



November 8, 2022

Swedish Orphan Biovitrum AB
c/o Advyzom LLC
Rula Ibrahim-Saker, PharmD
U.S. Agent
335 Snyder Ave.
Berkeley Heights, NJ 07922

RE: Emergency Use Authorization 109

Dear Dr. Ibrahim-Saker:

This letter is in response to Swedish Orphan Biovitrum AB's (Sobi) request that the Food and Drug Administration (FDA or Agency) issue an Emergency Use Authorization (EUA) for the emergency use of Kineret (anakinra) for the treatment of coronavirus disease 2019 (COVID-19) in certain hospitalized patients, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes coronavirus disease 2019 (COVID-19).¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

Kineret is an Interleukin-1 (IL-1) receptor antagonist. IL-1 is involved in inflammatory diseases and additionally, IL-1 is linked to acute severe lung inflammation in COVID-19. Kineret is FDA-approved for several indications³; however, Kineret is not approved for the treatment of COVID-19.

Based on the totality of scientific evidence available to FDA, including data from the clinical trial SAVE-MORE (NCT04680949): a randomized, double-blind, placebo-controlled study to

¹ U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3. February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020).

³ The FDA-approved labeling for Kineret (anakinra) may be found at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/103950s51891bl.pdf

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, it is reasonable to believe that Kineret may be effective 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), as described in the Scope of Authorization (Section II), and when used under the conditions described in this authorization, the known and potential benefits of Kineret outweigh the known and potential risks of such product.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Kineret for the treatment COVID-19 in certain hospitalized adults, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Kineret for the treatment of COVID-19, when administered as described in the Scope of Authorization (Section II), meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Kineret may be effective 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 suPAR, as described in the Scope of Authorization (Section II), and that, when used under the conditions described in this authorization, the known and potential benefits of Kineret outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to 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 suPAR.^{4,5}

⁴ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁵ Veklury (remdesivir), a SARS-CoV-2 nucleotide analog RNA polymerase inhibitor, is an FDA-approved alternative for the treatment of COVID-19 in hospitalized adults with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) who are at risk of progressing to severe respiratory failure. Veklury has demonstrated antiviral activity against SARS-CoV-2; whereas Kineret is an IL-1 receptor antagonist that blocks the IL-1 signaling pathway, which is involved in inflammatory diseases and thought to contribute to inflammation and worsening of COVID-19, offering a different mechanism of action. Olumiant (baricitinib), a Janus kinase (JAK) inhibitor, is an FDA-approved alternative for the treatment of COVID-19 in hospitalized adults with pneumonia requiring

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Kineret may only be used by healthcare providers to treat 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 for progressing to severe respiratory failure and are likely to have an elevated suPAR.⁶
- The use of Kineret covered by this authorization must be in accordance with the authorized Fact Sheets.

Product Description

The authorized Kineret is supplied in a single-use preservative free, prefilled glass syringe with a 29-gauge needle. Each prefilled glass syringe contains 100 mg of Kineret per 0.67 mL. Kineret is distributed in a 1 x 7 syringe dispensing pack containing 7 syringes (NDC 66658-234-07). Kineret is to be administered by subcutaneous injection.

The authorized storage and handling information for Kineret is included in the authorized Fact Sheet for Healthcare Providers.

Kineret is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and to patients and caregivers, respectively, through Sobi's website at www.KineretRxHCP.com/EUA (referred to as the "authorized labeling"):

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) for Kineret
- Fact Sheet for Patients and Caregivers: Emergency Use Authorization (EUA) of Kineret for Coronavirus Disease 2019 (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Kineret, when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh the known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Kineret may be effective for the

supplemental oxygen and non-invasive ventilation. Kineret offers an alternative mechanism of action as an IL-1 receptor antagonist. IL-1 is another component of the complex hyperinflammatory response thought to contribute to worsening of COVID-19. In addition, Kineret has a subcutaneous route of administration; whereas, Olumiant is available as tablets, offering an alternative route of administration to some patients who are hospitalized (e.g. for patients who are unable to swallow tablets).

⁶ See Section 1.1 of the authorized Fact Sheet for Healthcare Providers for criteria to identify patients who are at risk of progressing to severe respiratory failure and likely to have an elevated suPAR.

treatment of COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Kineret (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Kineret under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Kineret is authorized 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 for progressing to severe respiratory failure and are likely to have an elevated suPAR, as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Sobi and Authorized Distributors⁷

- A. Sobi and authorized distributor(s) will ensure that Kineret is distributed and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers as described in Section II of this Letter of Authorization.
- B. Sobi and authorized distributor(s) will ensure that appropriate storage is maintained until the product is delivered to healthcare facilities and/or healthcare providers.
- C. Sobi and authorized distributor(s) will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., U.S. government agencies, state and local government authorities, authorized distributors, healthcare facilities, healthcare providers) involved in distributing or receiving Kineret. Sobi will provide to all relevant stakeholders a copy of this Letter of Authorization and communicate any subsequent amendments that might be made to this Letter of Authorization and its authorized accompanying materials (i.e., Fact Sheets).
- D. Sobi may request changes to this authorization, including to the authorized Fact Sheets for Kineret. Any request for changes to this EUA must be submitted to the Office of

⁷ “Authorized Distributor(s)” are identified by Sobi as an entity or entities allowed to distribute the authorized Kineret.

