09-J0000-67

Original Effective Date: 06/15/07

Reviewed: 10/14/20

Revised: 01/01/21

Subject: Abatacept (Orencia®) Injection and Infusion

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:

Abatacept (Orencia), a modulator of T-lymphocyte activation, was first approved as an intravenous (IV) infusion by the US Food and Drug Administration (FDA) in December 2005 for adult rheumatoid arthritis (RA) and then in April 2008 for polyarticular juvenile idiopathic arthritis (JIA) in pediatric patients 6 years of age and older. In July 2011, a subcutaneous (SQ) injection was approved for the treatment of RA. In March 2017, the FDA-approved indication for the SQ injection was expanded to include the treatment of JIA in pediatric patients 2 years of age and older. Abatacept (as sponsored by the innovator drug company) has been granted orphan drug designation by the FDA for “treatment of idiopathic inflammatory myopathy (IMM)” in February 2017 and “treatment of giant cell arteritis” in February 2017.

Abatacept’s mechanism of action is distinct from the available non-biological disease-modifying anti-rheumatic drugs (DMARDs) and other biologics (e.g., tumor necrosis factor antagonists [TNFs], interleukin antagonists). Abatacept is a human protein designed to selectively inhibit T-cell activation, a process that plays a central role in the immunopathogenesis of RA. It exerts this mechanism of action by binding to the natural ligands CD80 and CD86, ultimately preventing CD80 and CD86 interaction with CD28 on the T-lymphocyte. Additionally, abatacept indirectly inhibits the production of inflammatory cytokines and auto-antibodies, which are also hypothesized to play a role in the pathogenesis of RA.

RHEUMATOID DISORDERS

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.

Polyarticular Juvenile Idiopathic Arthritis (PJIA)

Juvenile idiopathic arthritis (JIA) is arthritis that begins before the 16th birthday and persists for at least 6 weeks with other known conditions excluded. Polyarticular juvenile idiopathic arthritis (PJIA) is a subset of JIA. The ACR defines PJIA as arthritis in more than 4 joints during their disease course and excludes systemic JIA. Treatment goals are aimed at achieving clinically inactive disease and to prevent long-term morbidities, including growth disturbances, joint contractures and destruction, functional limitations, and blindness or visual impairment from chronic uveitis.

The ACR 2019 guidelines recommend the following treatment approach for PJIA:

- NSAIDs are conditionally recommended as adjunct therapy
- DMARD therapy:
    - Methotrexate (MTX) is conditionally recommended over leflunomide and sulfasalazine
    - Subcutaneous MTX is conditionally recommended over oral MTX
- Intraarticular glucocorticoids are conditionally recommended as adjunct therapy and conditionally recommended for bridging only in patients with moderate to high disease activity
- Strongly recommend against chronic low-dose glucocorticoid use, irrespective of disease activity and/or risk factors
- Strongly recommend combination use of a DMARD and infliximab
- Initial therapy for all patients:
    - DMARD is strongly recommended over NSAID monotherapy
    - MTX monotherapy is conditionally recommended over triple DMARD therapy
    - DMARD is conditionally recommended over a biologic
    - Initial biologic therapy may be considered for patients with risk factors and involvement of high-risk joints (e.g., cervical spine, wrist, hip), high disease activity, and/or those judged by their physician to be at high risk of disabling joint damage
- Subsequent therapy:
    - Low disease activity:
        - Escalating therapy (e.g., intraarticular glucocorticoid injections, optimization of DMARD dose, trial of MTX if not already done, and adding or changing biologic agent)
    - Moderate to high disease activity:
        - Add a biologic to original DMARD over changing to a second DMARD or changing to triple DMARD therapy
        - Switch to a non-TNF biologic if currently treated with first TNF ± DMARD over switching to another TNF (unless the patient had good initial response to first TNF)
        - TNF, abatacept, or tocilizumab (depending on prior biologics received) over rituximab after trial of second biologic

Systemic Juvenile Idiopathic Arthritis (SJIA)

Systemic juvenile idiopathic arthritis (SJIA) is a subset of JIA. The ACR defines SJIA as arthritis in ≥1 joint for at least 6 weeks' duration in a child less than 16 years of age with or preceded by a fever of at least 2 weeks' duration that is documented to be daily ("quotidian") for at least 3 days and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis. Goals of therapy for SJIA includes control of active inflammation and symptoms, and the prevention of a number of disease and/or treatment related morbidities, such as growth disturbances, joint damage, and functional limitations.

