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## Subject: Sarilumab (Kevzara®) Injection

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### DESCRIPTION:

Sarilumab (Kevzara) is an injectable human monoclonal antibody that binds specifically to both soluble and membrane-bound interleukin-6 (IL-6) receptors. The IL-6 receptor plays a major role in regulating the underlying disease pathophysiology and clinical manifestations of rheumatoid arthritis (RA). In patients with RA, elevated levels of IL-6 in serum and synovial fluid are closely associated with synovitis, systemic inflammation, bone metabolism, fatigue, and joint destruction. Sarilumab was approved by the US Food and Drug Administration (FDA) in May 2017 for “treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).” Sarilumab is the second anti-IL-6 agent to be approved by the FDA for the treatment of RA. Tocilizumab (Actemra) was the first anti-IL-6 agent to be approved by the FDA for RA in January 2010. Siltuximab (Sylvant) is also an anti-IL-6 agent but works by binding to IL-6 itself as opposed to the IL-6 receptor. Siltuximab is FDA-approved for the treatment of multicentric Castleman disease only.

### Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is the most common inflammatory autoimmune arthritis in adults. The main goal of therapy is to achieve remission, but additional goals include decrease inflammation, relieve symptoms, prevent joint and organ damage, improve physical function/overall well-being, and reduce long term complications. The choice of therapy depends on several factors, including the severity of disease activity when therapy is initiated and the response of the patient to prior therapeutic interventions.

American College of Rheumatology (ACR) guidelines list the following guiding principles in the treatment of RA:

- RA requires early evaluation, diagnosis, and management
- Treatment decisions should follow a shared decision-making process
- Treatment decisions should be reevaluated within a minimum of 3 months based on efficacy and tolerability of the DMARD(s) chosen
- Recommendations are limited to DMARDs approved by the US FDA for treatment of RA:
  - csDMARDs: hydroxychloroquine, sulfasalazine, methotrexate (MTX), leflunomide
  - bDMARDs: TNF inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), T cell costimulatory inhibitor (abatacept), IL-6 receptor inhibitors (tocilizumab, sarilumab), anti-CD20 antibody (rituximab)
  - tsDMARDs: JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
- Triple therapy refers to hydroxychloroquine, sulfasalazine, and either methotrexate or leflunomide
- Biosimilars are considered equivalent to FDA-approved originator bDMARDs
- Recommendations referring to bDMARDs exclude rituximab unless patients have had an inadequate response to TNF inhibitors (in order to be consistent with FDA approval) or have a history of lymphoproliferative disorder for which rituximab is an approved therapy
- Treat-to-target refers to a systematic approach involving frequent monitoring of disease activity using validated instruments and modifications of treatment to minimize disease activity with the goal of reaching a predefined target (low disease activity or remission)

ACR guidelines are broken down by previous treatment and disease activity:

- DMARD-naïve patients with moderate-to-high disease activity initial treatment:
  - MTX monotherapy is strongly recommended over hydroxychloroquine, sulfasalazine, bDMARDs monotherapy, tsDMARD monotherapy, or combination of MTX plus a non-TNF bDMARD or tsDMARD
  - MTX monotherapy is conditionally recommended over leflunomide, dual or triple csDMARD therapy, or combination MTX plus a TNF inhibitor
- DMARD-naïve patients with low disease activity initial treatment
  - Hydroxychloroquine is conditionally recommended over other csDMARDs
  - Sulfasalazine is conditionally recommended over MTX
  - MTX is conditionally recommended over leflunomide
- Initial therapy in csDMARD-treated patients, but MTX naïve, with moderate-to high disease activity:
  - MTX monotherapy is conditionally recommended over combination MTX and a bDMARD or tsDMARD
- Treatment Modifications in patients treated with DMARDs who are not at target:
  - Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy for patients taking maximally tolerated doses of MTX who are not at target

- Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target

Early use of DMARD, particularly MTX, is recommended as soon as possible following diagnosis of RA. Dosing of MTX for RA is once weekly dosing with starting doses at 7.5 mg or 15 mg once weekly. MTX dose is increased as tolerated and as needed to control symptoms and signs of RA disease. The usual target dose is at least 15 mg weekly, and the usual maximum dose is 25 mg weekly. ACR defines optimal dosing for RA treatments as 1) dosing to achieve a therapeutic target derived from mutual patient-clinician consideration of patient priorities and 2) given for at least 3 months before therapy escalation or switching. For patients who are unable to take MTX, hydroxychloroquine, sulfasalazine, or leflunomide are other DMARD options. In patients resistant to initial MTX treatment, combination DMARD (e.g., MTX plus sulfasalazine or hydroxychloroquine or a TNF-inhibitor) is recommended.

For patients who are resistant to MTX after 3 months of treatment at optimal doses (usually 25 mg per week), it is recommended to either use DMARD triple therapy with MTX plus sulfasalazine and hydroxychloroquine or combination of MTX with TNF inhibitor. Triple therapy regimen has been found to be of similar clinical efficacy to MTX with biologics in several randomized trials, including in patients with high level of disease activity or with adverse prognostic features. The use of triple therapy has been shown to be highly cost-effective compared with combining a biologic with MTX, providing comparable or near comparable clinical benefit. The use of biologic with MTX combination is preferred when patients have high disease activity and clinical benefit from a more rapid response is needed and when patients who do not achieve satisfactory response within 3 months with non-biologic triple therapy following an inadequate response to MTX therapy.

## POSITION STATEMENT:

### Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

**NOTE:** The self-administered products with prerequisites for certain indications are as follows:

**Table 1**

Disease State	Step 1		Step 2 (Directed to ONE step 1 agent)	Step 3a (Directed to TWO step 1 agents)	Step 3b (Directed to TWO agents from step 1 and/or step 2)	Step 3c (Directed to THREE step 1 agents)
	Step 1a	Step 1b (Directed to ONE TNF inhibitor) NOTE: Please see Step 1a for preferred TNF inhibitors				
Rheumatoid Disorders						

Ankylosing Spondylitis (AS)	SQ: Cosentyx, Enbrel, Humira	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Simponi, Taltz	N/A	N/A
Nonradiographic Axial Spondyloarthritis (nr-axSpA)	SQ: Cimzia, Cosentyx	Oral: Rinvoq	N/A	SQ: Taltz	N/A	N/A
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	SQ: Enbrel, Humira	Oral: Xeljanz	SQ: Actemra (Humira is required Step 1 agent)	N/A	SQ: Orencia	N/A
Psoriatic Arthritis (PsA)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Orencia, Simponi, Taltz	N/A	N/A
Rheumatoid Arthritis	SQ: Enbrel, Humira	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Actemra (Humira is required Step 1 agent)	Oral: Olumiant SQ: Cimzia, <b>Kevzara</b> , Kineret, Orencia, Simponi	N/A	N/A
<b>Dermatological Disorders</b>						
Hidradenitis Suppurativa (HS)	SQ: Humira	N/A	N/A	N/A	N/A	N/A
Psoriasis (PS)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	N/A	N/A	SQ: Cimzia, Ilumya	N/A	SQ: Siliq, Taltz  Oral: Sotyktu
<b>Inflammatory Bowel Disease</b>						
Crohn's Disease	SQ: Humira, Skyrizi, Stelara	N/A	N/A	SQ: Cimzia (Humira is a required Step 1 agent)	N/A	N/A
Ulcerative Colitis	SQ: Humira, Stelara	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Simponi (Humira is required Step 1 agent)	N/A	Zeposia (Humira, Rinvoq, Stelara, OR Xeljanz/Xeljanz XR are required Step agents)	N/A

Othe						
Uveiti	SQ: Humira	N/A	N/A	N/A	N/A	N/A
Indications Without Prerequisite Biologic Immunomodulators						
Alopecia Areata (AA)						
Atopic Dermatitis						
Deficiency of IL-1 Receptor Antagonist (DIRA)						
Enthesitis Related Arthritis (ERA)						
Giant Cell Arteritis (GCA)	N/A	N/A	N/A	N/A	N/A	N/A
Neonatal-Onset Multisystem Inflammatory Disease (NOMID)						
Systemic Juvenile Idiopathic Arthritis (SJIA)						
Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)						

