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# Anifrolumab

Updated: September 20, 2023.

# OVERVIEW

## Introduction

Anifrolumab is a human monoclonal antibody to the type 1 interferon receptor which is used in the therapy of moderate-to-severe systemic lupus erythematous. Anifrolumab has been linked to a low incidence of transient serum enzyme elevations during therapy and has not been linked to instances of clinically apparent liver injury.

## Background

Anifrolumab (an" i frol' ue mab) is a human monoclonal IgG1 antibody to the type 1 interferon (IFN) receptor subunit 1 which is used to treat adults with moderate-to-severe systemic lupus erythematosus (SLE). Anifrolumab binds to type 1 interferon receptors blocking their activation and induction of interferon related genes. This monoclonal antibody has been shown to be effective in reducing disease activity in patients with systemic lupus erythematosus, a disease marked by elevated levels of soluble interferon gene induced proteins with immune dysregulation and production of pathogenic autoantibodies and immune complexes. Anifrolumab was approved for use in the United States in 2021 and current indications are for treatment of adult patients with active, autoantibody positive systemic lupus erythematosus (SLE) who are receiving standard therapy. Its beneficial effects have not been demonstrated in patients with severe lupus nephritis or central nervous system involvement. Anifrolumab is available under the brand name Saphnelo in single dose vials of 300 mg in 2 mL. The recommended dose is 300 mg given as an intravenous infusion (over 30 minutes) every 4 weeks. Adverse effects include infusion reactions, upper respiratory symptoms and infections, bronchitis, cough, and herpes zoster. Rare but potentially serious side effects include severe hypersensitivity reactions (angioedema or anaphylaxis), severe infections, and possibly malignancies. The potential of reactivation of latent infections such as tuberculosis and hepatitis B from anifrolumab is not clear. Patients receiving anifrolumab should not receive live viral vaccines.

## Hepatotoxicity

In preregistration controlled trials, elevations in serum aminotransferase levels were uncommon (less than 1%) and no more frequent during anifrolumab than with placebo therapy. Elevations in aminotransferase levels above 5 times the ULN were less common on anifrolumab than placebo therapy, and there were no reports of clinically apparent liver injury attributed to anifrolumab. Since its approval and more widescale use, there have been no case reports of liver injury with jaundice linked to anifrolumab therapy. Reactivation of hepatitis B as well as immune-mediated hepatitis can occur with use of immunosuppressive monoclonal antibodies such as infliximab and adalimumab, but instances have not been reported with anifrolumab.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

## Mechanism of Injury

There is little evidence that anifrolumab is a cause of liver injury, and mechanisms by which it occurs is not clear but might result from immune modulation.

## Outcome and Management

The serum aminotransferase elevations that have been reported during anifrolumab therapy were generally transient, mild and asymptomatic and did not require dose modification or delay in therapy. Elevations above 5 times the upper limit of normal should lead to more careful monitoring and suspension of further infusions, at least until levels return to normal or near normal levels. There is no evidence of cross sensitivity to hepatic reactions among the various monoclonal antibodies.

Drug Class: Monoclonal Antibodies, Immunosuppressive Agents

Other Drugs for Systemic Lupus Erythematosus: Belimumab

# PRODUCT INFORMATION

**REPRESENTATIVE TRADE NAMES**

Anifrolumab – Saphnelo®

**DRUG CLASS**

Immunosuppressive Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

# CHEMICAL FORMULA AND STRUCTURE

| DRUG | CAS REGISTRY NO. | MOLECULAR FORMULA | STRUCTURE |
|---|---|---|---|
| Anifrolumab | 1326232-46-5 | Monoclonal Antibody | Not Available |

# ANNOTATED BIBLIOGRAPHY

References updated: 20 September 2023

Abbreviations: PML, progressive multifocal leukoencephalopathy; SLE, systemic lupus erythematosus.

Zimmerman HJ. Drugs used to treat rheumatic and musculospastic disease. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 517-54.

*(Expert review of hepatotoxicity published in 1999, before the availability of most monoclonal antibody therapies).*

Reuben A. Hepatotoxicity of immunosuppressive drugs. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2011, pp. 569-91.

*(Review of hepatotoxicity of immunosuppressive agents does not mention anifrolumab).*

Krensky AM, Azzi JR, Hafler DA. Immunosuppressants and toleragens. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 637-53.

*(Textbook of pharmacology and therapeutics).*

FDA: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761123Orig1s000MultidisciplineR.pdf

*(FDA website with product labels and initial multidiscipline clinical review of the safety and efficacy of anifrolumab based on results from 1,123 adults treated in 3 controlled trials, stated that the safety results were generally favorable with adverse events reported in 87% of anifrolumab vs 79% of placebo recipients, and serious adverse events in 12% vs 17% including serious infections in 4.8% vs 5.6%, herpes zoster in 12% vs 3%, hypersensitivity reactions in 2.6% vs 0.6%, and ALT elevations above 5 times ULN in 0.3% vs 0.8%).*

Furie R, Khamashta M, Merrill JT, Werth VP, Kalunian K, Brohawn P, Illei GG, et al.; CD1013 Study Investigators. Anifrolumab, an anti-interferon-α receptor monoclonal antibody, in moderate-to-severe systemic lupus erythematosus. Arthritis Rheumatol. 2017;69:376-386. PubMed PMID: 28130918.