SJIA treatment depends on the presence of active systemic features and physician global assessment score (MD global) and active joint count (AJC):

- Active systemic features and varying degrees of synovitis:
  - Initial therapy: anakinra, glucocorticoids (oral or IV) monotherapy, or NSAID monotherapy
  - Continued disease activity despite initial therapy:
    - 1 month of anakinra: canakinumab, tocilizumab, MTX, leflunomide, or TNF inhibitor
    - 2 weeks of glucocorticoids (GC): anakinra, canakinumab, tocilizumab, MTX, or leflunomide
    - 1 month of NSAIDs: GC monotherapy, anakinra, canakinumab, or tocilizumab
- Without active systemic features and varying degrees of synovitis:
  - Initial therapy: MTX, leflunomide, NSAID monotherapy, or intra-articular GC
  - Continued disease activity despite initial therapy:
    - 3 months of MTX or leflunomide: abatacept, anakinra, TNF inhibitor, or tocilizumab
    - 1 month of NSAIDs: anakinra, MTX, or leflunomide
    - Following initial intra-articular GC joint injection: anakinra, MTX, or leflunomide
  - Continued disease activity despite second line therapy:
    - 1 month of anakinra: abatacept, MTX, leflunomide, TNF inhibitor, or tocilizumab
    - 3 months of MTX or leflunomide: abatacept, anakinra, TNF inhibitor, or tocilizumab

Psoriatic Arthritis (PsA)

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis, most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis, particularly spondyloarthritis and RA, and other management strategies of the cutaneous manifestations of psoriasis.

The American Academy of Dermatology (AAD) recommends initiating MTX in most patients with moderate to severe PsA. After 12 to 16 weeks of MTX therapy with appropriate dose escalation, the AAD recommends adding or switching to a TNF inhibitor if there is minimal improvement on MTX monotherapy.

The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and the following:

- Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient and health care provider to be due to PsA based on the presence of one of the following:

- Actively inflamed joints
- Dactylitis
- Enthesitis
- Axial disease
- Active skin and/or nail involvement
- Extraarticular manifestations such as uveitis or inflammatory bowel disease

- Disease severity includes level of disease activity at a given time point and the presence/absence of poor prognostic factors and long-term damage
- Severe PsA disease includes the presence of 1 or more of the following:
  - Erosive disease
  - Elevated markers of inflammation (ESR, CRP) attributable to PsA
  - Long-term damage that interferes with function (i.e., joint deformities)
  - Highly active disease that causes a major impairment in quality of life
  - Active PsA at many sites including dactylitis, enthesitis
  - Function limiting PsA at a few sites
  - Rapidly progressive disease
- Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, local glucocorticoid injections
- Treatment recommendations for active disease:
  - Treatment naïve patients first line options include oral small molecules (OSM), TNF biologics, IL-17 inhibitor, and IL-12/23 inhibitor
    - OSM (i.e., methotrexate [MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe psoriasis, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitor
    - Biologics (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe psoriasis
  - Previous treatment with OSM and continued active disease:
    - Switch to a different OSM (except apremilast) in patients without severe PsA or severe PS, contraindications to TNF biologics, prefers oral therapy OR add on apremilast to current OSM therapy
    - May add another OSM (except apremilast) to current OSM therapy for patients that have exhibited partial response to current OSM in patients without severe PsA or severe PS, contraindications to TNF biologics, or prefers oral therapy
    - Biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) monotherapy
  - Previous treatment with a biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) and continued active disease:
    - Switch to another biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) monotherapy or add MTX to the current TNF biologic

POSITION STATEMENT:

Site of Care: If intravenous abatacept (Orencia) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

Comparative Effectiveness

The Food and Drug Administration 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) of the subcutaneous formulation of abatacept in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary. This statement does not apply to the intravenous (IV) formulation of abatacept.

