuals) IV every 4 weeks for 48 weeks. The individuals continued to receive standard therapy for SLE and there was a mandatory attempt to taper the OC dose after 8 weeks through week 40 if the individual was on a prednisone-equivalent dose of 10 mg/d or more. The proportion of individuals who had a BICLA response at week 52 in the anifrolumab (Saphnelo) group was 47.8 percent versus 31.5 percent in the placebo group (*P*=0.001). For the subpopulation of individuals with a high IFN, 48.0 percent in the anifrolumab (Saphnelo) group and 30.7 percent in the placebo group had a BICLA response at week 52 (*P*=0.002). The proportion of individuals able to decrease and sustain a lower OC dose was 47.0 percent in the anifrolumab (Saphnelo) group and 30.2 percent in the placebo group (*P*=0.01). The proportion of individuals able to decrease their CLASI score by 50 percent or more was 49.0 percent in the anifrolumab (Saphnelo) group and 25.0 percent in the placebo group (*P*=0.04). The proportion of individuals with a decrease by 50 percent or more in the swollen/tender joint count was 42.2 percent in the anifrolumab (Saphnelo) and 37.5 percent in the placebo group (*P*=0.55). The annualized flare rate was 0.43 in the anifrolumab (Saphnelo) group and 0.64 in the placebo group (*P*=0.08).

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria

highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

Chatham WW, Furie R, Saxena A, et al. Long-term safety and efficacy of anifrolumab in adults with systemic lupus erythematosus: results of a phase II open-label extension study. *Arthritis Rheumatol*. 2021;73(5):816-825.

Elsevier's Clinical Pharmacology Compendium. Anifrolumab-fnia (Saphnelo™). [Clinicalkey Web site]. 08/11/2021. Available at: https://www.clinicalkey.com/phamacology/ [via subscription only]. Accessed August 13, 2021.

Furie R, Khamashta M, Merrill JT, et al. Anifrolumab, an anti-interferon-a receptor monoclonal antibody, in moderate-to-severe systemic lupus erythematosus. *Arthritis Rheumatol*. 2017;69(2):376-386.

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.

Furie RA, Morand EF, Bruce IN, et al. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomized, controlled, phase 3 trial. *Lancet Rheumatology*. 2019;1(4):e208-e219.

IBM Micromedex® DRUGDEX® (electronic version). Anifrolumab-fnia (Saphnelo™). [Micromedex Web site]. IBM Watson Health, Greenwood Village, Colorado, USA. 08/11/2021. Available at: https://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed August 13, 2021.

Lexi-Drugs Compendium. Anifrolumab-fnia (Saphnelo™). [Lexicomp Online Web site]. 08/02/2021. Available at: https://online.lexi.com/lso/action/home [via subscription only]. Accessed August 13, 2021.

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.

Saphnelo™ (anifrolumab-fnia) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP. 07/2021. Available at: https://www.saphnelo.com/. Accessed August 13, 2021.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Labeling for Anifrolumab-fnia (Saphnelo™). [FDA Web site]. 07/30/2021. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed August 13, 2021.

Wallace DJ. Overview of the management and prognosis of systemic lupus erythematosus in adults. [Up To Date website]. 04/19/2021. Available at: https://www.uptodate.com/contents/overview-of-the-management-and-prognosis-of-systemic-lupus-erythematosus-in-adults/print?search=anifrolumab&source=search_result&selectedTitle=2~2&usage_type=default&display_rank=1 [via subscription only]. Accessed August 13, 2021.

Wallace DJ and Gladman DD. Clinical manifestations and diagnosis of systemic lupus erythematosus in adults. [Up To Date website]. 12/10/2019. Available at: https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-systemic-lupus-erythematosus-in-adults?search=systemic lupus erythematosus&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1 [via subscription only]. Accessed August 13, 2021.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)

M32.0 Drug-induced systemic lupus erythematosus
M32.8 Other forms of systemic lupus erythematosus
M32.9 Systemic lupus erythematosus, unspecified
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
M32.19 Other organ or system involvement in systemic lupus erythematosus

HCPCS Level II Code Number(s)
J0491 Injection, anifrolumab-fnia, 1 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.140c:

09/16/2024	This version of the policy will become effective 09/16/2024. This Policy has been updated to communicate the classification criteria of systemic lupus erythematosus. Additionally, continuation therapy with specified criteria has been added.

Revisions From MA08.140b:

05/07/2024	The policy has been reviewed and reissued to communicate the Company's continuing position on anifrolumab-fnia (Saphnelo™).
9/5/2023	The policy has been reviewed and reissued to communicate the Company's continuing position on anifrolumab-fnia (Saphnelo™).
06/01/2022	The policy has been reviewed and reissued to communicate the Company's continuing position on anifrolumab-fnia (Saphnelo™).
04/01/2022	This version of the policy will become effective 04/01/2022. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following HCPCS codes have been **removed** from this policy: J3590: Unclassified biologics

	C9086: Injection, anifrolumab-fnia, 1mg The following HCPCS code has been **added** to this policy: J0491: Injection, anifrolumab-fnia, 1 mg

Revisions From MA08.140a:

01/01/2022	This version of the policy will become effective 01/01/2022. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following HCPCS code has been **removed** from this policy: C9399: Unclassified drug or biological The following HCPCS code has been **added** to this policy: C9086: Injection, anifrolumab-fnia, 1mg

Revisions From MA08.140:

10/11/2021	The following new policy has been developed to communicate the Company's coverage criteria for anifrolumab-fnia (Saphnelo™). The policy will become effective 10/11/2021.

Version Effective Date:
09/16/2024
Version Issued Date:
09/16/2024
Version Reissued Date:
05/07/2024