Immunology and Inflammation/Office of New Drugs/Center for Drug Evaluation and Research. Such changes require appropriate authorization prior to implementation.⁸

- E. Sobi may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of Kineret as described in this Letter of Authorization and authorized labeling, without FDA’s review and concurrence, when necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling for Kineret are prohibited. If the Agency notifies Sobi that any instructional and educational materials are inconsistent with the authorized labeling, Sobi must cease distribution of such instructional and educational materials. Furthermore, as part of its notification, the Agency may also require Sobi to issue corrective communication(s).
- F. Sobi will report to FDA all serious adverse events and medication errors potentially related to Kineret use that are reported to Sobi using either of the following options.

Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the [FDA SRP](#) web page.

Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the [FAERS electronic submissions](#) web page.

Submitted reports under both options must state: “Kineret use for COVID-19 under Emergency Use Authorization (EUA).” For reports submitted under Option 1, include this language at the beginning of the question “Describe Event” for further analysis. For reports submitted under Option 2, include this language at the beginning of the “Case Narrative” field.

- G. All manufacturing, packaging, and testing sites for both drug substance and drug product used for EUA supply will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.
- H. Sobi will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with drug product distributed under this EUA for Kineret that includes the following:

⁸ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study; (8) new strengths of the authorized product, new product sources (e.g., of active pharmaceutical ingredient) or of product components. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence is required from the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER and the Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist.

- Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or
- Information concerning any microbiological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information must be submitted for all potentially impacted lots.

Sobi will include in its notification to the Agency whether the batch, or batches, in question will be recalled.

If not included in its initial notification, Sobi must submit information confirming that Sobi has identified the root cause of the significant quality problems, taken corrective action, and provide a justification confirming that the corrective action is appropriate and effective. Sobi must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

- I. Sobi will manufacture Kineret to meet all quality standards and per the manufacturing process and control strategy as detailed in Sobi's EUA request. Sobi will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product, without notification to and concurrence by the Agency as described under Condition D.
- J. Through a process of inventory control, Sobi and authorized distributor(s) will maintain records regarding distribution of Kineret (i.e., lot numbers, quantity, receiving site, receipt date).
- K. Sobi must provide the following information to the Agency:
 1. Sobi will provide the necessary data and/or information validating the use of the alternative patient identification method to suPAR⁹ at baseline in patients with positive direct SARS-CoV-2 viral testing, who are hospitalized, requiring oxygen, with evidence of COVID-19 pneumonia. Sobi will pre-specify the analyses to examine the correlation, sensitivity, specificity, positive predictive value, and negative predictive value, between suPAR and the alternative patient identification method. Sobi must submit a data analysis plan no later than January 31, 2023. Sobi must submit a final analysis report no later than May 31, 2023.
 2. Sobi will provide the data and/or information necessary to support the submission of a marketing application under the appropriate regulatory pathway, as determined by the Center for Devices and Radiological Health

⁹ Supra at Note 6.

(CDRH), for a suPAR test for commercial use in the United States. Sobi has agreed to submit a marketing application to CDRH no later than January 31, 2025.

- L. Sobi and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom Kineret Is Distributed and Healthcare Providers Administering Kineret

- M. Healthcare facilities and healthcare providers will ensure that they are aware of the Letter of Authorization, and the terms herein, and that the authorized Fact Sheets are made available to healthcare providers and to patients and caregivers, respectively, through appropriate means, prior to administration of Kineret as described in the Scope of Authorization (Section II) under this EUA.
- N. Healthcare facilities and healthcare providers receiving Kineret will track all serious adverse events and medication errors that are considered to be potentially related to Kineret use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form (www.fda.gov/medwatch/report.htm), or complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (these forms can be found via link above). Call [1-800-FDA-1088](tel:1-800-FDA-1088) for questions. Submitted reports must state, “Kineret use for COVID-19 under Emergency Use Authorization” at the beginning of the question “Describe Event” for further analysis. A copy of the completed FDA Form 3500 must also be provided to Sobi per the instructions in the authorized labeling.
- O. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the product is administered consistent with the terms of this letter and the authorized labeling.
- P. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensing and administration of Kineret for the use authorized in this letter (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered).
- Q. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Sobi and/or FDA. Such records will be made available to Sobi, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

- R. All descriptive printed matter, advertising, and promotional materials relating to the use of Kineret under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the Act, as applicable, and FDA implementing regulations. References to “approved

labeling”, “permitted labeling”, or similar terms in these requirements shall be understood to refer to the authorized labeling for the use of Kineret under this authorization. In addition, such materials shall:

- Be tailored to the intended audience.
 - Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i), 21 CFR 200.200 and 21 CFR 201.100(f).
 - Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
 - Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.
 - Be submitted to FDA accompanied by Form FDA-2253 for consideration at least 14 calendar days prior to initial dissemination or first use.
- S. Sobi may disseminate descriptive printed matter, advertising, and promotional materials relating to the emergency use of Kineret that provide accurate descriptions of safety results and efficacy results on a clinical endpoint(s) from the clinical trial(s) summarized in the authorized labeling. Such materials must include any limitations of the clinical trial data as described in the authorized labeling. Sobi may not imply that Kineret is FDA-approved for its authorized use by making statements such as “Kineret is safe and effective for the treatment of COVID-19.”
- T. All descriptive printed matter, advertising, and promotional material, relating to the use of Kineret under this authorization clearly and conspicuously shall state that:
- Kineret has not been approved, but has been authorized for emergency use by FDA under an EUA, 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 suPAR; and
 - 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.

