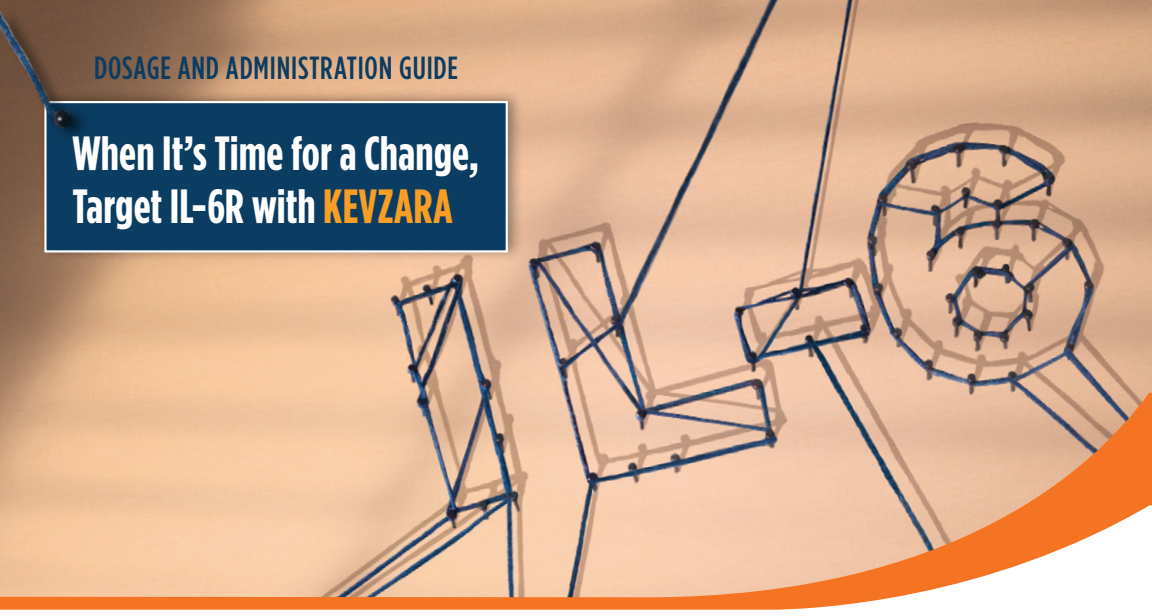
DOSAGE AND ADMINISTRATION GUIDE

When It's Time for a Change, Target IL-6R with KEVZARA



IL-6R=interleukin-6 receptor.

INDICATION

KEVZARA is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

KEVZARA® (sarilumab) injection
200 mg | 150 mg

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS INFECTIONS

Patients treated with KEVZARA are at increased risk for developing serious infections that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving KEVZARA. Most patients who developed infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Avoid use of KEVZARA in patients with an active infection.

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before KEVZARA use and during therapy. Treatment for latent infection should be initiated prior to KEVZARA use.**
- **Invasive fungal infections, such as candidiasis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral and other infections due to opportunistic pathogens.**

Closely monitor patients for signs and symptoms of infection during treatment with KEVZARA. If a serious infection develops, interrupt KEVZARA until the infection is controlled.

Consider the risks and benefits of treatment with KEVZARA prior to initiating therapy in patients with chronic or recurrent infection.

Please see additional Important Safety Information throughout, and click here to see full Prescribing Information, including **Boxed WARNING.**

KEVZARA®
(sarilumab) injection
200 mg | 150 mg

For your adult patients with moderately to severely active RA who have had an inadequate response/intolerance to one or more DMARD(s)

THE PRE-FILLED, BUTTON-FREE KEVZARA PEN

A real-world usability study in patients with RA demonstrated:

Overall, **98%** of patients were **"satisfied"** to **"very satisfied"** with the KEVZARA pen[1]*†

Ergonomically designed to help address dexterity issues

Button-free injection activation

Transparent window for visual feedback during injection

Automatic needle cover to help prevent needlestick injuries after injection

Audible clicks signal the beginning and end of injection

Grip strips to help with holding the pen

Easy-to-remove cap 90% of patients with RA responded that the cap was easy to very easy to remove in the EASY study†

*55% of patients had past experience with self-injection. All patients were trained on the use of the KEVZARA pen prior to first injection.[1]

†**EASY Study Description:** A 12-week, global, phase 3, randomized, multicenter, open-label study of 217 adult patients with active moderate-to-severe rheumatoid arthritis designed to assess usability of the KEVZARA pen, of which 108 patients were randomized to the KEVZARA pen. The primary endpoint was defined as number of validated product technical failures (product technical complaint with validated technical cause). One of the secondary objectives was to assess satisfaction with the KEVZARA pen. A total of 600 successful injections were reported during the 12-week study period.[1]

Please visit KEVZARAhcp.com for KEVZARA Instructions for Use.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATION

Do not use KEVZARA in patients with known hypersensitivity to sarilumab or any of the inactive ingredients.

