KINERET EMERGENCY USE AUTHORIZATION **FOR COVID-19**

Kineret® (anakinra)

EMERGENCY USE AUTHORIZATION (EUA) FOR KINERET® (anakinra)

The FDA has issued an EUA for the emergency use of KINERET for the treatment of COVID-19 in hospitalized adults with positive results of direct SARS-CoV-2 viral testing with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) who are at risk of progressing to severe respiratory failure, and likely to have an elevated plasma soluble urokinase plasminogen activator receptor (suPAR). However, KINERET is not approved for this use.

The emergency use of KINERET is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of drugs during the COVID-19 pandemic, information on available alternatives, and additional information on COVID-19.

CONTRAINDICATIONS

KINERET is contraindicated in patients with known hypersensitivity to *E. coli* derived proteins, anakinra, or any components of the product.

Please see additional Important Safety Information throughout and accompanying EUA Fact Sheet for Healthcare Providers.

KINERET® (anakinra) for the treatment of COVID-19[1]

The SAVE-MORE study[1]

The SAVE-MORE study was a randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of KINERET in adult (≥18 years) patients with COVID-19 pneumonia who were at risk of developing severe respiratory failure (SRF). SRF was defined as pO2/FiO2 <150 mm Hg necessitating high-flow oxygenation (HFO), noninvasive ventilation (NIV), or mechanical ventilation (MV).

All patients were hospitalized adults with COVID-19 pneumonia, radiologically confirmed by chest x-ray or CT, but had not progressed to SRF. All enrolled patients in this study were required to have a plasma suPAR level ≥6 ng/mL.

Primary endpoint[1]

The primary endpoint of the study was the 11-point WHO Clinical Progression ordinal Scale (CPS), which was compared between the 2 arms of treatment by day 28. The 11-point WHO-CPS provides a measure of illness severity across a range from 0 (not infected), 1-3 (mild disease), 4-5 (hospitalized—moderate disease), 6-9 (hospitalized—severe disease with increasing degrees of NIV, MV, and extra-corporeal membrane oxygenation [ECMO]), to 10 (dead).

Key exclusion criteria:

- pO2/FiO2 <150 mm Hg
- requirement for NIV, MV, or ECMO
- <1500 neutrophils/mm^3

suPAR, soluble urokinase plasminogen activator receptor.

Results[1]

At the start of treatment, 91% of patients had severe COVID-19 pneumonia and required low- or high-flow supplementary oxygen, and 9% of patients had moderate COVID-19 pneumonia. Eighty-six percent of patients received dexamethasone.

At 28 days, patients treated with KINERET had lower odds of more severe disease according to the WHO-CPS compared to placebo.[1,*]

Mortality at 28 days[1,†]

KINERET **3.2%** (13/405)

Placebo **6.9%** (13/189)

†Hazard ratio (HR): 0.48 (95% CI 0.22, 1.04); risk difference -3.7% (95% CI -7.7%, 0.3%).

Mortality at 60 days[1,2,‡,§]

KINERET **5.3%** (21/392)

Placebo **9.7%** (18/183)

‡HR: 0.56 (95% CI 0.30, 1.04); risk difference -4.4% (95% CI -9.2%, 0.4%).

SRF at 28 days[1,‖]

KINERET **21.2%** (86/405)

Placebo **32.8%** (62/189)

‖HR: 0.66 (95% CI 0.48, 0.92); risk difference -11.6% (95% CI -19.4%, -3.8%).

§Data from a post hoc analysis of derived binary endpoints.

*Odds ratio: 0.37 (95% CI 0.26 to 0.50). The endpoints were not multiplicity controlled.

IMPORTANT SAFETY INFORMATION

Serious Infections. KINERET has been associated with an increased incidence of serious infections (2%) vs. placebo (< 1%) in clinical trials of patients with rheumatoid arthritis (RA). In a placebo-controlled study in COVID-19 patients, serious infections were observed in 9.1% of patients (37/405) treated with KINERET and 16.4% of patients (31/189) treated with placebo. In patients with COVID-19, monitor for signs and symptoms of new infections during and after treatment with KINERET. There is limited information regarding the use of KINERET in patients with COVID-19 and concomitant active serious infections. The risks and benefits of treatment with KINERET in COVID-19 patients with other concurrent infections should be considered.

Please see additional Important Safety Information throughout and accompanying EUA Fact Sheet for Healthcare Providers.

Kineret® (anakinra)

Safety[1]

The safety data are based on the evaluation of 405 KINERET-treated patients and 189 placebo-treated patients who were hospitalized with COVID-19 pneumonia in the SAVE-MORE trial. During the study, there were 18 (4.4%) deaths in the KINERET arm and 17 (9.0%) in the placebo arm. Serious infections occurred in 37 patients (9.1%) in the KINERET arm and in 31 patients (16.4%) in the placebo arm.

