Saphnelo (anifrolumab-fnia)

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Introduction

- **Brand name:** Saphnelo
- **Generic name:** Anifrolumab-fnia
- **Pharmacologic class:** Type I interferon (IFN) receptor antagonist
- **Strength and Formulation:** 300mg/vial; soln for IV infusion after dilution; preservative-free
- **Manufacturer:** AstraZeneca Pharmaceuticals
- **How supplied:** Single-dose vial (2mL)—1
- **Legal Classification:** Rx

Indication

- Treatment of **adult** patients with **moderate** to **severe** systemic lupus erythematosus (**SLE**) who are receiving standard therapy.

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Limitations of Use

- Not for use in severe active lupus nephritis or severe active CNS lupus.

Dosage and Administration

- Given by IV infusion over 30 minutes.
- ≥18yrs: 300mg every 4 weeks.
- Missed infusion:
  - Administer as soon as possible. Maintain a minimum interval of 14 days between infusions.

Considerations for Specific Populations

- **Pregnancy:** Insufficient human data to assess drug-associated risk of birth defects and miscarriage.
  - *Pregnancy exposure registry: 877-693-9268*
- **Nursing mothers:** No data on presence of anifrolumab-fnia in human milk.
- **Pediatrics**: <18yrs: Not established.
- **Geriatrics**: Number of patients 65 years and older was not sufficient to determine difference in response.
- **Renal impairment**: No dose adjustment necessary.
- **Hepatic impairment**: No dose adjustment necessary.

Warnings and Precautions

- Increased risk of **serious infections** (respiratory, herpes zoster)
  - Active infection: avoid initiation until resolved or adequately treated.
  - Chronic infection, history of recurrent infections, or known risk factors for infection: consider benefit-risk for administration.
  - Consider interrupting anifrolumab-fnia if infection develops or if patient not responding to anti-infective treatment; monitor closely.
- Consider premedication prior to infusion for those with a history of hypersensitivity or infusion-related reactions.

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Warnings and Precautions

- Interrupt immediately if a serious infusion-related or hypersensitivity reaction occurs.
- Increased risk of malignancies with the use of immunosuppressants.
  - Consider individual benefit-risk in patients with known risk factors for the development or reoccurrence of malignancy.
  - In patients who develop malignancies, consider the benefit-risk of continued treatment.
- Update immunizations according to current guidelines prior to initiation.

Adverse Reactions

- **Most common (≥5%)**: Nasopharyngitis, upper respiratory tract infections, bronchitis, infusion-related reactions, herpes zoster, cough.

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Mechanism of Action

- Anifrolumab-fnia is a human IgG1κ monoclonal antibody that binds to subunit 1 of the type I interferon receptor, blocking the biologic activity of type I IFNs.
- Anifrolumab-fnia 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.

Clinical Trials

- Safety and efficacy were evaluated in three 52-week treatment period, multicenter, randomized, double-blind, placebo-controlled studies (Trial 1 [NCT01438489], Trial 2 [NCT02446912], and Trial 3 [NCT02446899]).
- All patients were ≥18yrs and had moderate to severe disease, with SLE Disease Activity Index 2000 (SLEDAI-2K) score ≥6, organ level involvement based on British Isles Lupus Assessment Group (BILAG) assessment, and Physician's Global Assessment score ≥1, despite receiving standard SLE therapy.

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Clinical Trial

Patient Demographics			
	Trial 1	Trial 2	Trial 3
Clinical Trial Identifier	NCT01438489	NCT02446912	NCT02446899
Baseline SLEDAI-2K Score			
Mean (SD)	10.9 (4.1)	11.3 (3.72)	11.5 (3.76)
≥10 points, n (%)	182 (60)	328 (72)	260 (72)
BILAG organ system scoring (≥1 A, n[%])	152 (50)	217 (48)	176 (49)
Positive Anti-dsDNA levels, n (%)	185 (77)	207 (45)	159 (44)
Baseline SLE treatment			
OCS, n (%)	258 (85)	381 (83)	292 (81)
Antimalarials, n (%)	219 (72)	334 (73)	252 (70)
Immunosuppressants, n (%)	150 (49)	214 (47)	174 (48)

OCS: oral corticosteroids

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Clinical Trial

- **Primary endpoint:**
  - **Trial 1:** Combined assessment of the SLE Responder Index (SRI-4) and the sustained reduction in OCS (<10mg/day and ≤OCS dose at week 1, sustained for 12 weeks) measured at week 24.
  - **Trials 2/3:** Improvement in disease activity evaluated at 52 weeks, measured by SRI-4 (Trial 2) and BILAG-Based Composite Lupus Assessment (BICLA) (Trial 3).
- **Secondary endpoint:**
  - **Trials 2/3:** Maintenance of OCS reduction, improvement in cutaneous SLE activity, and flare rate.

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Clinical Trial

SRI-4 Response Rate at Week 52						
	Trial 1		Trial 2		Trial 3	
	Placebo (N=102)	Anifrolumab-fnia (N=99)	Placebo (N=184)	Anifrolumab-fnia (N=180)	Placebo (N=182)	Anifrolumab-fnia (N=180)
SRI-4 Response Rate						
Responder, n (%)	41 (38.8)	62 (62.8)	79 (43.0)	88 (49.0)	68 (37.3)	100 (55.5)
Difference in Response Rates (95% CI)	24.0 (10.9, 37.2)		6.0 (-4.2, 16.2)		18.2 (8.1, 28.3)	

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Clinical Trial

BICLA Response Rate at Week 52						
	Trial 1		Trial 2		Trial 3	
	Placebo (N=102)	Anifrolumab-fnia (N=99)	Placebo (N=184)	Anifrolumab-fnia (N=180)	Placebo (N=182)	Anifrolumab-fnia (N=180)
BICLA Response Rate						
Responder, n (%)	27 (25.8)	54 (54.6)	55 (30.2)	85 (47.1)	57 (31.5)	86 (47.8)
Difference in Response Rates (95% CI)	28.8 (15.7, 41.9)		17.0 (7.2, 26.8)		16.3 (6.3, 26.3) *P* =.001	

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Clinical Trial

- SRI-4 Responder Analysis: Treatment with anifrolumab-fnia did not result in statistically significant improvements over placebo (primary endpoint of Trial 2).
- In Trial 3, among the 47% of patients with baseline OCS use ≥10mg/day, anifrolumab-fnia demonstrated a statistically significant difference in the proportion of patients able to reduce OCS by at least 25% to ≤7.5mg/day at week 40 and maintain the reduction through week 52 (*P* =.004).

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/saphnelo/