Please see additional Important Safety Information throughout, and click here to see full Prescribing Information, including **Boxed WARNING.**

KEVZARA OFFERS CONSISTENT EVERY-2-WEEK DOSING

The recommended starting dosage for KEVZARA is 200 mg once every 2 weeks, given as a subcutaneous injection[2]

- No dose adjustments are recommended based on age, gender, race, or weight
- KEVZARA can be used with or without MTX or other conventional DMARD(s)*
- Reduce the dose to 150 mg q2w for the management of neutropenia, thrombocytopenia, and elevated liver enzymes

AVAILABLE IN 2 FORMS OF ADMINISTRATION[2]

KEVZARA 200 mg | KEVZARA 150 mg

KEVZARA is available by prescription only.

Arthritis Foundation Ease of Use™

The KEVZARA packaging, pre-filled pen, and pre-filled syringe received an Arthritis Foundation Ease of Use Commendation after independent testing by experts and evaluation by people with arthritis. Products receiving the Commendation make certain aspects of life easier for people with RA.[3,4]

KEVZARA comes in a pre-filled syringe or a pre-filled, button-free pen.
Both should be refrigerated, but either **can be kept at room temperature (≤77°F) for up to 14 days,** if needed.[1,2]

*Dosing of MTX and other conventional DMARD(s) may vary.
MTX=methotrexate; DMARD(s)=disease-modifying antirheumatic drug(s); q2w=every 2 weeks.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

- ***Infections.*** Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving immunosuppressive agents for rheumatoid arthritis (RA). The most frequently observed serious infections with KEVZARA included pneumonia and cellulitis. Among opportunistic infections, TB, candidiasis, and pneumocystis were reported with KEVZARA.
  - Hold treatment with KEVZARA if a patient develops a serious infection or an opportunistic infection.

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200 mg | 150 mg

For your adult patients with moderately to severely active RA who have had an inadequate response/intolerance to one or more DMARD(s)

DOSING CONSIDERATIONS FOR PATIENT MANAGEMENT

RECOMMENDED DOSAGE MODIFICATIONS

- Reduce dose to 150 mg once every 2 weeks in case of neutropenia, thrombocytopenia, and elevated liver enzymes[2]
- If a patient develops a serious infection, hold treatment with KEVZARA until the infection is controlled[2]

GENERAL CONSIDERATIONS FOR ADMINISTRATION

- KEVZARA initiation is not recommended in patients with an absolute neutrophil count (ANC) less than 2000 per mm^3, platelet count less than 150,000 per mm^3, or who have ALT or AST above 1.5 times the upper limit of normal (ULN)[2]

DOSAGE MODIFICATIONS[2]

LAB VALUE	RECOMMENDATION
Low absolute neutrophil count (cells/mm^3)	
ANC >1000	**Maintain** current dosage of KEVZARA.
ANC 500-1000	**Hold** treatment with KEVZARA until ANC >1000. KEVZARA can then be resumed at 150 mg every 2 weeks and increased to 200 mg every 2 weeks as clinically appropriate.
ANC <500	**Discontinue** KEVZARA.
Low platelet count (cells/mm^3)	
50,000-100,000	**Hold** treatment with KEVZARA until platelets >100,000. KEVZARA can then be resumed at 150 mg every 2 weeks and increased to 200 mg every 2 weeks as clinically appropriate.
<50,000	If confirmed by repeat testing, **discontinue** KEVZARA.
Liver enzyme abnormalities	
ALT >1 to ≤3 x ULN	**Consider** dosage modification of concomitant DMARDs as clinically appropriate.
ALT >3 to ≤5 x ULN	**Hold** treatment with KEVZARA until ALT <3 x ULN. KEVZARA can then be resumed at 150 mg every 2 weeks and increased to 200 mg every 2 weeks as clinically appropriate.
ALT >5 x ULN	**Discontinue** KEVZARA.

ANC=absolute neutrophil count; ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Patients with latent TB should be treated with standard antimycobacterial therapy before initiating KEVZARA. Consider anti-TB therapy prior to initiation of KEVZARA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but having risk factors for TB infection.
- Consider the risks and benefits of treatment prior to initiating KEVZARA in patients who have: chronic or recurrent infection, a history of serious or opportunistic infections, underlying conditions in addition to RA that may predispose them to infection, been exposed to TB, or lived in or traveled to areas of endemic TB or endemic mycoses.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Viral reactivation has been reported with immunosuppressive biologic therapies. Cases of herpes zoster were observed in clinical studies with KEVZARA.

- ***Laboratory Abnormalities.*** Treatment with KEVZARA was associated with decreases in absolute neutrophil counts (including neutropenia), and platelet counts; and increases in transaminase levels and lipid parameters (LDL, HDL cholesterol, and/or triglycerides). Increased frequency and magnitude of these elevations were observed when potentially hepatotoxic drugs (e.g., MTX) were used in combination with KEVZARA. Assess neutrophil count, platelet count, and ALT/AST levels prior to initiation with KEVZARA. Monitor these parameters 4 to 8 weeks after start of therapy and every 3 months thereafter. Assess lipid parameters 4 to 8 weeks after start of therapy, then at 6 month intervals.
- ***Gastrointestinal Perforation.*** GI perforation risk may be increased with concurrent diverticulitis or concomitant use of NSAIDs or corticosteroids. Gastrointestinal perforations have been reported in clinical studies, primarily as complications of diverticulitis. Promptly evaluate patients presenting with new onset abdominal symptoms.
- ***Immunosuppression.*** Treatment with immunosuppressants may result in an increased risk of malignancies. The impact of treatment with KEVZARA on the development of malignancies is not known but malignancies have been reported in clinical studies.
- ***Hypersensitivity Reactions.*** Hypersensitivity reactions have been reported in association with KEVZARA. Hypersensitivity reactions that required treatment discontinuation were reported in 0.3% of patients in controlled RA trials. Injection site rash, rash, and urticaria were the most frequent hypersensitivity reactions. Advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylaxis or other hypersensitivity reaction occurs, stop administration of KEVZARA immediately. Do not administer KEVZARA to patients with known hypersensitivity to sarilumab.
- ***Active Hepatic Disease and Hepatic Impairment.*** Treatment with KEVZARA is not recommended in patients with active hepatic disease or hepatic impairment, as treatment with KEVZARA was associated with transaminase elevations.
- ***Live Vaccines.*** Avoid concurrent use of live vaccines during treatment with KEVZARA due to potentially increased risk of infections. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving KEVZARA.

ADVERSE REACTIONS

- The most common serious adverse reactions were infections. The most frequently observed serious infections included pneumonia and cellulitis. The most common adverse reactions (occurred in at least 3% of patients treated with KEVZARA + DMARDs) are neutropenia, increased ALT, injection site erythema, upper respiratory infections, and urinary tract infections.

DRUG INTERACTIONS

- Exercise caution when KEVZARA is co-administered with CYP substrates with a narrow therapeutic index (e.g. warfarin or theophylline), or with CYP3A4 substrates (e.g. oral contraceptives or statins) as there may be a reduction in exposure which may reduce the activity of the CYP3A4 substrate.
- Elevated interleukin-6 (IL-6) concentration may down-regulate CYP activity such as in patients with RA and hence increase drug levels compared to subjects without RA. Blockade of IL-6 signaling by IL-6Rα antagonists such as KEVZARA might reverse the inhibitory effect of IL-6 and restore CYP activity, leading to altered drug concentrations.

USE IN SPECIFIC POPULATIONS

- KEVZARA should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. Because monoclonal antibodies could be excreted in small amounts in human milk, the benefits of breastfeeding and the potential adverse effects on the breastfed child should be considered along with the mother's clinical need for KEVZARA.
- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to KEVZARA during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.
- Use caution when treating the elderly.

Advise patients to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

References: 1. Kivitz A, Baret-Cormel L, van Hoogstraten H, et al. Usability and patient preference phase 3 study of the sarilumab pen in patients with active moderate-to-severe rheumatoid arthritis. *Rheumatol Ther.* 2017. doi:10.1007/s40744-017-0090-2. **2.** KEVZARA [prescribing information]. Bridgewater, NJ: Sanofi/Regeneron Pharmaceuticals, Inc. **3.** Ease of use products. Arthritis Foundation website. http://www.arthritis.org/living-with-arthritis/tools-resources/ease-of-use. Accessed August 16, 2019. **4.** Data on file, Sanofi/Regeneron. Regeneron Sarilumab Evaluation Report of Consumer Product Accessibility for Users with Arthritis. February 2015.

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SUPPORT PATIENTS GETTING STARTED

KEVZARAconnect®

KevzaraConnect® provides eligible, commercially insured patients support getting started with and saving on KEVZARA:

Copay Card to help eligible patients pay as little as $0 per month for KEVZARA*

Call KevzaraConnect at **1-844-KEVZARA** (1-844-538-9272)

*Subject to an annual copay assistance amount of $15,000. Additional terms and conditions apply.

To order a free, one-time, 30-day supply of KEVZARA for your patients, visit our website and download the **KEVZARA Experience Voucher Form.**†

†Additional terms and conditions apply.

For more information, visit **KEVZARAhcp.com**

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SANOFI GENZYME REGENERON

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