The overall safety profile in KINERET-treated patients with COVID-19 is similar to that in KINERET-treated patients with rheumatoid arthritis, which is an FDA-approved indication.

Adverse Events Occurring in at Least 1% of Patients in the KINERET Arm and at Least 1% More Frequently Than Observed in the Placebo Arm Through Day 90[1]

ADVERSE REACTIONS	SoC + PLACEBO (n=189)[a] n (%)	SoC + KINERET (n=405)[a] n (%)
Transaminases increased	52 (27.5)	125 (30.8)
Gamma-glutamyltransferase increased	22 (11.7)	56 (13.8)
Leukopenia	2 (1.1)	14 (3.5)
Neutropenia	1 (0.5)	12 (3.0)
Rash	3 (1.5)	15 (3.7)
Hypernatremia	15 (7.9)	39 (9.6)
Constipation	14 (7.4)	37 (9.1)
Hyperkalemia	14 (7.4)	37 (9.1)
Anxiety	12 (6.3)	33 (8.1)
Hypothermia	8 (4.2)	30 (7.4)
Acute kidney injury	10 (5.2)	26 (6.3)

[a]Patients are counted once for each category regardless of the number of events.

SoC, standard of care.

Dosing[1]

The recommended dosage of KINERET for the treatment of adults with COVID-19 is **100 mg administered daily by subcutaneous injection for 10 days**.

Consider administration of KINERET 100 mg every other day by subcutaneous injection for a total of 5 doses over 10 days in patients who have severe renal insufficiency or end-stage renal disease (creatinine clearance <30 mL/min).

For more information and downloadable resources about the EUA of KINERET in COVID-19, please visit

https://kineretrxhcp.com/EUA.php

or scan the QR code below.

IMPORTANT SAFETY INFORMATION

Use with Tumor Necrosis Factor (TNF)-blocking agents is not recommended. The combination of KINERET with TNF-blocking agents and other anti-cytokine treatments has not been evaluated in COVID-19 patients.

Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported. If a severe hypersensitivity reaction occurs, administration of KINERET should be discontinued and appropriate therapy initiated.

Please see additional Important Safety Information throughout and accompanying EUA Fact Sheet for Healthcare Providers.

Kineret® (anakinra)

IMPORTANT SAFETY INFORMATION

Immunosuppression. The impact of treatment with KINERET on the development of malignancies in COVID-19 patients is not known.

Immunizations. Avoid live vaccines during treatment with KINERET.

Neutropenia. Patients receiving KINERET may experience a decrease in neutrophil counts. There is limited information on the effect of KINERET on the neutrophil count of patients with COVID-19. COVID-19 patients with < 1500 neutrophils/mm^3 were excluded from participation in the SAVE and SAVE-MORE studies. Therefore, assess neutrophil counts prior to initiating KINERET treatment for COVID-19 and monitor for neutropenia according to current clinical practices.

Serious Adverse Reactions

The safety data described in this section are based on a randomized placebo-controlled study of 405 KINERET-treated patients hospitalized with COVID-19 pneumonia (SAVE-MORE study). During the study, there were 18 (4.4%) deaths in the KINERET arm and 17 (9.0%) in the placebo arm. Serious infections occurred in 37 patients (9.1%) in the KINERET arm and in 31 patients (16.4%) in the placebo arm.

Most Common Adverse Reactions

The adverse reactions reported more frequently in patients receiving KINERET compared to placebo, at a frequency of at least 1% were transaminases increased, gamma-glutamyltransferase increased, leukopenia, neutropenia, rash, hypernatremia, constipation, hyperkalemia, anxiety, hypothermia, and acute kidney injury.

Refer to Section 6 Adverse Reactions of the FDA-approved Prescribing Information for additional information on adverse reactions associated with chronic use of KINERET.

These are not all the possible risks associated with KINERET. Please see the KINERET Fact Sheet for Health Care Providers at https://www.KineretRxHCP.com/EUA

Mandatory reporting is required for all serious adverse events and medication errors potentially related to KINERET within 7 calendar days from the onset of the event, using FDA Form-3500. For instructions on how to submit adverse event and medication error reports, using FDA Form-3500, see the KINERET Fact Sheet for Health Care Providers or visit www.fda.gov/medwatch/report.htm. You may also call FDA at 1-800-FDA-1088 or Sobi North America at 1-866-773-5274.

References: 1. Fact Sheet for Healthcare Providers: Emergency Use Authorization for KINERET. Stockholm, Sweden: Sobi, Inc. 2022. **2.** Data on file. Stockholm, Sweden: Sobi, Inc. 2022.

Kineret® (anakinra) sobi