\*Note: A trial of either or both Xeljanz products (Xeljanz and Xeljanz XR) collectively counts as ONE product

Initiation of sarilumab (Kevzara) meets the definition of medical necessity when **ALL** of the following are met (“1” to “6”):

1. **ONE** of the following (“a”, “b”, or “c”):
  - a. Information has been provided that indicates the member has been treated with sarilumab (starting on samples is not approvable) within the past 90 days
  - b. The prescriber states the member has been treated with sarilumab (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
  - c. **BOTH** of the following (“i” and “ii”):
    - i. Sarilumab will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific criteria are met
    - ii. **EITHER** of the following (“I” or “II”)
      - I. The member’s age is within FDA labeling for the requested indication for sarilumab

- II. The prescriber has provided information in support of using sarilumab for the member's age
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for RA) or the prescriber has consulted with a specialist in the area of the member's diagnosis
  3. Member does **NOT** have any FDA labeled contraindications to sarilumab
  4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the member has begun therapy for latent TB
  5. Member will **NOT** be using sarilumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
  6. **ANY** of the following ("a", "b", or "c"):
    - a. The dosage does not exceed 200 mg once every 2 weeks (14 days)
      - QL: 150 mg/1.14 mL pen – 2 pens (2.28 mL)/28 days
      - QL: 200 mg/1.14 mL pen – 2 pens (2.28 mL)/28 days
      - QL: 150 mg/1.14 mL syringe – 2 syringes (2.28 mL)/28 days
      - QL: 200 mg/1.14 mL syringe – 2 syringes (2.28 mL)/28 days
    - b. The requested quantity (dose) is greater than program's quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
    - c. The requested quantity (dose) is greater than the program's quantity limit and greater than the maximum FDA labeled dose **AND** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the prescriber has provided information in support of therapy with a higher dose for the requested indication (submitted copy required, e.g., clinical trials, phase III studies, guidelines required)

**Approval duration:** 12 months

**Table 2**

Diagnosis	Criteria
Moderately to severely active rheumatoid arthritis (RA)	<b>BOTH</b> of the following: 1. <b>ONE</b> of the following:

a. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3 months

**OR**

b. The member has tried and had an inadequate response to another conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA for at least 3 months

**OR**

c. The member has an intolerance or hypersensitivity to **ONE** of the following conventional agents (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA

**OR**

d. The member has an FDA labeled contraindication to **ALL** of the following conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA

**OR**

e. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA

**AND**

2. **ANY** of the following:

a. The member has tried and had an inadequate response to at least **TWO** of the following for at least 3 months:

- Enbrel (etanercept)
- Humira (adalimumab)
- Rinvoq (upadacitinib)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **TWO** of the following:

- Enbrel (etanercept)
- Humira (adalimumab)

	<ul style="list-style-type: none"> <li>• Rinvoq (upadacitinib)</li> <li>• Xeljanz/Xeljanz XR (tofacitinib)</li> </ul> <p><b>OR</b></p> <p>c. The member has an FDA labeled contraindication to <b>ALL</b> of the following:</p> <ul style="list-style-type: none"> <li>• Enbrel (etanercept)</li> <li>• Humira (adalimumab)</li> <li>• Rinvoq (upadacitinib)</li> <li>• Xeljanz/Xeljanz XR (tofacitinib)</li> </ul> <p><b>OR</b></p> <p>d. The prescriber has provided information indicating why <b>ALL</b> of the following are not clinically appropriate for the member, <b>AND</b> the prescriber has provided a complete list of previously tried agents for the requested indication:</p> <ul style="list-style-type: none"> <li>• Enbrel (etanercept)</li> <li>• Humira (adalimumab)</li> <li>• Rinvoq (upadacitinib)</li> <li>• Xeljanz/Xeljanz XR (tofacitinib)</li> </ul>
Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a