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	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

SUBCUTANEOUS ORENCIA (PHARMACY BENEFIT)

Initiation of subcutaneous abatacept (Orencia) 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 subcutaneous abatacept (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with subcutaneous abatacept (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. Subcutaneous abatacept 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 subcutaneous abatacept
            II. The prescriber has provided information in support of using subcutaneous abatacept for the member's age
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, 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 subcutaneous abatacept
4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the patient has begun therapy for latent TB
5. Member will **NOT** be using subcutaneous abatacept in combination with another biologic immunomodulator agent or Otezla
6. **ANY** of the following ("a", "b", or "c"):

a. The dosage does not exceed 125 mg once every week
   - QL: 50 mg/0.4 mL syringe - 4 syringes (1.6 mL)/28 days
   - QL: 87.5 mg/ 0.7 mL syringe - 4 syringes (2.8 mL)/28 days
   - QL: 125 mg/mL syringe - 4 syringes (4 mL)/28 days
   - QL: 125 mg/mL ClickJect autoinjector - 4 autoinjectors (4 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: 1. 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** 2. 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** 3. The member has an intolerance or hypersensitivity to **ONE** of the following conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** 4. 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** 5. 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)
Active psoriatic arthritis (PsA)	**BOTH** of the following: 1. **ONE** of the following:

	a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3 months **OR** b. The member has an intolerance or hypersensitivity to **ONE** of the conventional agents used in the treatment of PsA **OR** c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of PsA **OR** d. The member has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive) **OR** e. The member has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) **OR** f. The member's medication history indicates use of another biologic immunomodulator agent OR Otezla 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 PsA **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: • Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Otezla (apremilast) • Stelara (ustekinumab) • Tremfya (guselkumab) • 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:

	• Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Otezla (apremilast) • Stelara (ustekinumab) • Tremfya (guselkumab) • Xeljanz/Xeljanz XR (tofacitinib) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Otezla (apremilast) • Stelara (ustekinumab) • Tremfya (guselkumab) • 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: • Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Otezla (apremilast) • Stelara (ustekinumab) • Tremfya (guselkumab) • Xeljanz/Xeljanz XR (tofacitinib)
Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)	**BOTH** of the following: 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least 3 months **OR** b. The member has an intolerance or hypersensitivity to **ONE** of the

	conventional agents used in the treatment of PJIA **OR** c. The member has an labeled contraindication to **ALL** of the conventional agents used in the treatment of PJIA **OR** d. 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 PJIA 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: • Actemra (tocilizumab) • Enbrel (etanercept) • Humira (adalimumab) **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: • Actemra (tocilizumab) • Enbrel (etanercept) • Humira (adalimumab) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Actemra (tocilizumab) • Enbrel (etanercept) • Humira (adalimumab) **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: • Actemra (tocilizumab) • Enbrel (etanercept) • Humira (adalimumab)
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 subcutaneous abatacept (Orencia) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for subcutaneous abatacept has been previously approved by Florida Blue
2. Member has had clinical benefit with subcutaneous abatacept therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, 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 subcutaneous abatacept
5. Member will **NOT** be using subcutaneous abatacept in combination with another biologic immunomodulator agent or Otezla
6. **ANY** of the following ("a", "b", or "c"):
    a. The dosage does not exceed 125 mg once every week
        - QL: 50 mg/0.4 mL syringe - 4 syringes (1.6 mL)/28 days
        - QL: 87.5 mg/ 0.7 mL syringe - 4 syringes (2.8 mL)/28 days
        - QL: 125 mg/mL syringe - 4 syringes (4 mL)/28 days
        - QL: 125 mg/mL ClickJect autoinjector - 4 autoinjectors (4 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

INTRAVENOUS ORENCIA (MEDICAL BENEFIT)

Initiation of intravenous (IV) abatacept (Orencia) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "5"):

1. Intravenous abatacept is administered for an indication listed in **Table 3,** and **ALL** indication-specific and maximum-allowable dose criteria are met
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, 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 IV abatacept
4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the patient has begun therapy for latent TB