*(Among 305 adults with SLE treated with anifrolumab [300 or 1000 mg] vs placebo every 4 weeks for 52 weeks, clinical responses occurred in 63% and 54% vs 40%, while adverse event rates were higher with the higher dose including herpes zoster in 5.2% and 9.5% vs 2%; no mention of ALT elevations or hepatotoxicity).*

Morand EF, Furie R, Tanaka Y, Bruce IN, Askanase AD, Richez C, Bae SC, et al.; TULIP-2 Trial Investigators. Trial of anifrolumab in active systemic lupus erythematosus. N Engl J Med. 2020;382:211-221. PubMed PMID: 31851795.

*(Among 362 adults with SLE treated with anifrolumab vs placebo, response rates at 52 weeks was 48% vs 32% and adverse events 88% vs 84%, serious adverse events 8% vs 17%, herpes zoster 7.2% vs 1.1%, serious infections 2.8% vs 5.5%, and infusion reactions 14% vs 8%; no mention of ALT elevations or hepatotoxicity).*

Smith MA, Chiang CC, Zerrouki K, Rahman S, White WI, Streicher K, Rees WA, et al. Using the circulating proteome to assess type I interferon activity in systemic lupus erythematosus. Sci Rep. 2020;10:4462. PubMed PMID: 32157125.

*(Among 1,132 protein measurements from blood samples from patients with SLE, type 1 interferon induced genes were often elevated and patients could be categorized by high vs low levels).*

Anifrolumab (Saphnelo) for systemic lupus erythematosus. Med Lett Drugs Ther. 2021;63(1633):146-147. PubMed PMID: 34550961.

*(Concise review of the mechanism of action, clinical efficacy, safety, and costs of anifrolumab shortly after its approval as therapy of SLE in the US, discusses adverse events of upper respiratory infections, bronchitis, infusion reactions, herpes zoster, and cough, but does not mention ALT elevations or hepatotoxicity).*

Chatham WW, Furie R, Saxena A, Brohawn P, Schwetje E, Abreu G, Tummala R. Long-term safety and efficacy of anifrolumab in adults with systemic lupus erythematosus: results of a phase I open-label extension study. Arthritis Rheumatol. 2021;73:816-825. PubMed PMID: 33225631.

*(Among 218 adult participants with SLE in controlled trials of anifrolumab who were enrolled in an open label extension study, clinical responses were sustained, no new safety signals were observed and there were no liver related serious adverse events).*

Jayne D, Rovin B, Mysler EF, Furie RA, Houssiau FA, Trasieva T, Knagenhjelm J, et al. Phase II randomised trial of type I interferon inhibitor anifrolumab in patients with active lupus nephritis. Ann Rheum Dis. 2022;81:496-506. PubMed PMID: 35144924.

*(Among 147 adults with active lupus nephritis treated with standard therapy and anifrolumab [300 mg every 4 weeks or an intensive early regimen] or placebo, clinical response rates were similar among the three groups while herpes zoster was more frequent with anifrolumab [17% vs 8%]; no mention of ALT elevations or hepatotoxicity).*

Kalunian KC, Furie R, Morand EF, Bruce IN, Manzi S, Tanaka Y, Winthrop K, et al. A randomized, placebo-controlled phase III extension trial of the long-term safety and tolerability of anifrolumab in active systemic lupus erythematosus. Arthritis Rheumatol. 2023;75:253-265. PubMed PMID: 36369793.

*(Among 560 adults with SLE enrolled in a long term extension study of anifrolumab [300 mg every 4 weeks], adverse events occurred in 93% which were scored as serious in 26%, herpes zoster in 13% and severe infections in 10%, 1 case of anaphylaxis, and 12 malignancies; no mention of ALT elevations or hepatoxicity and no cases of active tuberculosis).*

Neupane B, Shukla P, Slim M, Martin A, Petri M, Bertsias GK, Kim AHJ, et al. Belimumab versus anifrolumab in adults with systemic lupus erythematosus: an indirect comparison of clinical response at 52 weeks. Lupus Sci Med. 2023;10:e000907. PubMed PMID: 37147022.

*(Analysis of 5 trials of belimumab and 3 of anifrolumab in adults with moderate-to-severe SLE found similar rates of clinical response to both agents; no analysis of adverse events).*

Kalunian KC, Furie R, Morand EF, Bruce IN, Manzi S, Tanaka Y, Winthrop K, et al. A randomized, placebo-controlled phase III extension trial of the long-term safety and tolerability of anifrolumab in active systemic lupus erythematosus. Arthritis Rheumatol. 2023;75:253-265. PubMed PMID: 36369793.

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