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Subject: Sarilumab (Kevzara®) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

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 recommend a treat-to-target approach in therapy, regardless of disease activity. ACR guidelines categorize therapy for those with early RA (disease duration <6 months) or established RA (disease duration ≥6 months) as follows:

- In general, MTX is the preferred initial DMARD therapy for most patients with RA with active disease.

- For early RA patients, the ACR recommends the following:
    - Naïve to therapy: DMARDs, methotrexate (MTX) preferred, as initial, monotherapy therapy unless contraindicated. Other DMARD monotherapy options include sulfasalazine, hydroxychloroquine, and leflunomide.
    - Moderate or high disease activity despite DMARD monotherapy: treatment with combination DMARDs or a TNF-inhibitor (e.g., adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) or a non-TNF inhibitor (abatacept, rituximab, or tocilizumab [excludes anakinra]), with or without MTX.
    - Moderate or high disease activity despite the previous DMARD or biologic therapy: addition of low-dose glucocorticoid (≤10 mg/day of prednisone or equivalent) to bridge therapy until therapeutic effects of DMARD is reached. ACR also recommends short-term (<3 months) with lowest dose of glucocorticoids for flares.
- For established RA patients, the ACR recommends the following:
    - Low disease activity and is DMARD naïve: DMARD monotherapy, MTX preferred, is recommended over a TNF-inhibitor.
    - Moderate or high disease and is DMARD naïve: DMARD monotherapy, MTX preferred, is recommended over double or triple DMARD therapy and tofacitinib.
    - Moderate-high disease activity despite DMARD monotherapy: combination DMARD therapy OR the addition of TNF inhibitor, non-TNF biologic, or tofacitinib with or without MTX is recommended rather than continuing DMARD monotherapy. Combination biologic therapy and MTX is recommended over biologic monotherapy.
    - Moderate or high disease despite TNF-inhibitor and not on DMARD: addition of one or two DMARD, rather than TNF-inhibitor monotherapy

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.[26-28] 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.[27,28] 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 preferred and non-preferred, self-administered products for certain indications are as follows:

Table 1

Disease State	Step 1 (Preferred)	Step 2 (Non-preferred directed to ONE step 1 agent)	Step 3a (Non-preferred directed to TWO step 1 agents)	Step 3b (Non-preferred directed to TWO agents from step 1 and/or step 2)	Step 3c (Non-preferred directed to THREE step 1 agents)
Rheumatoid Disorders					
Ankylosing Spondylitis (AS)	SQ: Cosentyx, Enbrel, Humira	N/A	SQ: Cimzia, Simponi, Taltz	N/A	N/A
Nonradiographic Axial Spondyloarthritis (nr-axSpA)	SQ: Cimzia, Cosentyx	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, Stelara, Tremfya Oral: Otezla, 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, **Kevzara**, Kineret, Orencia, Simponi	N/A	N/A
Dermatological Disorders					
Hidradenitis Suppurativa (HS)	SQ: Humira	N/A	N/A	N/A	N/A
Psoriasis (PS)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	N/A	SQ: Cimzia, Ilumya, Siliq	N/A	SQ: Taltz
Inflammatory Bowel Disease					
Crohn's Disease	SQ: Humira, Stelara	SQ: Cimzia (Humira is required Step 1 agent)	N/A	N/A	N/A
Ulcerative Colitis	SQ: Humira, Stelara	SQ: Simponi Oral: Xeljanz, Xeljanz XR	N/A	N/A	N/A
Other					
Uveitis	SQ: Humira	N/A	N/A	N/A	N/A

Indications Without Preferred Agents Required					
Giant Cell Arteritis (GCA) Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Systemic Juvenile Idiopathic Arthritis (SJIA)	N/A	N/A	N/A	N/A	N/A

*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 or Otezla
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 that 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)	**BOTH** of the following: 1. **ONE** 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, AHFS, or NCCN compendium recommended use 1 or 2a 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) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Enbrel (etanercept) • Humira (adalimumab) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib) **OR** d. The prescriber has provided information indicating why **ALL** of the following are not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried agents for the requested indication: • Enbrel (etanercept) • Humira (adalimumab) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib)
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 or Otezla
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 that 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^3, platelet count less than 150,000/ mm^3, 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^3 – maintain current dosage
  - ANC 500 to 1,000/mm^3 - hold treatment until ANC greater than 1,000/mm^3. Resume at 150 mg every two weeks and increased to 200 mg every two weeks as clinically appropriate.
  - ANC less than 500/mm^3 - discontinue
- Low Platelet Count
  - 50,000–100,000/mm^3 – hold treatment until platelets greater than 100,000/mm^3. Resume at 150 mg every two weeks and increased to 200 mg every two weeks as clinically appropriate.
  - Less than 50,000/mm^3 – 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.
- I**mmunosuppression**: 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:

The following codes may be used to describe:

HCPCS Coding

J3590	Unclassified biologics

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) Tablets, 09-J1000-86

\OTHER:

Table 3:

DMARD Generic Name	DMARD Brand Name
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

Severity	Criteria
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 10/14/20.

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.