Continuation of sarilumab (Kevzara) **meets the definition of medical necessity** when **ALL** of the following are met (“1” to “6”):

1. An authorization or reauthorization for sarilumab has been previously approved by Florida Blue
2. Member has had clinical benefit with sarilumab therapy
3. The prescriber is a specialist in the area of the member’s diagnosis (e.g., rheumatologist for RA) or the prescriber has consulted with a specialist in the area of the member’s diagnosis
4. Member does **NOT** have any FDA labeled contraindications to sarilumab
5. Member will **NOT** be using sarilumab in combination with another biologic immunomodulator agent (full list in “Other” section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following (“a”, “b”, or “c”):
  - a. The dosage does not exceed 200 mg once every 2 weeks (14 days)



- QL: 150 mg/1.14 mL pen – 2 pens (2.28 mL)/28 days
  - QL: 200 mg/1.14 mL pen – 2 pens (2.28 mL)/28 days
  - QL: 150 mg/1.14 mL syringe – 2 syringes (2.28 mL)/28 days
  - QL: 200 mg/1.14 mL syringe – 2 syringes (2.28 mL)/28 days
- b. The requested quantity (dose) is greater than program’s quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
- c. The requested quantity (dose) is greater than the program’s quantity limit and greater than the maximum FDA labeled dose **AND** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the prescriber has provided information in support of therapy with a higher dose for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

**Approval duration:** 12 months

## **DOSAGE/ADMINISTRATION:**

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER’S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

### **FDA-approved**

- Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)
- The recommended dosage of is 200 mg once every two weeks given as a subcutaneous injection. Reduce dose to 150 mg once every two weeks for management of neutropenia, thrombocytopenia and elevated liver enzymes. Sarilumab may be used as monotherapy or in combination with methotrexate (MTX) or other conventional DMARDs. Prior to initiating, test patients for latent tuberculosis. A patient may self-inject after proper training on preparation and administration. The pre-filled syringe should sit at room temperature for 30 minutes prior to injection. Rotate injection sites with each injection.
- Sarilumab initiation is **NOT** recommended in patients with an absolute neutrophil count (ANC) less than 2,000/mm<sup>3</sup>, platelet count less than 150,000/ mm<sup>3</sup>, or who have ALT or AST above 1.5 times the upper limit of normal (ULN).
- Avoid using sarilumab with biological DMARDs because of the possibility of increased immunosuppression and increased risk of infection.

### **Dose Adjustments**

- Low Absolute Neutrophil Count (ANC)

- ANC greater than 1,000/mm<sup>3</sup> – maintain current dosage
- ANC 500 to 1,000/mm<sup>3</sup> - hold treatment until ANC greater than 1,000/mm<sup>3</sup>. Resume at 150 mg every two weeks and increased to 200 mg every two weeks as clinically appropriate.
- ANC less than 500/mm<sup>3</sup> - discontinue
- Low Platelet Count
  - 50,000–100,000/mm<sup>3</sup> – hold treatment until platelets greater than 100,000/mm<sup>3</sup>. Resume at 150 mg every two weeks and increased to 200 mg every two weeks as clinically appropriate.
  - Less than 50,000/mm<sup>3</sup> – discontinue if confirmed by repeat testing
- Liver Enzyme Abnormalities
  - ALT greater than ULN to 3 times ULN or less – consider dosage modification of concomitant DMARDs as clinically appropriate.
  - ALT greater than 3 times ULN to 5 times ULN or less – hold treatment until ALT less than 3 times ULN. Resume at 150 mg every two weeks and increased to 200 mg every two weeks as clinically appropriate.
  - ALT greater than 5 times ULN - discontinue

#### **Drug Availability**

- 150 mg/1.14 mL and 200 mg/1.14 mL as single-dose pre-filled syringes or pre-filled pens that come in a package of two syringes or pens
- Refrigerate at 36°F to 46°F (2°C to 8°C) in original carton to protect from light. If needed, sarilumab may be stored at room temperature up to 77°F (25°C) up to 14 days in the outer carton.