5. Member will **NOT** be using IV abatacept in combination with another biologic immunomodulator agent or Otezla

Approval duration: 6 months

Table 3

Indications and Specific Criteria		
Indication	**Specific Criteria**	**Maximum Allowable Dose***
Active psoriatic arthritis (PsA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3 months **OR** 2. The member has an intolerance or hypersensitivity to **ONE** of the conventional agents used in the treatment of PsA **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of PsA **OR** 4. The member has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive) **OR** 5. The member has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) **OR** 6. The member's medication history indicates use of another biologic	Initial: o >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o 60 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o <60 kg: 500 mg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: o >100 kg: 1,000 mg every 4 weeks starting at week 8 o 60 to 100 kg: 750 mg every 4 weeks starting at week 8 o <60 kg: 500 mg every 4 weeks starting at week

	immunomodulator agent **OR** Otezla 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 PsA	
Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least 3 months **OR** 2. The member has an intolerance or hypersensitivity to **ONE** of the conventional agents used in the treatment of PJIA **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of PJIA **OR** 4. 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 PJIA	Initial dose: o >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o 75 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o <75 kg: 10 mg/kg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: o >100 kg: 1,000 mg every 4 weeks starting at week 8 o 75 to 100 kg: 750 mg every 4 weeks starting at week 8 o <75 kg: 10 mg/kg every 4 weeks starting at
Moderately to severely active rheumatoid arthritis (RA)	**ONE** of the following: 1. 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** 2. 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** 3. The member has an intolerance or	Initial: o >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o 60 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o <60 kg: 500 mg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: o >100 kg: 1,000 mg every 4

	hypersensitivity to **ONE** of the following conventional agents (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** 4. 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** 5. 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	weeks starting at week 8 o 60 to 100 kg: 750 mg every 4 weeks starting at week 8 o <60 kg: 500 mg every 4 weeks starting at week 8
Chronic graft-versus-host disease (GVHD)	**ALL** of the following: 1. The member has previously received an allogeneic HSCT **AND** 2. Abatacept will be used as additional therapy in conjunction with systemic corticosteroids **AND** 3. The member has steroid-refractory disease	Initial: o >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o 60 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) o <60 kg: 500 mg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: o >100 kg: 1,000 mg every 4 weeks starting at week 8 o 60 to 100 kg: 750 mg every 4 weeks starting at week 8 o <60 kg: 500 mg every 4 weeks starting at week 8
Immune checkpoint inhibitor-related adverse effects	**ALL** of the following: 1. Member has been receiving treatment with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab,	o >100 kg: 1,000 mg X 1 dose; may repeat one additional dose if the member does not have adequate improvement in symptoms.

	pembrolizumab, atezolizumab, avelumab, durvalumab) **AND** 2. The member severe or life-threatening myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities (Grade 3 or 4) **AND** 3. Member has had an inadequate response to, intolerable adverse effects with, or a contraindication to an adequate trial of systemic corticosteroid treatment **AND** 4. The members immune checkpoint inhibitor therapy will be either permanently discontinued or held during treatment with abatacept	○ 60 to 100 kg: 750 mg X 1 dose; may repeat one additional dose if the member does not have adequate improvement in symptoms. ○ <60 kg: 500 mg X 1 dose; may repeat one additional dose if the member does not have adequate improvement in symptoms.
Orphan Indications		
Giant cell arteritis (GCA)	**ONE** of the following: 1. The member has tried and had an inadequate response to systemic corticosteroids (e.g., prednisone, methylprednisolone) used in the treatment of GCA for at least 7 to 10 days **OR** 2. The member has an intolerance or hypersensitivity to systemic corticosteroids used in the treatment of GCA **OR** 3. The member has an FDA labeled contraindication to **ALL** systemic corticosteroids **OR** 4. 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	Initial: ○ >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) ○ 60 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) ○ <60 kg: 500 mg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: ○ >100 kg: 1,000 mg every 4 weeks starting at week 8 ○ 60 to 100 kg: 750 mg every 4 weeks starting at week 8 ○ <60 kg: 500 mg every 4 weeks starting at week 8