If the Agency notifies Sobi that any descriptive printed matter, advertising, or promotional materials do not meet the terms set forth in Conditions R through T of this EUA, Sobi must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency’s notification. Furthermore, as part of its notification, the Agency may also require Sobi to issue corrective communication(s).

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

Patrizia A.
Cavazzoni -S



Digitally signed by
Patrizia A. Cavazzoni -S
Date: 2022.11.08
18:28:17 -05'00'

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR KINERET

HIGHLIGHTS OF EMERGENCY USE AUTHORIZATION (EUA)

These highlights of the EUA do not include all the information needed to use KINERET® under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for KINERET®.

KINERET® (anakinra) injection, for subcutaneous use

Original EUA Authorized Date: 11/2022

-----EUA FOR KINERET-----

The U.S. Food and Drug Administration has issued an EUA for the emergency use of KINERET for the treatment of coronavirus disease 2019 (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.

See Section 1.1 for criteria to identify patients who are at risk of progressing to severe respiratory failure and likely to have an elevated plasma suPAR.

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.

-----DOSAGE AND ADMINISTRATION-----

- The recommended dosage of KINERET in adults with COVID-19 is 100 mg administered daily by subcutaneous injection for 10 days. (2.1)
- In COVID-19 patients who have severe renal insufficiency or end stage renal disease (creatinine clearance < 30 mL/min, estimated from serum creatinine levels) consider a dose of 100 mg of KINERET administered every other day for 5 total doses over 10 days. (2.2)

-----DOSAGE FORMS AND STRENGTHS-----

Injection: 100 mg/0.67 mL solution in a single-use prefilled syringe for subcutaneous injection. (3)

-----CONTRAINDICATIONS-----

Known hypersensitivity to E coli-derived proteins, anakinra, or to any component of the product. (4)

-----WARNINGS AND PRECAUTIONS-----

- KINERET has been associated with an increase of serious infections in patients with rheumatoid arthritis. (5.1)

- KINERET is not recommended for use in combination with Tumor Necrosis Factor (TNF) blocking agents. (5.2)
- Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported. (5.3)
- The impact of treatment with KINERET on the development of malignancies is not known. (5.4)
- Avoid live vaccines during treatment with KINERET. (5.5)
- Neutropenia can occur with treatment with KINERET. Assess neutrophil counts prior to initiating KINERET treatment. COVID-19 patients with < 1500 neutrophils/mm³ were excluded from study participation. (5.6)

-----ADVERSE REACTIONS-----

Most common adverse reactions (incidence ≥ 1%) are transaminases increased, neutropenia, rash, and injection site reactions. (6.1)

You or your designee must report all SERIOUS ADVERSE EVENTS or MEDICATION ERRORS potentially related to KINERET (1) by submitting FDA Form 3500 [online](#), (2) by [downloading](#) this form and then submitting by mail or fax, or (3) contacting the FDA at 1-800-FDA-1088 to request this form. Please also provide a copy of this form to Swedish Orphan Biovitrum at email medinfo.us@sobi.com or call 1-866-773-5274 (6.2).

-----DRUG INTERACTIONS-----

KINERET is not recommended for use in combination with TNF blocking agents. (7.1)

-----USE IN SPECIFIC POPULATIONS-----

Renal Impairment: This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. (8.6)

See PATIENT AND PARENTS/CAREGIVER FACT SHEET.

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FULL FACT SHEET FOR HEALTHCARE PROVIDERS

1 EMERGENCY USE AUTHORIZATION

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of KINERET for the treatment of coronavirus disease 2019 (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) [see Section (1.1)].

Justification for Emergency Use of Drugs During the COVID-19 Pandemic

There is currently an outbreak of Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2, a novel coronavirus. The Secretary of HHS has declared that:

- A public health emergency related to COVID-19 has existed since January 27, 2020.
- Circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic (March 27, 2020 declaration).

An EUA is a FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency that affects the national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition.
- Based on the totality of the available scientific evidence (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that:
 - The product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition; and
 - The known and potential benefits of the product - when used to diagnose, prevent, or treat such disease or condition - outweigh the known and potential risks of the product, taking into consideration the material threat posed by the biological agent(s).
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the serious or life-threatening disease or condition.

Information Regarding Available Alternatives for the EUA Authorized Use

Veklury (remdesivir), a SARS-CoV-2 nucleotide analog RNA polymerase inhibitor, is an FDA-approved alternative for the treatment of COVID-19 in hospitalized adults with pneumonia requiring supplemental oxygen (low or high-flow oxygen) who are at risk of progressing to severe respiratory failure. Veklury has demonstrated antiviral activity against SARS-CoV-2; whereas KINERET is an IL-1 receptor antagonist that blocks the IL-1 signaling pathway, which is involved in inflammatory diseases and thought to contribute to inflammation and worsening of COVID-19, offering a different mechanism of action.