## **PRECAUTIONS:**

### **Boxed Warning**

- **WARNING: RISK OF SERIOUS INFECTIONS**
  - Patients treated with Kevzara are at increased risk for developing serious infections that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving Kevzara. Most patients who developed infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
  - Avoid use of Kevzara in patients with an active infection.
  - Reported infections include:
    - Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before Kevzara use and during therapy. Treatment for latent infection should be initiated prior to Kevzara use.
    - Invasive fungal infections, such as candidiasis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
    - Bacterial, viral and other infections due to opportunistic pathogens.

- Closely monitor patients for signs and symptoms of infection during treatment with Kevzara. If a serious infection develops, interrupt Kevzara until the infection is controlled.
- Consider the risks and benefits of treatment with Kevzara prior to initiating therapy in patients with chronic or recurrent infection.

### **Contraindications**

- Patients with known hypersensitivity to sarilumab or any of the inactive ingredients

### **Precautions/Warnings**

- **Serious Infections:** Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving immunosuppressive agents including sarilumab for RA. The most frequently observed serious infections with sarilumab included pneumonia and cellulitis. Avoid sarilumab use in patients with an active infection, including localized infections.
  - **Tuberculosis:** Evaluate patients for TB risk factors and test for latent infection prior to initiating treatment. Treat patients with latent TB with standard antimycobacterial therapy before initiating sarilumab
  - **Viral Reactivation:** Viral reactivation has been reported with immunosuppressive biologic therapies. Cases of herpes zoster were observed in clinical studies with sarilumab. The risk of Hepatitis B reactivation with is unknown since patients who were at risk for reactivation were excluded.
- **Laboratory Abnormalities**
  - **Neutropenia:** Treatment with sarilumab was associated with a higher incidence of decrease in absolute neutrophil count (ANC). Assess neutrophil count prior to initiation of therapy and monitor neutrophil count 4 to 8 weeks after start of therapy and every 3 months thereafter. Adjust the dose as needed based on ANC results.
  - **Thrombocytopenia:** Treatment with sarilumab was associated with a reduction in platelet counts in clinical studies. Assess platelet count prior to initiation of therapy and monitor platelets 4 to 8 weeks after start of therapy and every 3 months thereafter. Adjust the dose as needed based on platelet counts.
  - **Elevated Liver Enzymes:** Treatment with sarilumab was associated with a higher incidence of transaminase elevations. These elevations were transient and did not result in any clinically evident hepatic injury in clinical studies. Increased frequency and magnitude of these elevations were observed when potentially hepatotoxic drugs (e.g., MTX) were used in combination. Assess ALT/AST levels prior to initiation of treatment and monitor ALT and AST levels 4 to 8 weeks after start of therapy and every 3 months thereafter. Adjust the dose as needed based on transaminase elevations.
  - **Lipid Abnormalities:** Treatment with sarilumab was associated with increases in lipid parameters such as LDL-C, HDL-C, and/or triglycerides. Assess lipid parameters approximately 4 to 8 weeks following initiation of treatment, then at approximately 6-month intervals. Manage patients according to clinical guidelines for the management of hyperlipidemia.

- **Gastrointestinal (GI) Perforation:** Gastrointestinal perforations have been reported in clinical studies. Risk may be increased with concurrent diverticulitis or concomitant use of NSAIDs or corticosteroids. Promptly evaluate acute abdominal signs or symptoms.
- **Immunosuppression:** Treatment with immunosuppressants may result in an increased risk of malignancies. The impact of treatment with sarilumab on the development of malignancies is not known but malignancies were reported in clinical studies.
- **Hypersensitivity reactions:** Hypersensitivity reactions have been reported in association with sarilumab. Injection site rash, rash, and urticaria were the most frequent hypersensitivity reactions.
- **Active Hepatic Disease and Hepatic Impairment:** Treatment with sarilumab is not recommended in patients with active hepatic disease or hepatic impairment, as treatment was associated with transaminase elevations.
- **Live vaccines:** Avoid concurrent use of live vaccines during treatment with sarilumab due to the risk of infection. Follow vaccination guidelines.