	for the treatment of GCA	
Idiopathic inflammatory myopathy (IMM) [includes dermatomyositis (DM) and polymyositis (PM)]	**BOTH** of the following: 1. The members diagnosis has been confirmed by muscle biopsy **AND** 2. The member disease is refractory to at least 3 months of continuous combination treatment with a corticosteroid and an immunosuppressant (either azathioprine or methotrexate), **OR** the member has intolerable adverse effects with or a contraindication to either treatment	Initial: ○ >100 kg: 1,000 mg every 2 weeks for 3 total doses (week 0, 2, and 4) ○ 60 to 100 kg: 750 mg every 2 weeks for 3 total doses (week 0, 2, and 4) ○ <60 kg: 500 mg every 2 weeks for 3 total doses (week 0, 2, and 4) Maintenance: ○ >100 kg: 1,000 mg every 4 weeks starting at week 8 ○ 60 to 100 kg: 750 mg every 4 weeks starting at week 8 ○ <60 kg: 500 mg every 4 weeks starting at week 8
Prevention of Graft versus Host Disease (GVHD)	**BOTH** of the following 1. Member will receive an allogeneic HSCT the day following the first dose **AND** 2. The use of conventional treatment with methotrexate and a calcineurin inhibitor needs to be avoided	Not to exceed the FDA-approved maximum dosage
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	Maximum dose supported by the FDA labeled indication or maximum dose supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a
*The maximum allowable dose can be exceeded if (1) the dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication, OR (2) 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)		

Continuation of **intravenous (IV)** abatacept **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for IV abatacept has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition in **Table 3** [except prevention of GVHD - see initiation criteria], **OR** the member previously met **ALL** indication-specific initiation criteria
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, 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 IV abatacept
4. Member has had clinical benefit with IV abatacept therapy
5. Member will **NOT** be using IV abatacept in combination with another biologic immunomodulator agent or Otezla
6. **EITHER** of the following ("a" or "b"):
    a. The member's dosage does not exceed the following based on their weight and indication for use:
        - Rheumatoid arthritis, psoriatic arthritis, GCA, chronic CVHD,and IMM
            - >100 kg: 1,000 mg every 4 weeks
            - 60 to 100 kg: 750 mg every 4 weeks
            - <60 kg: 500 mg every 4 weeks
        - JIA
            - >100 kg: 1,000 mg every 4 weeks
            - 75 to 100 kg: 750 mg every 4 weeks
            - <75 kg: 10 mg/kg every 4 weeks
    b. The dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication, **OR** 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:

Abatacept is indicated for treatment of the following indications

- For reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis in adults, as monotherapy or concomitantly with disease-modifying anti-rheumatic drugs (DMARDs) other than tumor-necrosis factor (TNF) antagonists
- For reducing signs and symptoms in patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis, as monotherapy or in combination with methotrexate

- For the treatment of adult patients with active psoriatic arthritis (PsA)

ADULT RHEUMATOID ARTHRITIS

Abatacept is administered as an intravenous (IV) or subcutaneous (SQ) injection.

- IV infusions should be administered as a 30-minute infusion utilizing weight range-based dosing specified in Table 4. Following the initial IV administration, an IV infusion should be administered at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.

Table 4

Table 2: Abatacept IV dose in adult RA persons		
Body weight	**Dose**	**Number of vials**
Less than 60 kg	500 mg	2
60 to 100 kg	750 mg	3
More than 100 kg	1,000 mg	4
Each vial provides 250 mg of abatacept for administration		

- Following a single IV loading dose (as per body weight categories listed in Table 1), the first 125 mg SQ injection of abatacept should be given within a day, followed by 125 mg SQ injections once weekly.
    - Persons unable to receive an infusion may initiate weekly injections of SQ abatacept without an IV loading dose
    - Persons transitioning from abatacept IV therapy to SQ administration should administer the first SQ dose instead of the next scheduled IV dose.

JUVENILE IDIOPATHIC ARTHRITIS

- The recommended intravenous dosage for persons aged 6 to 17 years of age:
    - Less than 75 kg: 10 mg/kg IV on week 0, 2, 4, and every 4 weeks thereafter
    - Greater than 75 kg: use adult IV dosing regimen, not to exceed a maximum dose of 1,000 mg
    - Intravenous dosing has not been studied in patients younger than 6 years of age
- The recommended subcutaneous dosage for persons aged 2 to 17 years of age:
    - 10 to less than 25 kg: 50 kg once weekly
    - 25 to less than 50 kg: 87.5 mg once weekly
    - 50 kg or more: 125 mg once weekly

ADULT PSORIATIC ARTHRITIS

Abatacept is administered as an intravenous (IV) or subcutaneous (SQ) injection with or without non-biological DMARDs.

- IV infusions should be administered as a 30-minute infusion utilizing weight range-based dosing specified in Table 2. Following the initial IV administration, an IV infusion should be administered at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.

- The SQ injections administered once weekly without the need for an IV loading dose. Persons transitioning from abatacept IV therapy to SQ administration should administer the first SQ dose instead of the next scheduled IV dose.

Drug Availability:

- Intravenous infusion:
  - 250 mg lyophilized powder in a single use vial
- Subcutaneous injection:
  - 50 mg/0.4 mL, 87.5 mg/0.7 mL, and 125 mg/mL single-dose prefilled glass syringes
  - 125 mg/mL solution in a single-dose prefilled autoinjector (ClickJect)

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Warnings:

- **Concomitant Use with TNF Antagonists:** concomitant use with a TNF antagonist can increase the risk of infections and serious infections.
- **Hypersensitivity:** hypersensitivity, anaphylaxis, and anaphylactoid reactions have occurred following abatacept administration.
- **Infections:** persons with a history of recurrent infections or underlying conditions predisposing to infections may experience more infections; discontinue if a serious infection occurs.
- **Tuberculosis:** screen for latent TB infection prior to initiating therapy. Members testing positive should be treated prior to initiating abatacept.
- **Immunizations:** live vaccines should not be given concurrently or within three months of discontinuation. Members with juvenile idiopathic arthritis should be brought up to date with all immunizations prior to abatacept therapy. Abatacept may blunt the effectiveness of some immunizations based on its mechanism of action.
- **Chronic Obstructive Pulmonary Disease (COPD):** Persons with COPD may develop more frequent respiratory events.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J0129	Injection, abatacept, 10mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

D89.810 – D89.813	Graft-versus-host disease

I30.8	Other forms of acute pericarditis [for immune checkpoint inhibitor-related adverse effects ONLY]
I30.9	Acute pericarditis, unspecified [for immune checkpoint inhibitor-related adverse effects ONLY]
I40.8	Other acute myocarditis [for immune checkpoint inhibitor-related adverse effects ONLY]
I40.9	Acute myocarditis, unspecified [for immune checkpoint inhibitor-related adverse effects ONLY]
I44.0 - I44.39	Atrioventricular and left bundle-branch block [for immune checkpoint inhibitor-related adverse effects ONLY]
I45.0 – I45.9	Other conduction disorders [for immune checkpoint inhibitor-related adverse effects ONLY]
I47.0	Re-entry ventricular arrhythmia [for immune checkpoint inhibitor-related adverse effects ONLY]
I49.9	Cardiac arrhythmia, unspecified [for immune checkpoint inhibitor-related adverse effects ONLY]
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.59	Other psoriatic arthropathy
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
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.89	Other juvenile arthritis, multiple sites
M31.5	Giant cell arteritis with polymyalgia rheumatica
M31.6	Other giant cell arteritis
M33.00 – M33.09	Juvenile dermatopolymyositis
M33.10 – M33.19	Other dermatopolymyositis
M33.20 – M33.29	Polymyositis
M33.90 – M33.99	Dermatopolymyositis, 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 Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date. LCD Abatacept (L33257) was retired effective 12/15/2018. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

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

DEFINITIONS:

DMARD: 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).

Psoriatic arthritis (PsA): joint inflammation that occurs in about 5% to 10% of people with psoriasis (a common skin disorder). It is a severe form of arthritis accompanied by inflammation, psoriasis of the skin or nails, and a negative test for rheumatoid factor. Enthesitis refers to inflammation of entheses, the site where ligaments or tendons insert into the bones. It is a distinctive feature of PsA and does not occur with other forms of arthritis. Common locations for enthesitis include the bottoms of the feet, the Achilles' tendons, and the places where ligaments attach to the ribs, spine, and pelvis.

Rheumatoid arthritis: An inflammatory disease of the synovium, or lining of the joint that results in pain stiffness, and swelling of multiple joints. The inflammation may extend to other joints and cause bone and cartilage erosion, joint deformities, movement problems, and activity limitations.

RELATED GUIDELINES:

Adalimumab (Humira), 09-J0000-46

Anakinra (Kineret), 09-J0000-45

Apremilast (Otezla) Tablet, 09-J2000-19

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

Ixekizumab (Taltz), 09-J2000-62

Rituximab (Rituxan), 09-J0000-59

Sarilumab (Kevzara), 09-J2000-87

Tocilizumab (Actemra) Injection, 09-J1000-21

Tofacitinib (Xeljanz, Xeljanz XR) Tablets, 09-J1000-86

OTHER:

Table 5: Conventional Synthetic DMARDs

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

Table 6: 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

REFERENCES:

1. Bansback N, Phibbs CS, Sun H, et al; CSP 551 RACAT Investigators. Triple Therapy Versus Biologic Therapy for Active Rheumatoid Arthritis: A Cost-Effectiveness Analysis. Ann Intern Med. 2017 Jul 4;167(1):8-16.
2. Beukelman T, Atkar NM, Saag KG, et al. 2011 American College of Rheumatology Recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res 2011;63(4):465-82.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: www.clinicalpharmacilogy-ip.com. Accessed 9/29/20.
4. Coates LC, Kavanaugh A, Mease PJ et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis: Treatment Recommendations for Psoriatic Arthritis 2015. Arthritis Rheumatol 2016;68:1060–71
5. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. [cited 2020 Sep 29]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/.
6. Genant HK, Peterfy CG, Westhovens R, Becker JC, Aranda R, Vratsanos G, Teng J, Kremer JM. Abatacept inhibits structural damage progression in rheumatoid arthritis: results from the long-term extension of the AIM trial. Ann Rheum Dis. 2007 Dec 17.
7. Genovese MC, Schiff M, Luggen M, et al. Longterm safety and efficacy of abatacept through 5 years of treatment in patients with rheumatoid arthritis and an inadequate response to tumor necrosis factor inhibitor therapy. J Rheumatol. 2012 Aug;39(8):1546-54.
8. Graudal N, Hubeck-Graudal T, Tarp S, et al. Effect of combination therapy on joint destruction in rheumatoid arthritis: a network meta-analysis of randomized controlled trials. PLoS One. 2014 Sep 22;9(9):e106408.
9. Hellmich B, Agueda A, Monti S, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2019 Jul 3. pii: annrheumdis-2019-215672. [Epub ahead of print]
10. Karlsson JA, Neovius M, Nilsson JA, et al. Addition of infliximab compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in early rheumatoid arthritis: 2-year quality-of-life results of the randomised, controlled, SWEFOT trial. Ann Rheum Dis. 2013 Dec;72(12):1927-33.
11. Krause ML, Amin A, and Makol A. Use of DMARDs and biologics during pregnancy and lactation in rheumatoid arthritis: what the rheumatologist needs to know. Ther Adv Musculoskelet Dis. 2014 Oct; 6(5): 169–184.
12. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 9/29/20.
13. Menter A, Strober BE, Kaplan DH et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019 Apr;80(4):1029-1072. Epub 2019 Feb 13.
14. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 9/29/20.
15. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2020. Hematopoietic Cell Transplantation (HCT): Pre-Transplant Recipient Evaluation and Management of Graft-Versus-Host Disease. Available at https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed 9/29/20.
16. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2020. Management of Immunotherapy-Related-Toxicities. Available at https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed 9/29/20.

17. Orencia (abatacept) [package insert]. Bristol-Myers Squibb Co. Princeton (NJ): June 2020.
18. Peper SM, Lew R, Mikuls T, et al. Rheumatoid Arthritis Treatment After Methotrexate: The Durability of Triple Therapy Versus Etanercept. Arthritis Care Res (Hoboken). 2017 Oct;69(10):1467-1472.
19. Rahimi R, Nikfar S, Rezaie A, et al. Pregnancy outcome in women with inflammatory bowel disease following exposure to 5-aminosalicylic acid drugs: a meta-analysis. Reprod. Toxicol;2008:25,271–275.
20. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Rheumatol. 2019 Jun;71(6):846-863. Epub 2019 Apr 25.
21. Salliot C, Dougados M, Gossec L. Risk of serious infections during rituximab, abatacept and anakinra therapies for rheumatoid arthritis: meta-analyses of randomized placebo-controlled trials. Ann Rheum Dis. 2008 Jan 18.
22. Scott DL, Ibrahim F, Farewell V, et al. Tumour necrosis factor inhibitors versus combination intensive therapy with conventional disease modifying anti-rheumatic drugs in established rheumatoid arthritis: TACIT non-inferiority randomised controlled trial. BMJ. 2015 Mar 13;350:h1046.
23. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan;71(1):5-32. Epub 2018 Nov 30.
24. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2016 Jan;68(1):1-25.
25. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977.
26. Tynjälä P, Vähäsalo P, Tarkiainen M, et al. Aggressive combination drug therapy in very early polyarticular juvenile idiopathic arthritis (ACUTE-JIA): a multicentre randomised open-label clinical trial. Ann Rheum Dis. 2011 Sep;70(9):1605-12.
27. van Vollenhoven RF, Geborek P, Forslind K, et al. Conventional combination treatment versus biological treatment in methotrexate-refractory early rheumatoid arthritis: 2 year follow-up of the randomised, non-blinded, parallel-group Swefot trial. Lancet. 2012 May 5;379(9827):1712-20.
28. Vera-Llonch M, Massarotti E, Wolfe F, et al. Cost-effectiveness of abatacept in patients with moderately to severely active rheumatoid arthritis and inadequate response to methotrexate. Rheumatology (Oxford). 2008 Apr; 47(4): 535-41.
29. Weinblatt ME, Schiff M, Valente R, et al. Head-to-head comparison of subcutaneous abatacept versus adalimumab for rheumatoid arthritis: findings of a phase IIIb, multinational, prospective, randomized study. Arthritis Rheum. 2013 Jan;65(1):28-38.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Coverage Committee on 10/14/20.

GUIDELINE UPDATE INFORMATION:

06/15/07	New Medical Coverage Guideline.
10/15/07	Revision; consisting of updating ICD-9 coding.
05/15/08	Review and revision; consisting of adding new JIA indication, updating dosage and administration section, updating references and updating ICD-9 file.

09/15/09	Review and revision; consisting of updating references and updating precautions.
04/15/10	Revision; consisting of adding specific continuation criteria.
08/15/10	Review and revision; consisting of updating references, description and precautions.
02/15/11	Revision; consisting of formatting changes and ICD-10 codes.
08/15/11	Review and revision to guideline; consisting of updating coding and references.
11/15/11	Revision to guideline; consisting of adding new dosage formulation and maximum dose.
08/15/12	Review and revision to guideline; consisting of updating position statement, precautions, exceptions and references.
09/15/12	Revision to guideline; consisting of modifying continuation criteria.
04/15/13	Revision to guideline; consisting of revising and reformatting position statement; revising and reformatting description, dosage/administration, and precautions sections; updating references and related guidelines.
09/15/13	Review and revision to guideline; consisting of updating quantity limit, adding Orphan drug indications, program exceptions, and updating references.
01/01/14	Revision to guideline; consisting of updating preferred language.
04/15/14	Revision to guideline; consisting of revising position statement.
09/15/14	Review and revision to guideline; consisting of updating position statement, references, coding, and related guidelines.
09/15/15	Review and revision to guideline; consisting of updating description section, position statement, billing/coding, and references.
10/01/15	Revision consisting of update to Program Exceptions section.
12/15/15	Revision consisting of ICD-10 coding updates.
09/15/16	Review and revision to guideline consisting of updating description section, position statement, billing/coding, and references.
06/15/17	Revision to guideline consisting of updating description section, position statement, dosage/administration section, and references based on expanded FDA-approval of JIA indication to age 2 years of age and older and new SQ dosage recommendations for JIA.
10/15/17	Review and revision to guideline consisting of updating description, position statement, dosage/administration, coding/billing, definitions, related guidelines, and references.
01/01/18	Revision to guideline consisting of updating the preferred self-administered biologic products according to indication for use. Secukinumab is now a preferred product for psoriatic arthritis, and use of three preferred products is required. 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, billing/coding, related guidelines, and references.
10/15/19	Review and revision to guideline consisting of updating the position statement, related guidelines, program exceptions, and references.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
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, other, and definitions.
01/01/21	Review and revision to guideline consisting of updating the position statement, billing/coding, and references.