

# Sarilumab

## Indications/Dosage

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### Labeled

- rheumatoid arthritis

### Off-Label

- coronavirus disease 2019 (COVID-19) †
- severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection †

† Off-label indication

**INVESTIGATIONAL USE: For adjunctive use in the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection†, the virus that causes coronavirus disease 2019 (COVID-19)†**

### Intravenous dosage

- **Adults**

Efficacy has not been established. Due to a lack of clinical data, the National Institutes of Health (NIH) COVID-19 treatment guidelines do not give recommendations for or against the use of IL-6 receptor inhibitors, such as sarilumab.[\[65314\]](#) 400 mg IV once is being evaluated in combination with antiviral therapy.[\[65188\]](#) [\[65189\]](#) [\[65190\]](#) [\[65249\]](#) The 200 mg dose is being removed from manufacturer-sponsored trials based on preliminary results.[\[65188\]](#) [\[65190\]](#)

### Subcutaneous dosage

- **Adults**

Efficacy has not been established. Due to a lack of clinical data, the National Institutes of Health (NIH) COVID-19 treatment guidelines do not give recommendations for or against the use of IL-6 receptor inhibitors, such as sarilumab.[\[65314\]](#) 200 or 400 mg subcutaneously once is being evaluated in combination with antiviral therapy.[\[65191\]](#) [\[65254\]](#) [\[65351\]](#) [\[65352\]](#) [\[65353\]](#)

## For the treatment of moderately- to severely- active rheumatoid arthritis in patients who have had an inadequate response or intolerance to one or more disease modifying antirheumatic drugs

### Subcutaneous dosage

- **Adults**

200 mg subcutaneously once every 2 weeks is the usual and recommended dose, as monotherapy or in combination with methotrexate or other conventional DMARDs (cDMARDs). Interrupt treatment and then resume at a reduced dose of 150 mg subcutaneously once every 2 weeks for the management of neutropenia, thrombocytopenia, or elevated liver enzymes, as directed in manufacturer label.[\[61976\]](#) Do not use with other biological DMARDs because of the possibility of increased immunosuppression and increased risk of infection; such combinations have not been studied.[\[61976\]](#)

## Therapeutic Drug Monitoring

### Prior to initiation of treatment

Check the patient's ANC, platelet count, and liver function tests (ALT/AST concentrations) before sarilumab initiation. Test for latent tuberculosis. In adults, sarilumab is not recommended for patients with an ANC less than  $2,000/\text{mm}^3$ , a platelet count less than  $150,000/\text{mm}^3$ , or an ALT or AST greater than 1.5 times the upper limit of normal (ULN).[\[61976\]](#)

### During treatment

Check ANC, platelet count, and liver function tests 4 to 8 weeks after sarilumab initiation and then every 3 months during therapy. Serum lipid profile should be checked 4 to 8 weeks after sarilumab initiation and then approximately every 6 months during therapy.[\[61976\]](#)

### Dosage modifications for neutropenia, thrombocytopenia, or elevated liver enzymes

*Absolute neutrophil count (ANC) 500 to  $1000/\text{mm}^3$* : Hold sarilumab and restart when ANC more than 1000 cells/ $\text{mm}^3$  with 150 mg subcutaneously every 2 weeks and increased to 200 mg subcutaneously every 2 weeks as clinically appropriate.

*Absolute neutrophil count (ANC) less than  $500/\text{mm}^3$* : Discontinue sarilumab.

*Platelet count 50,000 to 100,000/mm<sup>3</sup>*: Hold sarilumab and restart when platelet count is more than 100,000/mm<sup>3</sup> with 150 mg subcutaneously every 2 weeks and increased to 200 mg subcutaneously every 2 weeks as clinically appropriate.

*Platelet count less than 50,000/mm<sup>3</sup>*: Repeat test; discontinue sarilumab if confirmed.

*Hepatic enzyme abnormalities*: Dosage interruption or modifications are recommended based on the degree of abnormality occurring during treatment, as evidenced by the degree of AST/ALT elevations above the upper limit of normal (ULN).<sup>[61976]</sup>

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## Maximum Dosage Limits

- Adults  
200 mg/dose subcutaneously every 2 weeks.
  - Geriatric  
200 mg/dose subcutaneously every 2 weeks.
  - Adolescents  
Safety and efficacy have not been established.
  - Children  
Safety and efficacy have not been established.
  - Infants  
Safety and efficacy have not been established.
- 

## Patients with Hepatic Impairment Dosing

*Prior to treatment initiation*: Do not initiate treatment with sarilumab if baseline AST/ALT is more than 1.5 times the upper limit of normal (ULN).

*Hepatic enzyme elevations occurring during treatment*:

*AST and/or ALT up to 3 times the ULN or less*: Dose modify concomitant DMARDs, if appropriate.

*AST and/or ALT greater than 3 times the ULN up to 5 times the ULN, confirmed by repeat testing*: Interrupt sarilumab dosing until AST/ALT is less than 3 times the ULN. Then, resume sarilumab at 150 mg subcutaneously every 2 weeks and then increase to 200 mg subcutaneously every 2 weeks as clinically appropriate. If liver enzymes are persistently elevated, consider treatment discontinuation.

*AST and/or ALT greater than 5 times the ULN: Discontinue sarilumab.*[61976]

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## Patients with Renal Impairment Dosing

*CrCl 30 mL/minute or more:* No dosage adjustment needed.

*CrCl less than 30 mL/minute:* Sarilumab has not been studied in patients with severe renal impairment.[61976]

† Off-label indication

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## References

**61976** – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

**65188** – Regeneron Pharmaceuticals. Evaluation of the efficacy and safety of sarilumab in hospitalized patients with COVID-19. Retrieved April 2, 2020: Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/study/NCT04315298?term=sarilumab&draw=2>.

**65189** – Assistance Publique – Hopitaux de Paris. Cohort multiple randomized controlled trials open-label of immune modulatory drugs and other treatments in COVID-19 patients – sarilumab trial – CORIMUNO-19-SARI (CORIMUNO-SARI). Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04324073?term=sarilumab&draw=3&rank=2>.

**65190** – Sanofi. Sarilumab COVID-19. Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04327388?cond=Coronavirus&intr=sarilumab&draw=2&rank=2>.

**65191** – Henriksen M. Anti-il6 treatment of serious COVID-19 disease With threatening respiratory failure (TOCIVID). Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04322773?cond=Coronavirus&intr=sarilumab&draw=2&rank=3>.

**65249** – Assistance Publique – Hopitaux de Paris. Study of Immune Modulatory Drugs and Other Treatments in COVID-19 Patients: Sarilumab, Azithromycin, Hydroxychloroquine Trial - CORIMUNO-19 - VIRO (CORIMUNO-VIRO). Retrieved April 13, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04341870?term=sarilumab&cond=SARS-CoV+2&draw=2&rank=1>

**65254** – Benfield T. Efficacy and safety of novel treatment options for adults with COVID-19 pneumonia (CCAP). Retrieved April 14, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04345289?cond=COVID&intr=Baricitinib&draw=2&rank=4>.

**65314** – COVID-19 Treatment Guidelines Panel. Coronavirus Diseases 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Accessed May 12, 2020. Available at on the World Wide Web at: <https://covid19treatmentguidelines.nih.gov/>.

**65351** – Maimonides Biomedical Research Institute of Cordoba. Clinical trial of sarilumab in adults With COVID-19 (SARICOR). Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04357860?cond=COVID&intr=Sarilumab&draw=2&rank=5>.

**65352** – Garcia de Vicuna Pinedo M. Efficacy of subcutaneous sarilumab in hospitalised patients with moderate-severe COVID-19 infection (SARCOVID) (SARCOVID). Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04357808?cond=COVID&intr=Sarilumab&draw=2&rank=2>.

**65353** – Branch-Elliman W. Sarilumab for Patients With Moderate COVID-19 Disease: A Randomized Controlled Trial With a Play-The-Winner Design. Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04359901?cond=COVID&intr=Sarilumab&draw=2&rank=1>.

## How Supplied

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Sarilumab Solution for injection
<a href="#">KEVZARA 150mg/1.14mL Pre-Filled Pen Solution for Injection</a> (00024-5920) (Sanofi U.S. LLC)
<a href="#">KEVZARA 150mg/1.14mL Prefilled Syringe Solution for Injection</a> (00024-5908) (Sanofi U.S. LLC)
<a href="#">KEVZARA 200mg/1.14mL Pre-Filled Pen Solution for Injection</a> (00024-5922) (Sanofi U.S. LLC)
<a href="#">KEVZARA 200mg/1.14mL Prefilled Syringe Solution for Injection</a> (00024-5910) (Sanofi U.S. LLC)

## Description/Classification

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### Description

Sarilumab is an injectable interleukin-6 (IL-6) receptor antagonist. In patients with inflammatory diseases such as rheumatoid arthritis, IL-6 concentrations correlate with disease activity and joint or tissue damage. Sarilumab is used for the treatment of adults with moderate to severe rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).[61976] Sarilumab was FDA approved in May 2017.

*Updates for coronavirus disease 2019 (COVID-19):*

Due to a lack of clinical data, the National Institutes of Health (NIH) COVID-19 treatment guidelines do not give recommendations for or against the use of IL-6 receptor inhibitors, such as sarilumab.[65314] Based on preliminary data from a study of another IL-6 receptor antibody, studies have begun to evaluate the use of sarilumab for COVID-19.[65188][65189][65190][65191][65249][65351][65352][65353] The 200 mg dose used in severe hospitalized patients is being removed from manufacturer-sponsored trials based on preliminary results; however, the 400 mg dose is still being studied in critical hospitalized patients.[65188][65190] Both doses are being studied outside of manufacturer-sponsored trials.[65189][65191][65249][65254][65351][65352][65353]

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## Classifications

- [Antineoplastic and Immunomodulating Agents](#)
  - [Agents that Suppress the Immune System](#)
    - [Interleukin-6 \(IL-6\) Inhibitors](#)

- [Musculo-Skeletal System](#)
  - [Antiinflammatory Agents and Antirheumatic Agents](#)
    - [Specific Anti-Rheumatic Agents](#)
      - [Anti-Rheumatic Monoclonal Antibodies](#)

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## References

**61976** – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

**65188** – Regeneron Pharmaceuticals. Evaluation of the efficacy and safety of sarilumab in hospitalized patients with COVID-19. Retrieved April 2, 2020: Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/study/NCT04315298?term=sarilumab&draw=2>.

**65189** – Assistance Publique – Hopitaux de Paris. Cohort multiple randomized controlled trials open-label of immune modulatory drugs and other treatments in COVID-19 patients – sarilumab trial – CORIMUNO-19-SARI (CORIMUNO-SARI). Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04324073?term=sarilumab&draw=3&rank=2>.

**65190** – Sanofi. Sarilumab COVID-19. Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04327388?cond=Coronavirus&intr=sarilumab&draw=2&rank=2>.

**65191** – Henriksen M. Anti-il6 treatment of serious COVID-19 disease With threatening respiratory failure (TOCIDVID). Retrieved April 2, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04322773?cond=Coronavirus&intr=sarilumab&draw=2&rank=3>.

**65249** – Assistance Publique – Hopitaux de Paris. Study of Immune Modulatory Drugs and Other Treatments in COVID-19 Patients: Sarilumab, Azithromycin, Hydroxychloroquine Trial - CORIMUNO-19 - VIRO (CORIMUNO-VIRO). Retrieved April 13, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04341870?term=sarilumab&cond=SARS-CoV+2&draw=2&rank=1>

**65254** – Benfield T. Efficacy and safety of novel treatment options for adults with COVID-19 pneumonia (CCAP). Retrieved April 14, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04345289?cond=COVID&intr=Baricitinib&draw=2&rank=4>.

**65314** – COVID-19 Treatment Guidelines Panel. Coronavirus Diseases 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Accessed May 12, 2020. Available at on the World Wide Web at: <https://covid19treatmentguidelines.nih.gov/>.

**65351** – Maimonides Biomedical Research Institute of Cordoba. Clinical trial of sarilumab in adults With COVID-19 (SARICOR). Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04357860?cond=COVID&intr=Sarilumab&draw=2&rank=5>.

**65352** – Garcia de Vicuna Pinedo M. Efficacy of subcutaneous sarilumab in hospitalised patients with moderate-severe COVID-19 infection (SARCOVID) (SARCOVID). Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04357808?cond=COVID&intr=Sarilumab&draw=2&rank=2>.

**65353** – Branch-Elliman W. Sarilumab for Patients With Moderate COVID-19 Disease: A Randomized Controlled Trial With a Play-The-Winner Design. Retrieved April 28, 2020. Available on the World Wide Web at: <https://clinicaltrials.gov/ct2/show/NCT04359901?cond=COVID&intr=Sarilumab&draw=2&rank=1>.

# Administration Information

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## General Administration Information

For storage information, see the specific product information within the How Supplied section.

## Route-Specific Administration

### Injectable Administration

- For subcutaneous administration only.
- Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit. The injection solution should be clear and colorless to pale yellow. Do not use the injection if it is cloudy, discolored or contains particles, or if any part of the prefilled syringe or prefilled pen appears to be damaged.[\[61976\]](#)

### Subcutaneous Administration

- The injection may be given by the patient or patient's caregiver after proper training in subcutaneous injection technique and a healthcare practitioner determines that it is appropriate.

#### *Prefilled Syringe:*

- Remove the prefilled syringe from the refrigerator and allow it to sit at room temperature outside of the carton for 30 minutes. Do not warm sarilumab in any other way.
- Do not uncap the needle until ready to inject. Do not get rid of any air bubbles in the syringe.
- Pick an injection site such as the front of a thigh or the abdomen except for the 2-inch area around the navel. If a caregiver or healthcare professional will administer, they can also use the patient's outer area of an upper arm. Do not inject into skin that is tender, damaged, or has bruises or scars.
- Rotate injection sites with each injection.
- Remove the needle cap immediately before injection, and gently pinch a cleaned area of skin between the thumb and index finger. Using a dart-like motion, insert the needle at a 45-degree angle. Gently push the plunger all the way down to inject the full amount in the prefilled syringe.
- Check that the syringe is empty and then pull the needle out at the same angle it was inserted. Do not rub the injection site.
- Dispose of the used syringe in an FDA-cleared sharps disposal container right away after use. Do not recap after use. Do not re-use the syringe.
- *Storage:* The prefilled syringes should be stored in the refrigerator in the original container to protect sarilumab from light. The prefilled syringes may be stored in the carton at room temperature up to 25 degrees C (77 degrees F) for up to 14 days. Dispose of any prefilled syringes left at room temperature for more than 14 days.[\[61976\]](#)

#### *Prefilled Pen:*

- Remove the prefilled pen from the refrigerator and allow it to sit at room temperature outside of the carton for 60 minutes. Do not warm sarilumab in any other way.

- Do not remove the orange cap until ready to inject.
  - Pick an injection site such as the front of a thigh or the abdomen except for the 2-inch area around the navel. If a caregiver or healthcare professional will administer, they can also use the patient's outer area of an upper arm. Do not inject into skin that is tender, damaged, or has bruises or scars.
  - Rotate injection sites with each injection.
  - Twist or pull off the orange cap immediately before injection, and do not touch the yellow needle cover. Place the yellow needle cover on the skin at a 90-degree angle, making sure the window is visible. Press down and hold firmly against the skin. There will be an audible 'click' when the injection starts. Continue to hold the pen firmly against the skin until the entire window becomes solid yellow and the full dose is administered; the complete injection may take up to 15 seconds. There will be a second 'click' when the injection is complete.
  - Remove the pen from the skin and the needle will automatically cover. Do not rub the injection site.
  - Dispose of the used pen in an FDA-cleared sharps disposal container right away after use. Do not replace the orange cap after use. Do not re-use the pen.
  - *Storage:* The prefilled pens should be stored in the refrigerator in the original container to protect sarilumab from light. The prefilled pens may be stored in the carton at room temperature up to 25 degrees C (77 degrees F) in the carton for up to 14 days. Dispose of any prefilled pens left at room temperature for more than 14 days.[\[61976\]](#)
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## Clinical Pharmaceutics Information

From Trissel's 2™ Clinical Pharmaceutics Database

### Sarilumab

#### 1. pH Range

pH is 6.0.

## References

Kevzara (sarilumab) injection package insert. Bridgewater, NJ. Sanofi-Aventis U.S. LLC. 2018; Apr

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## References

**61976** – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

## Adverse Reactions

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- anaphylactoid reactions
- antibody formation
- candidiasis
- elevated hepatic enzymes
- erythema
- GI perforation



- hypercholesterolemia
  - hyperlipidemia
  - hypertriglyceridemia
  - infection
  - injection site reaction
  - neutropenia
  - new primary malignancy
  - pharyngitis
  - pruritus
  - rash
  - thrombocytopenia
  - urticaria
- 

Patients treated with sarilumab are at increased risk for developing a serious infection, including bacterial or viral infections or reactivation of viral infections, that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving sarilumab. Most patients who developed an infection were taking concomitant immunosuppressants such as methotrexate or corticosteroids. During and after treatment with sarilumab, closely monitor all patients for the development of signs and symptoms of infection including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection before sarilumab use. If a serious infection develops, interrupt sarilumab until the infection is controlled.[\[61976\]](#) Infections of various types have been reported during clinical trials. During sarilumab plus DMARD placebo-controlled clinical trials, upper respiratory tract infections were reported in 3% and 4% of patients receiving sarilumab 200 mg and 150 mg, respectively (2% placebo). Urinary tract infections were reported in 3% of both sarilumab treatment groups (2% placebo). Naso-pharyngitis also was reported. The rate of serious infections in the 200 mg and 150 mg group was 3.8 to 4.3 and 3 to 4.4 events per 100 patient-years, respectively, compared to 2.5 to 3.1 events per 100 patient-years for placebo. Serious infections reported included pneumonia, cellulitis, and opportunistic infections. Viral reactivation has been reported with the use of immunosuppressive biologic therapies. Herpes zoster was reported in 0.8% and 0.6% of those receiving sarilumab 200 mg and 150 mg, respectively (0.5% placebo). Oral herpes simplex infection occurred in less than 2% of rheumatoid arthritis patients who received sarilumab in clinical trials. No cases of hepatitis B reactivation were observed in the trials; however, patients who screened positive for hepatitis were excluded from clinical trials. Among opportunistic infections, tuberculosis (pulmonary or extrapulmonary disease), candidiasis, and Pneumocystis infections were reported with sarilumab. Patients have presented with disseminated rather than localized disease and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids. Carefully consider the risks and benefits of sarilumab in patients with chronic or recurrent infection.[\[61976\]](#)

Gastrointestinal perforations have been reported during sarilumab clinical trials. Reports of GI perforation were primarily reported as complications of diverticulitis including lower GI perforation and abscesses. One patient experienced a gastrointestinal perforation during sarilumab clinical trials (0.11 events per 100 patient-years). In the long-term safety population, the overall rate of GI perforation was consistent with rates of the controlled periods of the studies. Most patients that developed GI perforations were taking concomitant nonsteroidal anti-inflammatory medications (NSAIDs) or corticosteroids. The contribution of these concomitant medications to the development of GI perforations is not known.[\[61976\]](#)

Sarilumab may cause neutropenia; neutrophil counts should be assessed before and during treatment. During sarilumab plus DMARD placebo-controlled clinical trials, decreases in neutrophil counts to less than 1000/mm<sup>3</sup> occurred in 6% and 4% of the patients in the sarilumab 200 mg and 150 mg groups, respectively (0% placebo). Severe decreases in neutrophil counts to less than 500/mm<sup>3</sup> were reported in 0.7% of both sarilumab treatment groups. Neutropenia was not associated with the occurrence of infections, including serious infections.[\[61976\]](#)

Sarilumab may cause thrombocytopenia; platelet counts should be assessed before and during treatment. During sarilumab plus DMARD placebo-controlled clinical trials, decreases in platelet counts to less than 100,000/mm<sup>3</sup> occurred in 1% and 0.7% of those receiving sarilumab 200 mg and 150 mg, respectively (0% placebo). Treatment-related reduction in platelets was not associated with bleeding events in clinical trials.[\[61976\]](#)

Sarilumab is associated with elevated hepatic enzymes. Liver function tests should be assessed before and during sarilumab treatment. In those experiencing elevated liver enzymes, modification of the treatment regimen

(i.e., dose reduction or interruption) usually results in a decrease or normalization of the liver enzyme. During sarilumab plus DMARD placebo-controlled trials, AST greater than the upper limit of normal (ULN) to 3 times ULN or less were reported in 30% of patients receiving sarilumab 200 mg and 27% of those receiving 150 mg compared to 15% of those receiving placebo. AST elevations of greater than 3 times the ULN to 5 times the ULN were reported in 1% of those receiving any dose of sarilumab (0% for placebo), and AST greater than 5 times ULN were reported in 0.2% to 0.7% of those receiving sarilumab (0% for placebo). Similarly, ALT greater than the ULN to 3 times ULN or less were reported in 43% of patients receiving sarilumab 200 mg and 38% of those receiving 150 mg compared to 25% of those receiving placebo. ALT elevations of greater than 3 times the ULN to 5 times the ULN were reported in 3% to 4% of those receiving any dose of sarilumab (1% for placebo), and ALT greater than 5 times ULN were reported in 0.7% to 1% of those receiving sarilumab (0% for placebo). These increases in liver enzymes were not associated with clinically relevant increases in direct bilirubin or evidence of hepatitis or hepatic impairment.[61976]

An injection site reaction may occur with the use of sarilumab. In clinical trials, injection site reactions were reported in 7% and 6% of patients who received sarilumab 200 mg and sarilumab 150 mg, respectively. Injection site reactions included pruritus (2%) and erythema (4% to 5%).[61976]

Hypersensitivity reactions have been reported with the administration of sarilumab. Reactions that required treatment discontinuation were reported in 0.2 to 0.3% of patients. Injection site rash, rash (unspecified), and urticaria were reported most frequently. Advise patients to seek medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylactoid reactions or other hypersensitivity reaction occurs, immediately stop the administration of sarilumab.[61976]

Sarilumab may cause hyperlipidemia, including hypercholesterolemia and hypertriglyceridemia. Lipid parameters should be assessed during sarilumab treatment. During sarilumab plus DMARD placebo-controlled trials, lipid parameters were measured 4 weeks following sarilumab initiation. Among those receiving sarilumab 150 mg, the mean LDL cholesterol increased by 12 mg/dL, mean triglycerides increased by 20 mg/dL, and mean HDL increased by 3 mg/dL. Among those receiving sarilumab 200 mg, the mean LDL increased by 16 mg/dL, mean triglycerides increased by 27 mg/dL, and mean HDL increased by 3 mg/dL. In the long-term safety population, the observations in lipid parameters were consistent with what was observed in the placebo-controlled studies.[61976]

Sarilumab may increase the risk for a new primary malignancy. In the 52-week placebo-controlled trial, 9 malignancies (exposure-adjusted event rate of 1 event per 100 patient-years) were reported in patients receiving sarilumab and a DMARD compared to 4 malignancies (exposure-adjusted event rate of 1 event per 100 patient-years) in the control group. In the long-term safety population, the rate of malignancies was consistent with the rate observed in the placebo-controlled period.[61976]

In patients treated with sarilumab monotherapy, 9.2% of patients exhibited an ADA response with 6.9% of patients also exhibiting neutralizing antibodies (NAbs). Prior to the administration of sarilumab, 2.3% of patients exhibited an ADA response. In the pre-rescue population, 4% of patients treated with sarilumab 200 mg plus DMARD and 5.7% of patients treated with sarilumab 150 mg plus DMARD exhibited an anti-drug antibody (ADA) response, compared with 1.9% of patients receiving placebo plus DMARD. Neutralizing antibodies (NAb) were detected in 1% of patients on sarilumab 200 mg plus DMARD and 1.6% of patients on sarilumab 150 mg + DMARD (versus 0.2% of patients on placebo plus DMARD). No correlation was observed between antibody formation and adverse events or loss of efficacy.[61976]

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## References

**61976** – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

# Contraindications/Precautions

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Absolute contraindications are italicized.

- breast-feeding
  - children
  - corticosteroid therapy
  - diabetes mellitus
  - diverticulitis
  - fungal infection
  - geriatric
  - GI perforation
  - hepatic disease
  - hepatitis
  - human immunodeficiency virus (HIV) infection
  - hypercholesterolemia
  - hyperlipidemia
  - hypertriglyceridemia
  - immunosuppression
  - infants
  - infection **B**
  - influenza
  - labor
  - neonates
  - neoplastic disease
  - neutropenia
  - obstetric delivery
  - pregnancy
  - sepsis
  - thrombocytopenia
  - tuberculosis
  - vaccination
- 

Sarilumab is contraindicated for use in patients with *known hypersensitivity to sarilumab or any of its inactive ingredients*. Hypersensitivity reactions were reported in sarilumab clinical trials.[\[61976\]](#)

Patients who receive sarilumab are at increased risk for developing serious infections that may lead to hospitalization or death. Infections include active tuberculosis and invasive fungal infections including candidiasis and pneumocystis. Bacterial, viral, and other infections due to opportunistic pathogens have been reported. Most patients who developed serious infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Patients with an invasive fungal infection may present with disseminated disease, and tuberculosis may present as pulmonary or extrapulmonary disease. Evaluate patients for tuberculosis risk factors before starting sarilumab. Also, test patients for latent tuberculosis before and during sarilumab receipt. Initiate treatment for latent infection before sarilumab use. Consider anti-tuberculosis therapy prior to sarilumab initiation for 2 patient groups: patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed and patients with a negative test for latent tuberculosis but with risk factors for tuberculosis infection. Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient. Carefully consider the risks and benefits of sarilumab before initiating therapy in patients with chronic or recurrent infection, who have been exposed to tuberculosis, with a history of a serious or opportunistic infection, with underlying conditions that may predispose them to infection (e.g., patients with advanced or uncontrolled diabetes mellitus, human immunodeficiency virus (HIV) infection, or immunosuppression), or who have resided or traveled in areas of endemic tuberculosis or endemic mycoses. Sarilumab initiation is not recommended for patients with an absolute neutrophil count (ANC) less than 2,000/mm<sup>3</sup>, sarilumab discontinuation is advised for an ANC less than 500/mm<sup>3</sup>, and sarilumab interruption is advised for an ANC between 500/mm<sup>3</sup> and 1,000/mm<sup>3</sup>. Closely monitor patients for the development of signs and symptoms of infection during and after sarilumab treatment; signs and symptoms of acute inflammation may be lessened due to suppression of the acute phase reactants. Consider the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to taking sarilumab. Viral reactivation has been observed during immunosuppressive biologic therapies. Do not administer sarilumab to a patient with an active infection including localized infections. If a serious infection such as sepsis or influenza or an opportunistic infection develops, interrupt sarilumab receipt until the infection is controlled. If a new infection

develops during sarilumab receipt, complete a prompt and complete diagnostic workup appropriate for an immunocompromised patient, initiate appropriate antimicrobial therapy, and closely monitor the patient.[61976]

Initiation of sarilumab therapy is not recommended in patients with thrombocytopenia defined as a platelet count less than  $150,000/\text{mm}^3$  or for neutropenia defined as an absolute neutrophil count (ANC) below  $2,000/\text{mm}^3$ . Thrombocytopenia and neutropenia have occurred with sarilumab, and drug interruption, dose reduction, or discontinuation may be needed. Assess platelet count and ANC before sarilumab receipt, 4 to 8 weeks after sarilumab initiation, and every 3 months thereafter.[61976]

Sarilumab is not recommended in patients with active hepatic disease or hepatic impairment. Initiation of sarilumab is not recommended in patients who have ALT or AST more than 1.5 times the upper limit of normal (ULN). Hepatic enzyme elevations observed in clinical trials with sarilumab did not result in any clinically evident hepatic injury. Elevated transaminases have been noted with sarilumab, and drug interruption, dose reduction, or discontinuation may be needed. Assess liver function tests (LFTs) before sarilumab receipt, 4 to 8 weeks after start of therapy, and every 3 months thereafter. Consider assessing other liver function tests such as bilirubin when clinically indicated. The safety and efficacy of sarilumab have not been studied in patients with hepatic impairment including patients with positive hepatitis B virus (HBV) or hepatitis C virus (HCV) serology. The risk of hepatitis B reactivation with sarilumab is unknown since patients who were at risk for reactivation were excluded from clinical trials.[61976]

Gastrointestinal (GI) perforations have been reported in clinical studies, primarily as complications of diverticulitis. Use with caution in patients with diverticulitis. GI perforation risk may be increased with concurrent diverticulitis or concomitant use of NSAIDs or in those receiving corticosteroid therapy. Promptly evaluate patients presenting with new onset abdominal symptoms.[61976]

Sarilumab is an immunosuppressant; therefore, sarilumab may affect host defenses against neoplastic disease. The impact of sarilumab on the development of malignancies is unknown, but malignancies were observed in clinical studies. Consider the risks and benefits of sarilumab before treatment initiation in patients with a known malignancy. Also, consider the risks and benefits of sarilumab continuation in patients who develop a malignancy.[61976]

Cautious use of sarilumab may be warranted for patients with hyperlipidemia, hypercholesterolemia, or hypertriglyceridemia. Increased total cholesterol, increased HDL-C, increased LDL-C, and increased triglycerides may occur with sarilumab. Assess lipid parameters approximately 4 to 8 weeks after sarilumab initiation and subsequently at approximately 6 month intervals. Manage patients according to clinical guidelines [e.g., National Cholesterol Educational Program (NCEP)] for the management of hyperlipidemia.[61976]

Live virus vaccines should not be given concurrently with sarilumab due to the potential increase in risk of infection. The safety of live virus vaccination in patients receiving sarilumab has not been established. No data exist on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab should be in accordance with current vaccination guidelines regarding immunosuppressive agents.[61976]

Limited available data are not sufficient to determine whether the use of sarilumab during human pregnancy is associated with risk for major birth defects or miscarriage. Monoclonal antibodies, like sarilumab, are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third trimester. This may affect immune response in the in utero exposed infant. Concentrations of immunoglobulin G (IgG), in response to antigen challenge, may be reduced in the fetus/infant of treated mothers. Consider risks and benefits prior to administering live or live-attenuated vaccines to neonates or infants who were exposed to sarilumab in utero. In an animal reproduction study, consisting of a combined embryo-fetal and pre- and postnatal development study with monkeys that received intravenous administration of sarilumab, there was no evidence of embryotoxicity or fetal malformations with exposures up to approximately 84 times the maximum recommended human dose (MRHD). Animal data suggest sarilumab may affect labor and obstetric delivery. Inhibition of IL-6 signaling may interfere with cervical ripening and dilatation and myometrial contractile activity, leading to potential delays in parturition. For mice deficient in IL-6, parturition was delayed

relative to wild-type mice without this deficiency. Administration of recombinant IL-6 to the deficient mice restored the normal timing of delivery. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to sarilumab during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.[61976]

There is no information available on the presence of sarilumab in human milk or its effects on the breast-fed infant or milk production. Maternal immunoglobulin G (IgG) is present in human milk. The effects of local exposure on the gastrointestinal tract and potential limited systemic exposure to the infant are unknown. Consider the developmental and health benefits of breast-feeding along with the mother's clinical need for sarilumab and the potential adverse effects on the breast-fed infant from sarilumab or the underlying maternal condition.[61976]

During clinical trials, the rate of serious infections among geriatric patients was higher compared to that of patients less than 65 years of age. Because there is a higher incidence of infections in the elderly in general, cautious use of sarilumab use is advised.[61976]

The safety and efficacy of sarilumab have not been established in pediatric patients (adolescents, children or infants).[61976]

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## References

61976 – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

## Mechanism of Action

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Sarilumab binds to both soluble and membrane-bound interleukin-6 (IL-6) receptors (sIL-6R and mIL-6R), and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T-cells and B-cells, lymphocytes, monocytes, and fibroblasts. IL-6 has been shown to be involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.[61976]

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## References

61976 – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

## Pharmacokinetics

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Sarilumab is administered subcutaneously. The volume of distribution at steady state is 7.3 L. Sarilumab is eliminated by parallel linear and non-linear pathways. At higher concentrations, the elimination is predominately through the linear, non-saturable proteolytic pathway. At lower concentrations, non-linear saturable target-

mediated elimination predominates. The half-life is concentration-dependent. At steady-state following administration of 150 mg or 200 mg subcutaneously every 2 weeks, the half-life is up to 8 or 10 days, respectively. After the last steady-state dose of 150 mg and 200 mg, the median times to non-detectable concentration are 28 and 43 days, respectively. Sarilumab is expected to be degraded into small peptides and amino acids via catabolic pathways, similar to endogenous IgG. Monoclonal antibodies are not eliminated via renal or hepatic pathways.[61976]

Decreases in C-reactive protein to within normal ranges were seen as early as week 2 after single-dose administration of sarilumab 150 mg or 200 mg during trials in adult patients with rheumatoid arthritis. Treatment with sarilumab resulted in decreases in serum amyloid A and fibrinogen and increases in hemoglobin and serum albumin.[61976]

*Affected cytochrome P450 (CYP450) isoenzymes and drug transporters:* various CYP450 isoenzymes

The formation of CYP450 enzymes may be suppressed by increased concentrations of cytokines, such as IL-6, during chronic inflammation. Thus, it is expected that the formation of CYP450 enzymes could be normalized during sarilumab receipt leading to increased metabolism of drugs that are CYP450 substrates. Exercise caution when coadministering sarilumab with CYP3A4 substrate drugs where a decrease in effectiveness is undesirable. The effect of sarilumab on CYP450 enzyme activity may persist for several weeks after stopping the medication. [61976]

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## Route-Specific Pharmacokinetics

- **Subcutaneous Route**

When administered subcutaneously, the time to maximum concentration (T<sub>max</sub>) was 2 to 4 days. At steady state, exposure (AUC) increased 2-fold with an increase in dose from 150 mg to 200 mg every 2 weeks. Steady-state was reached in 14 to 16 weeks with a 2- to 3-fold accumulation compared to single-dose exposure. For the 150 mg every 2 week regimen, the estimated mean (+/- SD) steady-state AUC was 202 +/- 120 mg x day/L, the minimum concentration (C<sub>min</sub>) was 6.35 +/- 7.54 mg/L, and the maximal concentration (C<sub>max</sub>) was 20 +/- 9.2 mg/L. For the 200 mg every 2 week regimen, the estimated mean (+/- SD) steady-state AUC, C<sub>min</sub>, and C<sub>max</sub> were 395 +/- 207 mg x day/L, 16.5 +/- 14.1 mg/L, and 35.6 +/- 15.2 mg/L, respectively.[61976]

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## Special Populations

- **Renal Impairment**

Mild (CrCl 60 to 90 mL/minute) and moderate (CrCl 30 to 60 mL/minute) renal impairment does affect the exposure of sarilumab; however, the effect is not sufficient enough to warrant dose adjustment. Patients with severe renal impairment have not been studied.[61976]

- **Geriatric**

Age does not affect the pharmacokinetic profile of sarilumab.[61976]

- **Gender Differences**

Gender does not affect the pharmacokinetic profile of sarilumab.[61976]

- **Ethnic Differences**

Race does not affect the pharmacokinetic profile of sarilumab.[61976]

- **Obesity**

Although body weight influenced the pharmacokinetics of sarilumab, no dose adjustments are recommended.[61976]

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## References

61976 – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

## Pregnancy/Breast-feeding

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### Pregnancy

Limited available data are not sufficient to determine whether the use of sarilumab during human pregnancy is associated with risk for major birth defects or miscarriage. Monoclonal antibodies, like sarilumab, are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third trimester. This may affect immune response in the in utero exposed infant. Concentrations of immunoglobulin G (IgG), in response to antigen challenge, may be reduced in the fetus/infant of treated mothers. Consider risks and benefits prior to administering live or live-attenuated vaccines to neonates or infants who were exposed to sarilumab in utero. In an animal reproduction study, consisting of a combined embryo-fetal and pre- and postnatal development study with monkeys that received intravenous administration of sarilumab, there was no evidence of embryotoxicity or fetal malformations with exposures up to approximately 84 times the maximum recommended human dose (MRHD). Animal data suggest sarilumab may affect labor and obstetric delivery. Inhibition of IL-6 signaling may interfere with cervical ripening and dilatation and myometrial contractile activity, leading to potential delays in parturition. For mice deficient in IL-6, parturition was delayed relative to wild-type mice without this deficiency. Administration of recombinant IL-6 to the deficient mice restored the normal timing of delivery. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to sarilumab during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.[61976]

### Breast-Feeding

There is no information available on the presence of sarilumab in human milk or its effects on the breast-fed infant or milk production. Maternal immunoglobulin G (IgG) is present in human milk. The effects of local exposure on the gastrointestinal tract and potential limited systemic exposure to the infant are unknown. Consider the developmental and health benefits of breast-feeding along with the mother's clinical need for sarilumab and the potential adverse effects on the breast-fed infant from sarilumab or the underlying maternal condition.[61976]

## References

61976 – Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2018 Apr.

## Interactions

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### Level 2 (Major)

- Abatacept
- Adalimumab
- Anakinra
- Bacillus Calmette-Guerin Vaccine, BCG
- Baricitinib
- Canakinumab
- Certolizumab pegol
- Etanercept
- Golimumab
- Infliximab
- Influenza Virus Vaccine
- Intranasal Influenza Vaccine
- Live Vaccines
- Measles Virus; Mumps Virus; Rubella Virus; Varicella Virus Vaccine, Live
- Measles/Mumps/Rubella Vaccines, MMR
- Ofatumumab
- Rituximab
- Rituximab; Hyaluronidase
- Rotavirus Vaccine
- Rubella Virus Vaccine Live
- Secukinumab
- Smallpox and Monkeypox Vaccine, Live, Nonreplicating
- Smallpox Vaccine, Vaccinia Vaccine
- Tocilizumab
- Tofacitinib
- Tumor Necrosis Factor modifiers
- Typhoid Vaccine
- Upadacitinib
- Ustekinumab
- Varicella-Zoster Virus Vaccine, Live
- Yellow Fever Vaccine, Live

### Level 3 (Moderate)

- Alfentanil
- Amlodipine; Atorvastatin
- Apixaban
- Atorvastatin
- Atorvastatin; Ezetimibe
- Belladonna Alkaloids; Ergotamine; Phenobarbital
- Caffeine; Ergotamine
- Carbamazepine
- Cisapride
- Cyclosporine
- Dextromethorphan; Quinidine
- Dienogest; Estradiol valerate
- Dihydroergotamine
- Drospirenone
- Drospirenone; Estradiol
- Drospirenone; Ethinyl Estradiol
- Drospirenone; Ethinyl Estradiol; Levomefolate
- Ergotamine
- Estradiol; Levonorgestrel
- Estradiol; Norethindrone
- Estradiol; Norgestimate
- Ethinyl Estradiol
- Ethinyl Estradiol; Desogestrel
- Ethinyl Estradiol; Ethynodiol Diacetate
- Ethinyl Estradiol; Etonogestrel
- Ethinyl Estradiol; Levonorgestrel
- Ethinyl Estradiol; Levonorgestrel; Ferrous bisglycinate
- Ethinyl Estradiol; Levonorgestrel; Folic Acid; Levomefolate
- Ethinyl Estradiol; Norelgestromin
- Ethinyl Estradiol; Norethindrone
- Ethinyl Estradiol; Norethindrone Acetate
- Ethinyl Estradiol; Norethindrone Acetate; Ferrous fumarate
- Ethinyl Estradiol; Norethindrone; Ferrous fumarate



- Ethinyl Estradiol; Norgestimate
- Ethinyl Estradiol; Norgestrel
- Ethosuximide
- Everolimus
- Ezetimibe; Simvastatin
- Fentanyl
- Fosphenytoin
- Leuprolide; Norethindrone
- Levonorgestrel
- Lovastatin
- Lovastatin; Niacin
- Mestranol; Norethindrone
- Niacin; Simvastatin
- Norethindrone
- Norgestrel
- Oral Contraceptives
- Phenytoin
- Pimozide
- Quinidine
- Rivaroxaban
- Segesterone Acetate; Ethinyl Estradiol
- Simvastatin
- Simvastatin; Sitagliptin
- Sirolimus
- Tacrolimus
- Theophylline, Aminophylline
- Thioridazine
- Tizanidine
- Warfarin

**Abatacept:** (Major) Avoid the concomitant use of sarilumab with biological DMARDs, including selective costimulation modulators such as abatacept; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

**Adalimumab:** (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

**Alfentanil:** (Moderate) Monitor for evidence of reduced effect if alfentanil coadministration with sarilumab is necessary; alfentanil dosage adjustment may be needed. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as alfentanil, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Alfentanil is a CYP3A4 substrate and a narrow therapeutic index drug. [61976]

**Amlodipine; Atorvastatin:** (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as atorvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in exposure to another "statin" was noted in a drug interaction study. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Atorvastatin is a CYP3A4 substrate. [61976]

**Anakinra:** (Major) Avoid using sarilumab with other biological DMARDs including interleukin-1 receptor antagonists such as anakinra; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

**Apixaban:** (Moderate) Monitor for a decrease in efficacy of apixaban if used with sarilumab. Until more data are available, consider using an anticoagulant without dependence on CYP450 enzymes for metabolism (e.g., heparins, edoxaban). The formation of CYP450 enzymes may be suppressed by increased concentrations of cytokines such as IL-6 during chronic inflammation. It is expected that the activity of CYP450 enzymes could increase to normal concentrations during treatment with an IL-6 antagonist such as sarilumab; these effects on

CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes [including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4]. Apixaban is an in vitro substrate for CYP3A4. [52739] [61976] [65210]

Atorvastatin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as atorvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in exposure to another "statin" was noted in a drug interaction study. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Atorvastatin is a CYP3A4 substrate. [61976]

Atorvastatin; Ezetimibe: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as atorvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in exposure to another "statin" was noted in a drug interaction study. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Atorvastatin is a CYP3A4 substrate. [61976]

Bacillus Calmette-Guerin Vaccine, BCG: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Baricitinib: (Major) Avoid the concomitant use of sarilumab with other biological DMARDs such as baricitinib; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976] [63229]

Belladonna Alkaloids; Ergotamine; Phenobarbital: (Moderate) Monitor for decreased efficacy of ergotamine if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as ergotamine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Ergotamine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Caffeine; Ergotamine: (Moderate) Monitor for decreased efficacy of ergotamine if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as ergotamine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Ergotamine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Canakinumab: (Major) Avoid using sarilumab with other biological DMARDs including interleukin-1 receptor antagonists such as canakinumab; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Carbamazepine: (Moderate) Monitor carbamazepine concentrations and watch for decreased efficacy of carbamazepine if coadministration with sarilumab is necessary; adjust carbamazepine dosage as necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as carbamazepine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Carbamazepine is a substrate of both CYP1A2 and CYP3A4 and a narrow therapeutic index drug. [61976]

Certolizumab pegol: (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Cisapride: (Moderate) Monitor for decreased efficacy of cisapride if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as cisapride, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Cisapride is a CYP3A4 substrate and a narrow therapeutic index drug. [61976]

Cyclosporine: (Moderate) Monitor cyclosporine levels and adjust the dose of cyclosporine as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as cyclosporine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Cyclosporine is a CYP3A4 substrate and a narrow therapeutic index drug. [61976]

Dextromethorphan; Quinidine: (Moderate) Monitor quinidine levels and adjust the dose of quinidine as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as quinidine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Quinidine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Dienogest; Estradiol valerate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Dihydroergotamine: (Moderate) Monitor for decreased efficacy of dihydroergotamine if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as dihydroergotamine, may have

fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Dihydroergotamine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Drospirenone: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Drospirenone; Estradiol: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Drospirenone; Ethinyl Estradiol: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Drospirenone; Ethinyl Estradiol; Levomefolate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ergotamine: (Moderate) Monitor for decreased efficacy of ergotamine if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as ergotamine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Ergotamine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Estradiol; Levonorgestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Estradiol; Norethindrone: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Estradiol; Norgestimate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Etanercept: (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Ethinyl Estradiol: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Desogestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Ethynodiol Diacetate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Etonogestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Levonorgestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to

increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Levonorgestrel; Ferrous bisglycinate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Levonorgestrel; Folic Acid; Levomefolate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norelgestromin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norethindrone Acetate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norethindrone Acetate; Ferrous fumarate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norethindrone: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norethindrone; Ferrous fumarate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in

effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norgestimate: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethinyl Estradiol; Norgestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Ethosuximide: (Moderate) Monitor for reduced efficacy of ethosuximide, monitor drug concentrations, and adjust the dose of ethosuximide as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as ethosuximide, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Ethosuximide is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Everolimus: (Moderate) Monitor for clinical response in patients taking everolimus concurrently with sarilumab. For indications where therapeutic drug monitoring is appropriate, monitor everolimus trough concentrations and adjust the dose of everolimus accordingly. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as everolimus, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Everolimus is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Ezetimibe; Simvastatin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as simvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in simvastatin exposure was noted 1 week after a single sarilumab dose. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Simvastatin is a CYP3A4 substrate. [61976]

Fentanyl: (Moderate) Monitor for evidence of reduced pain control or opioid withdrawal if fentanyl coadministration with sarilumab is necessary; fentanyl dosage adjustment may be needed. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs

that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as fentanyl, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Fentanyl is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Fosphenytoin: (Moderate) Monitor fosphenytoin concentrations and watch for decreased efficacy of fosphenytoin if coadministration with sarilumab is necessary; adjust fosphenytoin dosage as necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as fosphenytoin, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Fosphenytoin is a substrate of both CYP2C9 and CYP2C19 and narrow therapeutic index drug. [61976]

Golimumab: (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Infliximab: (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Influenza Virus Vaccine: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Intranasal Influenza Vaccine: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Leuprolide; Norethindrone: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Levonorgestrel: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]



Live Vaccines: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Lovastatin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as lovastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in exposure to another "statin" was noted in a drug interaction study. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Lovastatin is a CYP3A4 substrate. [61976]

Lovastatin; Niacin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as lovastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in exposure to another "statin" was noted in a drug interaction study. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Lovastatin is a CYP3A4 substrate. [61976]

Measles Virus; Mumps Virus; Rubella Virus; Varicella Virus Vaccine, Live: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Measles/Mumps/Rubella Vaccines, MMR: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Mestranol; Norethindrone: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Niacin; Simvastatin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as simvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in simvastatin exposure was noted 1 week after a single sarilumab dose. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Simvastatin is a CYP3A4 substrate. [61976]

**Norethindrone:** (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

**Norgestrel:** (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

**Ofatumumab:** (Major) Avoid using sarilumab with other biological agents, including anti-CD20 monoclonal antibodies such as ofatumumab; coadministration has not been studied and may result in additive immunosuppression and an increased risk of infection. [61976]

**Oral Contraceptives:** (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

**Phenytoin:** (Moderate) Monitor phenytoin concentrations and watch for decreased efficacy of phenytoin if coadministration with sarilumab is necessary; adjust phenytoin dosage as necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as phenytoin, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Phenytoin is a substrate of both CYP2C9 and CYP2C19 and narrow therapeutic index drug. [61976]

**Pimozide:** (Moderate) Monitor for an altered patient response to pimozide if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as pimozide, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Pimozide a substrate of both CYP2D6 and CYP3A4 and narrow therapeutic index drug. [61976]

**Quinidine:** (Moderate) Monitor quinidine levels and adjust the dose of quinidine as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as quinidine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6,

CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Quinidine is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Rituximab: (Major) Avoid using sarilumab with other biological agents, including anti-CD20 monoclonal antibodies such as rituximab; coadministration has not been studied and may result in additive immunosuppression and an increased risk of infection. [49773] [61976]

Rituximab; Hyaluronidase: (Major) Avoid using sarilumab with other biological agents, including anti-CD20 monoclonal antibodies such as rituximab; coadministration has not been studied and may result in additive immunosuppression and an increased risk of infection. [49773] [61976]

Rivaroxaban: (Moderate) Monitor for a decrease in efficacy of rivaroxaban if used with sarilumab. Until more data are available, consider using an anticoagulant without dependence on CYP450 enzymes for metabolism (e.g., heparins, edoxaban). The formation of CYP450 enzymes may be suppressed by increased concentrations of cytokines such as IL-6 during chronic inflammation. It is expected that the activity of CYP450 enzymes could increase to normal concentrations during treatment with an IL-6 antagonist such as sarilumab; these effects on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes [including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4]. Rivaroxaban is a substrate for CYP3A4/5. [44854] [61976] [65210]

Rotavirus Vaccine: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Rubella Virus Vaccine Live: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Secukinumab: (Major) Avoid using sarilumab with other biological DMARDs, such as secukinumab; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Segesterone Acetate; Ethinyl Estradiol: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as combined hormonal oral contraceptives, where a decrease in effectiveness is undesirable. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. [61976]

Simvastatin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as simvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in simvastatin exposure was noted 1 week after a single sarilumab dose. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Simvastatin is a CYP3A4 substrate. [61976]

Simvastatin; Sitagliptin: (Moderate) Utilize caution with concomitant use of sarilumab and CYP3A4 substrate drugs, such as simvastatin, where a decrease in effectiveness is undesirable. Monitor lipid panels and adjust therapy as indicated. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. A 45% decrease in simvastatin exposure was noted 1 week after a single sarilumab dose. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Simvastatin is a CYP3A4 substrate. [61976]

Sirolimus: (Moderate) Monitor sirolimus levels and adjust the dose of sirolimus as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as sirolimus, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Sirolimus is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Smallpox and Monkeypox Vaccine, Live, Nonreplicating: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Smallpox Vaccine, Vaccinia Vaccine: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Tacrolimus: (Moderate) Monitor tacrolimus levels and adjust the dose of tacrolimus as appropriate if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as tacrolimus, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Tacrolimus is a CYP3A4 substrate and narrow therapeutic index drug. [61976]

Theophylline, Aminophylline: (Moderate) Monitor drug concentrations and watch for decreased efficacy of aminophylline or theophylline if coadministration with sarilumab is necessary; a dosage increase of these methylxanthines may be necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Aminophylline and Theophylline are CYP1A2 substrates and narrow therapeutic index drugs. [61976]

Thioridazine: (Moderate) Monitor for an altered patient response to thioridazine if coadministration with sarilumab is necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels

leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as thioridazine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Thioridazine is a CYP2D6 substrate and narrow therapeutic index drug. [61976]

Tizanidine: (Moderate) Monitor for reduced efficacy of tizanidine if coadministered with sarilumab. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as tizanidine, may have fluctuations in drug levels and therapeutic effect when sarilumab therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. In vitro, sarilumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Tizanidine is a CYP1A2 substrate and narrow therapeutic index drug. [61976]

Tocilizumab: (Major) Avoid using sarilumab with other biological DMARDs, such as tocilizumab; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [38283] [61976]

Tofacitinib: (Major) Avoid the concomitant use of sarilumab with other biological DMARDs such as tofacitinib; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [52315] [61976]

Tumor Necrosis Factor modifiers: (Major) Avoid the concomitant use of sarilumab with biological DMARDs, such as tumor necrosis factor (TNF) modifiers; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Typhoid Vaccine: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Upadacitinib: (Major) Avoid the concomitant use of sarilumab with other biological DMARDs, such as upadacitinib; coadministration has not been studied and may result in additive immunosuppression and an increased risk of infection. [61976] [64572]

Ustekinumab: (Major) Avoid the concomitant use of sarilumab with other biological DMARDs such as ustekinumab; coadministration has not been studied and may result in additive immunosuppression and increased risk of infection. [61976]

Varicella-Zoster Virus Vaccine, Live: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

Warfarin: (Moderate) Monitor the INR if sarilumab is coadministered with warfarin due to the potential for decreased warfarin efficacy; adjust the dose of warfarin as necessary. Inhibition of IL-6 signaling by sarilumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. Therefore, CYP450 substrates with a narrow therapeutic index, such as warfarin, may have fluctuations in drug levels and therapeutic effect when sarilumab

therapy is started or discontinued. This effect on CYP450 enzyme activity may persist for several weeks after stopping sarilumab. [28549] [61976]

Yellow Fever Vaccine, Live: (Major) Avoid concurrent use of live vaccines during treatment with sarilumab due to potentially increased risk of infections; clinical safety of live vaccines during sarilumab treatment has not been established. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving sarilumab. The interval between live vaccinations and initiation of sarilumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. [51778] [61976]

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## Monitoring Parameters

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- CBC with differential
- LFTs
- platelet count
- serum lipid profile
- tuberculin skin test

## US Drug Names

- KEVZARA

## **Global Drug names**

### Austria

- Kevzara - (Sanofi-Aventis)

### Belgium

- Kevzara - (Sanofi-Aventis)

### Canada

- Kevzara - (Sanofi-Aventis)

### Denmark

- Kevzara - (Sanofi)

### Finland

- Kevzara - (Sanofi-Aventis)

### Germany

- Kevzara - (Sanofi-Aventis)

### Ireland

- Kevzara - (Sanofi-Aventis)

### Israel

- Kevzara - (Sanofi-Aventis)

### Netherlands

- Kevzara - (Sanofi-Aventis)

### Poland

- Kevzara - (Sanofi-Aventis)

### Spain

- Kevzara - (Sanofi-Aventis)

### Sweden

- Kevzara - (Sanofi)

### Switzerland

- Kevzara - (Sanofi-Aventis)

United Kingdom

- Kevzara - (Genzyme)

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