## BILLING/CODING INFORMATION:

### HCPCS Coding

J3590	Unclassified biologics
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### ICD-10 Diagnosis Codes That Support Medical Necessity

M05.00 – M05.09	Felty's syndrome
M05.10 – M05.19	Rheumatoid lung disease with rheumatoid arthritis
M05.20 – M05.29	Rheumatoid vasculitis with rheumatoid arthritis
M05.30 – M05.39	Rheumatoid heart disease with rheumatoid arthritis
M05.40 – M05.49	Rheumatoid myopathy with rheumatoid arthritis
M05.50 – M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis
M05.60 – M05.69	Rheumatoid arthritis with involvement of other organs and systems
M05.70 – M05.79	Rheumatoid arthritis with rheumatoid factor without organ or systems involvement
M05.80 – M05.89	Other rheumatoid arthritis with rheumatoid factor
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00 – M06.09	Rheumatoid arthritis without rheumatoid factor
M06.20 – M06.29	Rheumatoid bursitis
M06.30 – M06.39	Rheumatoid nodule
M06.80 – M06.89	Other specified rheumatoid arthritis
M06.9	Rheumatoid arthritis, unspecified

## REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

## DEFINITIONS:

**DMARDs:** An acronym for disease-modifying antirheumatic drug. These are drugs that modify the rheumatic disease processes, and slow or inhibit structural damage to cartilage and bone. These drugs are unlike symptomatic treatments such as NSAIDs that do not alter disease progression. DMARDs can be further subcategorized. With the release of biologic agents (e.g., anti-TNF drugs), DMARDs were divided into either: (1) conventional, traditional, synthetic, or non-biological DMARDs; or as (2) biological DMARDs. However, with the release of newer targeted non-biologic drugs and biosimilars, DMARDs are now best categorized as: (1) conventional synthetic DMARDs (csDMARD) (e.g., MTX, sulfasalazine), (2) targeted synthetic DMARDs (tsDMARD) (e.g., apremilast, baricitinib, tofacitinib), and (3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

**Interleukin-6 (IL-6):** a protein that in humans is encoded by the IL6 gene. It acts as both a pro-inflammatory and anti-inflammatory cytokine. It is secreted by T cells and macrophages to stimulate immune response to trauma, especially burns or other tissue damage leading to inflammation.

**Rheumatoid arthritis:** usually occurs between ages 20 and 50. Inflammation begins in a joint, usually those of the fingers and hands, resulting in pain, swelling, redness, and eventually joint deformity. It is considered an autoimmune disease, which can affect the entire body, causing fatigue, weight loss, weakness, fever, and loss of appetite. It affects each person differently, with symptoms ranging from mild to debilitating. In many cases, it is difficult to control. In about one in six cases, rheumatoid arthritis becomes severely debilitating and can shorten the life of the person affected.

## RELATED GUIDELINES:

[Abatacept \(Orencia\), 09-J0000-67](#)

[Adalimumab \(Humira\), 09-J0000-46](#)

[Anakinra \(Kineret\), 09-J0000-45](#)

[Baricitinib \(Olumiant\), 09-J3000-10](#)

[Certolizumab Pegol \(Cimzia\), 09-J0000-77](#)

[Etanercept \(Enbrel\), 09-J0000-38](#)

[Golimumab \(Simponi, Simponi Aria\), 09-J1000-11](#)

[Infliximab Products \[infliximab \(Remicade\), infliximab-dyyb \(Inflectra\), and infliximab-abda \(Renflexis\)\], 09-J0000-39](#)

[Rituximab \(Rituxan\), 09-J0000-59](#)

[Tocilizumab \(Actemra\) Injection, 09-J1000-21](#)

[Tofacitinib \(Xeljanz, Xeljanz XR\) Oral Solution, Tablet, and Extended-Release Tablet, 09-J1000-86](#)

[Upadacitinib \(Rinvoq\), 09-J3000-51](#)