Olumiant (baricitinib), a Janus kinase (JAK) inhibitor, is an FDA-approved alternative for the treatment of COVID-19 in hospitalized adults with pneumonia requiring supplemental oxygen and non-invasive ventilation. KINERET offers an alternative mechanism of action as an IL-1 receptor antagonist. IL-1 is another component of the complex hyperinflammatory response thought to contribute to worsening of COVID-19. In addition, KINERET has a subcutaneous route of administration, whereas, Olumiant is available as tablets; thus KINERET is offering an alternative route of administration to some patients who are hospitalized (e.g. for patients who are unable to swallow tablets).

Other therapeutics are currently authorized for the same use as KINERET. For additional information on all products authorized for the treatment of COVID-19, please see <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policyframework/emergency-use-authorization>.

For information on clinical studies of KINERET and other therapies for the treatment of COVID-19, see www.clinicaltrials.gov.

1.1 Patient Population Identification

KINERET is authorized for emergency use 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 suPAR.

In the SAVE-MORE trial used to support the efficacy and safety of KINERET in COVID-19, key exclusion criteria were: pO₂/FiO₂ ratio < 150 mmHg, requirement for non-invasive ventilation (NIV), requirement for mechanical ventilation (MV), requirement for extra-corporeal membrane oxygenation (ECMO), and < 1500 neutrophils/mm³.

All enrolled patients were required to have a plasma soluble urokinase plasminogen activator receptor (suPAR) level ≥ 6 ng/mL [see *Clinical Studies (14.1)*]. The suPAR assay is not commercially available in the United States. In order to identify a comparable population as was studied in the SAVE-MORE trial, an alternative patient identification method was developed to select patients most likely to have suPAR ≥ 6 ng/mL based on commonly measured patient characteristics. Patients meeting at least three of the following eight criteria are considered likely to have suPAR ≥ 6 ng/mL at baseline:

1. Age ≥ 75 years
2. Severe pneumonia by WHO criteria¹
3. Current/previous smoking status
4. Sequential Organ Failure Assessment (SOFA)² score ≥ 3
5. Neutrophil-to-lymphocyte ratio (NLR) ≥ 7
6. Hemoglobin ≤ 10.5 g/dL
7. Medical history of ischemic stroke
8. Blood urea ≥ 50 mg/dL and/or medical history of renal disease

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage for COVID-19

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

Each syringe is intended for a single use. A new syringe must be used for each dose. Any unused portion after each dose should be discarded.

2.2 Renal Impairment

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 (defined as creatinine clearance < 30 mL/min, as estimated from serum creatinine levels) [see *Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)*].

2.3 Important Administration Instructions

The prescribed dose of KINERET should be administered according to the instructions for use and any unused portions discarded. After administration of KINERET it is essential to follow the proper procedure for disposal of syringes and any residual drug. See the “Instructions for Use” in the FDA-approved Prescribing Information for detailed instructions on the handling and injection of KINERET.

Do not use KINERET beyond the expiration date shown on the carton. Visually inspect the solution for particulate matter and discoloration before administration. There may be trace amounts of small, translucent-to-white amorphous particles of protein in the solution. The prefilled syringe should not be used if the solution is discolored or cloudy, or if foreign particulate matter is present. If the number of translucent-to-white amorphous particles in a given syringe appears excessive, do not use this syringe.

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 mg/0.67 mL solution in a single-use prefilled syringe for subcutaneous injection.

4 CONTRAINDICATIONS

KINERET is contraindicated in patients with known hypersensitivity to *E. coli* derived proteins, KINERET, or any components of the product [see *Warnings and Precautions (5.3)*].

5 WARNINGS AND PRECAUTIONS

5.1 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.

The safety and efficacy of KINERET in immunosuppressed patients or in patients with chronic infections have not been evaluated.

5.2 Use with TNF blocking Agents

An increased rate of serious infections was observed in patients with RA who received KINERET and etanercept concurrently (7%) compared with etanercept alone (0%). KINERET is not recommended for use in combination with TNF blocking agents.

The combination of KINERET with TNF blocking agents and other anti-cytokine treatments has not been evaluated in COVID-19 patients.

5.3 Hypersensitivity Reactions

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

5.4 Immunosuppression

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

5.5 Immunizations

In a placebo-controlled clinical trial (n = 126), no difference was detected in anti-tetanus antibody response between the KINERET and placebo treatment groups when the tetanus/diphtheria toxoids vaccine was administered concurrently with KINERET. No data are available on the effects of vaccination with other inactivated antigens, or COVID-19 vaccines, in patients receiving KINERET. No data are available on either the effects of live vaccination or the secondary transmission of infection by live vaccines in patients receiving KINERET. Therefore, avoid live vaccines during treatment with KINERET.

5.6 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/mm³ 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 [see *Adverse Reactions* (6.1)].

6 ADVERSE REACTIONS

6.1 Adverse Reactions from Clinical Studies

The following adverse reactions have been observed in the clinical studies of KINERET in COVID-19 that supported EUA. The adverse reaction rates observed in these clinical studies cannot be directly compared to rates in the clinical studies of KINERET for RA, Neonatal-Onset Multisystem Inflammatory Disease (NOMID), Deficiency of Interleukin-1 Receptor Antagonist (DIRA), and may not reflect the rates observed in clinical practice.

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. The adverse events reported more frequently in patients receiving Kineret compared to placebo, at a frequency of at least 1% are described in Table 1.

The overall safety profile in patients with COVID-19 treated with Kineret is similar to that in Kineret-treated patients with the approved indication RA.

Table 1. 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

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)

^aPatients are counted once for each category regardless of the number of events

6.2 Adverse Reactions from Spontaneous Reports

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

6.3 Required Reporting for Serious Adverse Events and Medication Errors

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events* and medication errors potentially related to KINERET within 7 calendar days from the healthcare provider's awareness of the event, using FDA Form 3500 (for information on how to access this form, see below). The FDA requires that such reports, using FDA Form 3500, include the following:

- Patient demographics and baseline characteristics (e.g., patient identifier, age or date of birth, gender, weight, ethnicity, and race)

- A statement “KINERET use for COVID-19 under Emergency Use Authorization (EUA)” under the “**Describe Event, Problem, or Product Use/Medication Error**” heading
- Information about the serious adverse event or medication error (e.g., signs and symptoms, test/laboratory data, complications, timing of drug initiation in relation to the occurrence of the event, duration of the event, treatments required to mitigate the event, evidence of event improvement/disappearance after stopping or reducing the dosage, evidence of event reappearance after reintroduction, clinical outcomes).
- Patient’s preexisting medical conditions and use of concomitant products
- Information about the product (e.g., dosage, route of administration, NDC #).

Submit adverse event and medication error reports, using Form 3500, to FDA MedWatch using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm
- Complete and submit a postage-paid FDA Form 3500 (<https://www.fda.gov/media/76299/download>) and return by:
 - Mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or
 - Fax to 1-800-FDA-0178, or
- Call 1-800-FDA-1088 to request a reporting form

In addition, please provide a copy of all FDA MedWatch forms to:

Sobi Inc

Email: medinfo.us@sobi.com or call at 1-866-773-5274

The prescribing health care provider and/or the provider’s designee is/are responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of KINERET.

*Serious adverse events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- Other important medical event, which may require a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

7 DRUG INTERACTIONS

No drug-drug interaction studies in human subjects have been conducted. Toxicologic and toxicokinetic studies in rats did not demonstrate any alterations in the clearance or toxicologic profile of either methotrexate or KINERET when the two agents were administered together.

7.1 TNF Blocking Agents

A higher rate of serious infections has been observed in patients treated with concurrent KINERET and etanercept therapy than in patients treated with etanercept alone [see *Warnings and Precautions* (5.2)]. Two percent of patients treated concurrently with KINERET and etanercept developed neutropenia (ANC < 1 x 10⁹/L). Use of KINERET in combination with TNF blocking agents is not recommended.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from retrospective studies and case reports on KINERET use in pregnant women are insufficient to identify a drug associated risk of major birth defects, miscarriage, or maternal and fetal adverse events. In animal reproduction studies, subcutaneous administration of anakinra to pregnant rats and rabbits during organogenesis demonstrated no evidence of fetal harm at doses up to 25 times the maximum recommended human dose (MRHD). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Human Data

The available data from retrospective studies and case reports of anakinra-exposed pregnancies have not identified an increased frequency or pattern of birth defects, miscarriage, or adverse maternal or fetal outcomes. An international multi-center retrospective study of pregnancy outcomes with interleukin-1 inhibitors reported on 23 anakinra-exposed pregnancies. There were 21 live births of healthy infants, 1 miscarriage, and 1 infant with left renal agenesis. The estimated background rate of detected renal malformations is 0.2-2% of all newborns. Overall, these data cannot definitively establish or exclude any anakinra-associated risks during pregnancy. Methodological limitations of these data include small sample size and the inability to control for confounders such as the timing of drug exposure, underlying maternal disease, and concomitant medication use.

Animal Data

Animal reproduction studies were conducted in rats and rabbits. In embryo-fetal development studies, anakinra was administered throughout the period of organogenesis at the subcutaneous doses of 12.5, 50, and 200 mg/kg/day to pregnant rats from gestation days (GD) 7 to 17 and pregnant rabbits from GD 6 to 18. In these studies, anakinra at doses up to 25 times the MRHD (on a mg/kg basis at maternal subcutaneous doses up to 200 mg/kg/day) revealed no evidence of harm to the fetus.

8.2 Lactation

Risk Summary

There are no data on the presence of anakinra in either human or animal milk or the effects on milk production. Available published data from a small retrospective study and postmarketing case reports do not establish an association between maternal anakinra use during lactation and adverse effects on breastfed infants. The limited clinical data during lactation precludes a clear determination of the risk of KINERET to an infant during lactation. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for KINERET and any potential adverse effects on the breastfed infant from KINERET or from the underlying maternal condition.

8.4 Pediatric Use

The emergency use of KINERET is not authorized or approved for the treatment of coronavirus disease 2019 (COVID-19) for pediatric patients less than 18 years of age.

8.5 Geriatric Use

In a placebo-controlled study in COVID-19 patients, 250/594 (42%) were 65 years of age or older (KINERET 172/405, placebo 78/189). No differences in safety or effectiveness were observed between these patients and younger adult patients, but greater sensitivity of some older individuals cannot be ruled out. Because there is a higher incidence of infections in the elderly population in general, caution should be used in treating the elderly. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

8.6 Renal Impairment

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function [see *Clinical Pharmacology (12.3)*].

KINERET has not been studied in COVID-19 patients with end-stage renal failure necessitating hemofiltration or peritoneal hemodialysis.

8.7 Hepatic Impairment

No formal studies have been conducted examining the pharmacokinetics of KINERET administered subcutaneously in patients with hepatic impairment.

10 OVERDOSAGE

In sepsis trials no serious toxicities attributed to KINERET were seen when administered at mean calculated doses of up to 35 times those given patients with COVID-19 over a 72-hour treatment period.

11 DESCRIPTION

KINERET (anakinra) is a recombinant, nonglycosylated form of the human interleukin-1 receptor antagonist (IL-1Ra). KINERET differs from native human IL-1Ra in that it has the addition of a single methionine residue at its amino terminus. KINERET consists of 153 amino acids and has a molecular weight of 17.3 kilodaltons. It is produced by recombinant DNA technology using an *E coli* bacterial expression system.

KINERET is supplied in single use prefilled glass syringes with 29 gauge needles as a sterile, clear, colorless-to-white, preservative free solution for daily subcutaneous (SC) administration. The solution may contain trace amounts of small, translucent-to-white amorphous proteinaceous particles. Each prefilled glass syringe contains: 0.67 mL (100 mg) of anakinra in a solution (pH 6.5) containing anhydrous citric acid (1.29 mg), disodium EDTA (0.12 mg), polysorbate 80 (0.70 mg), and sodium chloride (5.48 mg) in Water for Injection, USP.

The prefilled syringe contains an outer rigid plastic needle shield attached to an inner needle cover. The syringe or needle shield components are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

KINERET blocks the biologic activity of IL-1 alpha and beta by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL-1RI), which is expressed in a wide variety of tissues and organs.

Refer to **Section 12.1 Mechanism of Action** of the FDA-approved Prescribing Information for additional information on the mechanism of action in the approved indications for Kineret.

12.3 Pharmacokinetics

The pharmacokinetics of Kineret has not been studied in patients with COVID-19.

The absolute bioavailability of KINERET after a 70 mg subcutaneous bolus injection in healthy subjects (n = 11) is 95%.

In subjects with RA, maximum plasma concentrations of KINERET occurred 3 to 7 hours after subcutaneous administration of KINERET at clinically relevant doses (1 to 2 mg/kg; n = 18); the terminal half-life ranged from 4 to 6 hours. In RA patients, no unexpected accumulation of KINERET was observed after daily subcutaneous doses for up to 24 weeks.

The influence of demographic covariates on the pharmacokinetics of KINERET was studied using population pharmacokinetic analysis encompassing 341 patients receiving daily subcutaneous injection of KINERET at doses of 30, 75, and 150 mg for up to 24 weeks. The estimated KINERET clearance increased with increasing creatinine clearance and body weight. After adjusting for creatinine clearance and body weight, gender and age were not significant factors for mean plasma clearance.

In Neonatal-Onset Multisystem Inflammatory Disease (NOMID) patients, at a median SC dose of 3 mg/kg once daily and a median treatment time of 3.5 years, the median (range) steady-state serum exposure of anakinra was C_{max} 3628 (655–8511) ng/mL (n=16) and C_{24h} 203 (53–1979) ng/mL (n=16). The median (range) half-life of anakinra was 5.7 (3.1–28.2) hours (n=12). There was no obvious gender difference.

Patients With Renal Impairment: The mean plasma clearance of KINERET in subjects with mild (creatinine clearance 50-80 mL/min) and moderate (creatinine clearance 30-49 mL/min) renal insufficiency was reduced by 16% and 50%, respectively. In severe renal insufficiency and end stage renal disease (creatinine clearance < 30 mL/min¹), mean plasma clearance declined by 70% and 75%, respectively. Less than 2.5% of the administered dose of KINERET was removed by hemodialysis or continuous ambulatory peritoneal dialysis. Based on these observations, a dose schedule change should be considered for subjects with severe renal insufficiency or end stage renal disease [see *Dosage and Administration (2.2)*].

Patients with Hepatic Dysfunction: No formal studies have been conducted examining the pharmacokinetics of KINERET administered subcutaneously in patients with hepatic impairment.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies to evaluate the carcinogenic potential of KINERET were not conducted. KINERET had no effects on fertility and reproductive performance indices in male and female rats subcutaneous doses up to 200 mg/kg/day (approximately 25 times the MRHD on a mg/kg basis).

14 CLINICAL STUDIES

14.1 Clinical Study in COVID-19

SAVE-MORE (NCT04680949) 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), defined as $pO_2/FiO_2 < 150$ mmHg necessitating high flow oxygenation (HFO)/NIV/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 soluble urokinase plasminogen activator receptor (suPAR) level ≥ 6 ng/mL. The suPAR assay is not commercially available for use in the United States, [see *Emergency Use Authorization (1.1)*]. Key exclusion criteria were $pO_2/FiO_2 < 150$ mmHg, requirement for NIV, requirement for MV, requirement for ECMO, and < 1500 neutrophils/mm³. The mean age of participants was 61.9 years (standard deviation [SD] 12.1 years), and 57.9% were male.

Efficacy analyses at Day 28 were performed using all randomized patients who maintained consent for data usage comprising 594 patients of whom 189 patients were randomized to the placebo+Standard of Care (SoC) arm and 405 patients to the anakinra 100 mg daily+SoC arm for 10 days.

At the start of treatment, 91% of patients had severe COVID-19 pneumonia and required low- or high-flow supplementary oxygen, 9% of patients had moderate COVID-19 pneumonia. 86% of patients received dexamethasone.

The primary endpoint of the study was the 11-point WHO Clinical Progression ordinal Scale (CPS) which was compared between the two 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 ECMO) to 10 (dead).

Patients treated with KINERET had lower odds of more severe disease according to the WHO-CPS at Day 28 compared to placebo (odds ratio: 0.37 [95% CI 0.26 to 0.50]).

By Day 28, there were 13 deaths (6.9%) in the placebo arm and 13 deaths (3.2%) in the KINERET arm (hazard ratio (HR): 0.48 [95% CI 0.22, 1.04]; risk difference: -3.7% [95% CI -7.7%, 0.3%]). By Day 60, there were 18 deaths (9.7%) in the placebo arm and 21 deaths (5.3%) in the KINERET arm (HR: 0.56 [95% CI 0.30, 1.04]; risk difference -4.4% [95% CI -9.2%, 0.4%]).

By Day 28, there were 62 (32.8%) patients in the placebo arm and 86 (21.2%) patients in the KINERET arm with SRF (HR: 0.66 [95% CI 0.48, 0.92]; risk difference -11.6% [95% CI -19.4%, -3.8%]).

The endpoints were not multiplicity controlled.

15 REFERENCES

1. World Health Organization . (2020, March 13). *Clinical management of severe acute respiratory infection (SARI) when covid-19 disease is suspected*. Interim Guidance . Retrieved October 13, 2022, from <https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov>
2. HHS Technical Resources, Assistance Center, and Information Exchange. (2020, December 21). *Sofa score: What it is and how to use it in triage - hhs.gov*. SOFA Score: What it is and How to Use it in Triage. Retrieved October 13, 2022, from <https://files.asprtracie.hhs.gov/documents/aspr-tracie-sofa-score-fact-sheet.pdf>

16 HOW SUPPLIED/STORAGE AND HANDLING

KINERET is supplied in single-use preservative free, prefilled glass syringes with 29 gauge needles. Each prefilled glass syringe contains 100 mg of anakinra per 0.67 mL. The full syringe contains 100 mg anakinra. KINERET is dispensed in a 1 x 7 syringe dispensing pack containing 7 syringes (NDC 66658-234-07).

Storage

Store KINERET in the refrigerator at 2°C to 8°C (36°F to 46°F). **DO NOT FREEZE OR SHAKE.** Protect from light.

17 PATIENT COUNSELING INFORMATION

As a healthcare practitioner, you must communicate to the patient and/or caregiver information consistent with the “FACT SHEET FOR PATIENTS AND CAREGIVERS” (www.KineretRxHCP.com/EUA) and provide them with a copy of this Fact Sheet prior to administration of KINERET. However, if providing this information will delay the administration of KINERET to a degree that would endanger the life of a patient, the information must be provided to the parent and/or caregiver as soon as feasible after KINERET administration

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Fact Sheet for Patients and Caregivers Emergency Use Authorization (EUA) of KINERET® (anakinra) for Coronavirus Disease 2019 (COVID-19)

You are being given this fact sheet because your healthcare provider believes it is necessary to provide you with KINERET for the treatment of coronavirus disease 2019 (COVID-19). KINERET is authorized for emergency use 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 are likely to have an increased blood level of a certain substance called urokinase plasminogen activator receptor (suPAR) that may be a sign of increased risk of worsening of the disease. This fact sheet contains information to help you understand the risks and benefits of taking KINERET you have received or may receive.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to make KINERET available during the COVID-19 pandemic (for more details about an EUA please see **“What is an Emergency Use Authorization?”** at the end of this document). KINERET is not FDA-approved for this use. Read this Fact Sheet for information about KINERET and talk to your healthcare provider about your options or if you have any questions. It is your choice for you to take KINERET or stop it at any time.

What is COVID-19?

COVID-19 is an illness caused by a virus called a coronavirus. You can get COVID-19 through close contact with another person who has the virus. COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. People of all ages with severe, long lasting (chronic) medical conditions like heart disease, lung disease and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

What is KINERET?

KINERET is a prescription medicine called an interleukin-1 receptor antagonist (IL-1Ra). KINERET is an FDA-approved medicine used to reduce the signs and symptoms and slow the damage of moderate to severe active rheumatoid arthritis (RA) in people age 18 years and older when one or more other medicines for RA have not worked, to treat people with a form of Cryopyrin-Associated Periodic Syndromes (CAPS) called Neonatal-Onset Multisystem Inflammatory Disease (NOMID) and to treat people with Deficiency of Interleukin-1 Receptor Antagonist (DIRA). KINERET is not FDA-approved to treat COVID-19. KINERET is not authorized for COVID-19 patients younger than 18 years of age.

The FDA has authorized under an EUA 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 are likely to have an increased blood level of a certain substance called urokinase plasminogen activator receptor (suPAR) that may be a sign of increased risk of worsening of the disease. For more information on EUA, see the “What is an Emergency Use Authorization (EUA)?” section at the end of this Fact Sheet.

What should I tell my health care provider before I take KINERET?

Tell your healthcare provider if you:

- Have any allergies.
- Have kidney problems.
- Are pregnant or plan to become pregnant.
- Are breastfeeding or plan to breastfeed.
- Have any serious illnesses.
- Are scheduled to receive any vaccines. People using KINERET should not receive live vaccines.
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal supplements). KINERET and other medicines may affect each other and cause serious side effects. Especially, tell your healthcare provider if you take certain other medicines that affect your immune system called Tumor Necrosis Factor (TNF) blockers or anti-cytokines.

How will I receive KINERET?

- KINERET is given to you by injection under the skin as a single dose 1 time each day for a total of 10 days.
- If you have kidney problems or end stage renal disease (ESRD) you may be given 1 dose every other day, for up to 10 days (up to 5 doses in total).

Who should generally not take KINERET?

Do not take KINERET if:

- You are allergic to proteins made from bacteria called E.coli. Ask your healthcare provider if you are not sure.
- You are allergic to anakinra, the active ingredient in KINERET, or any of the ingredients in KINERET. For a complete list of ingredients in KINERET, refer to the Package Insert for KINERET (anakinra) at www.KineretRx.com

What are the important possible side effects of KINERET?

KINERET may cause serious side effects, including:

- **Allergic reactions.** Stop using KINERET and call your healthcare provider or get emergency help right away if you have any of these symptoms of an allergic reaction: swelling of your face, lips, mouth or tongue, trouble breathing, wheezing, severe

itching skin rash, hives, redness, or swelling outside of the injection site area, dizziness or fainting, fast heartbeat or pounding in your chest (tachycardia), sweating.

- **Low white blood cell count (neutropenia).** KINERET may cause you have a lower number of certain white blood cells (neutrophils). Neutrophils are important in fighting infections. You should have blood tests before starting treatment with KINERET

The most common side effects of KINERET include:

- **Increased levels of liver enzymes:** KINERET may cause you to have increased levels of the liver enzymes as determined after a blood test.
- **Rash.**
- **Injection site skin reactions.** The symptoms of injection site skin reactions may include: redness, swelling, bruising, itching, stinging.

What other treatment choices are there?

Olumiant (baricitinib) and Veklury (remdesivir) are FDA-approved medicines for the treatment of COVID-19 in certain hospitalized patients. Talk with your healthcare provider to see if those therapies are appropriate for you.

Like KINERET, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization> for more information on the emergency use of other medicines that are authorized by FDA to treat people with COVID-19. Your healthcare provider may talk with you about other medicines that are used for the treatment of COVID-19 or clinical trials for which you may be eligible.

It is your choice for you to be treated or not to be treated with KINERET. Should you decide not to receive it, it will not change your standard medical care.

What if I am pregnant or breastfeeding?

There is limited experience giving KINERET to pregnant women or breastfeeding mothers. It is unknown if KINERET passes into your breast milk. For a mother and unborn baby, the benefit of receiving KINERET may be greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

How do I report side effects with KINERET?

Contact your health care provider if there are any side effects that bother you or do not go away. Report side effects to **FDA MedWatch** at www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Sobi by calling 1-866-773-5274

How can I learn more about COVID-19?

- Ask your healthcare provider.
- Visit <https://www.cdc.gov/COVID19>.
- Contact your local or state public health department.

What is an Emergency Use Authorization (EUA)?

The United States FDA has made KINERET available under an emergency access mechanism called an Emergency Use Authorization (EUA) as a treatment for certain

patients with COVID-19. The EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

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 are likely to have an increased blood level of a certain substance called urokinase plasminogen activator receptor (suPAR) that may be a sign of increased risk of worsening of the disease, has not undergone the same type of review as an FDA-approved product for this indication. In issuing an EUA under the COVID-19 public health emergency, the FDA has determined, among other things, that based on the total amount of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective for diagnosing, treating, or preventing COVID-19, or a serious or life-threatening disease or condition caused by COVID-19; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such disease or condition, outweigh the known and potential risks of such product; and that there are no adequate, approved and available alternatives.

All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for KINERET is in effect for the duration of the COVID-19 declaration justifying emergency use of this product, unless terminated or revoked (after which the products may no longer be used under the EUA).

This Fact Sheet may be updated as new data become available. The most recent version of this Fact Sheet is available at www.KineretRxHCP.com/EUA for download.

Manufactured by:

Swedish Orphan Biovitrum AB (publ)

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Issued: 11/2022

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