## **OTHER:**

### **Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy**

Actemra (tocilizumab)

Adbry (tralokinumab-ldrm)

Arcalyst (rilonacept)

Avsola (infliximab-axxq)

Benlysta (belimumab)

Cimzia (certolizumab)

Cinqair (reslizumab)

Cosentyx (secukinumab)

Dupixent (dupilumab)

Enbrel (etanercept)

Entyvio (vedolizumab)

Fasenra (benralizumab)

Humira (adalimumab)

Ilaris (canakinumab)

Ilumya (tildrakizumab-asmn)

Inflectra (infliximab-dyyb)

Infliximab

Kevzara (sarilumab)

Kineret (anakinra)

Nucala (mepolizumab)

Orencia (abatacept)

Remicade (infliximab)

Renflexis (infliximab-abda)

Riabni (rituximab-arrx)

Rituxan (rituximab)

Rituxan Hycela (rituximab/hyaluronidase human)

Ruxience (rituximab-pvvr)

Siliq (brodalumab)

Simponi (golimumab)

Simponi Aria (golimumab)

Skyrizi (risankizumab-rzaa)

Stelara (ustekinumab)

Taltz (ixekizumab)

Tezspire (tezepelumab-ekko)

Tremfya (guselkumab)

Truxima (rituximab-abbs)

Tysabri (natalizumab)

Xolair (omalizumab)

**Table 3:**

<b>DMARD Generic Name</b>	<b>DMARD Brand Name</b>
Auranofin (oral gold)	Ridaura
Azathioprine	Imuran
Cyclosporine	Neoral, Sandimmune
Hydroxychloroquine	Plaquenil
Leflunomide	Arava
Methotrexate	Rheumatrex, Trexall
Sulfasalazine	Azulfidine, Azulfidine EN-Tabs

**Table 4: Grading of Severity of Rheumatoid Arthritis**

<b>Severity</b>	<b>Criteria</b>
Mild	Joint pain Inflammation of at least 3 joints No inflammation in tissues other than the joints Usually, a negative result on a rheumatoid factor test An elevated erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) level No evidence of bone or cartilage damage on x-rays
Moderate	Between 6 and 20 inflamed joints Usually no inflammation in tissues other than the joints An elevated ESR or CRP levels A positive rheumatoid factor test or anti-cyclic citrullinated peptide (anti-CCP) antibodies Evidence of inflammation but no evidence of bone damage on x-rays
Severe	More than 20 persistently inflamed joints or a rapid loss of functional abilities Elevated ESR or CRP levels Anemia related to chronic illness Low blood albumin level A positive rheumatoid factor test, often with a high level Evidence of bone and cartilage damage on x-ray Inflammation in tissues other than joints

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### COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/09/22.

### GUIDELINE UPDATE INFORMATION:

09/15/17	New Medical Coverage Guideline.
01/01/18	Revision to guideline consisting of updating the preferred self-administered biologic products according to indication for use. Tofacitinib (Xeljanz, Xeljanz XR) added as prerequisite therapy for rheumatoid arthritis indication.
07/01/18	Revision to guideline consisting of updating the position statement.
10/15/18	Review and revision to guideline consisting of updating the position statement, definitions, related guidelines, and references.
10/15/19	Review and revision to guideline consisting of updating the position statement, billing/coding, and references.
01/01/20	Revision to guideline consisting of updating the position statement due to changes in preferred and non-preferred products.
07/01/20	Revision to guideline consisting of updating the description, position statement, dosage/administration, and other section.
01/01/21	Review and revision to guideline consisting of updating the position statement and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
09/15/21	Update to Table 1 in Position Statement.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the description, position statement, related guidelines, other section, and references.
02/15/22	Update to Table 1 in Position Statement.
03/15/22	Revision to guideline consisting of updating the position statement and other sections.
05/15/22	Update to Table 1 in Position Statement.
07/15/22	Update to Table 1 in Position Statement.
09/15/22	Update to Table 1 in Position Statement.
01/01/23	Review and revision to guideline consisting of updating the position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination.