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# Subject: Certolizumab Pegol (Cimzia®) Injection

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## DESCRIPTION:

Certolizumab pegol (Cimzia) is one of five commercially available tumor necrosis factor (TNF) alpha inhibitors available, not counting biosimilars as separate products, in the United States. It was FDA approved for Crohn's disease in April 2008, for rheumatoid arthritis (RA) in May 2009, for psoriatic arthritis (PsA) in September 2013, for ankylosing spondylitis (AS) in October 2013, for plaque psoriasis in May 2018, for non-radiographic axial spondyloarthritis (nr-AxSp) in March 2019, and for polyarticular juvenile idiopathic arthritis (PJIA) in September 2024. Tumor necrosis factor, a proinflammatory cytokine, initiates the body's defense response to local injury by stimulating the production of inflammatory mediators and signaling immune cells. TNF may augment host defense mechanisms when in low concentration, but large amounts of TNF can lead to excessive inflammation and tissue deterioration. In rheumatoid arthritis, activated T-cells migrate into the synovial lining of the joint where TNF is released and joint destruction begins. The intestinal mucosa from patients with Crohn's disease or ulcerative colitis has been associated with high levels of TNF as compared to healthy individuals; a similar elevation in TNF has been demonstrated in patients with psoriasis. The National Comprehensive Cancer Network (NCCN) guidelines on the Management of Immunotherapy-Related-Toxicities now include all TNF alpha inhibitors as options to be considered for the management of moderate or severe immunotherapy-related inflammatory arthritis if no improvement after holding immunotherapy and treating with oral corticosteroids, or if unable to taper corticosteroids, or no response to conventional synthetic (cs)DMARDs.

**RHEUMATOID DISORDERS**

**Ankylosing spondylitis (AS)**

Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis, enthesitis, and a marked propensity for sacroiliac joint and spinal fusion. AS is distinguished by universal involvement with sacroiliac joint inflammation or fusion and more prevalent spinal ankylosis. Goals of treatment for AS are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstays of treatment have been NSAIDs and exercise, with the additional use of DMARDs in patients with peripheral arthritis. The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommend the following pharmacological treatment for AS:

- Stable AS: First line therapy with on demand NSAIDs; there is also a conditional recommendation for continuation of TNF inhibitor as monotherapy
- Active AS:
    - First line therapy with continuous NSAIDs and physical therapy
    - TNF inhibitor recommended for patients with active AS despite an adequate trial with NSAIDs
        - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
    - Recommendations for nonresponse to TNF therapy (all conditional):
        - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
        - Secondary nonresponse: switch to another TNF over a non-TNF biologic
        - Recommend against addition of sulfasalazine or MTX
        - Recommend against switching to a biosimilar of the failed TNF
    - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
    - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
    - DMARDs (i.e., methotrexate [MTX], sulfasalazine) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
    - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
    - If patient has concomitant inflammatory bowel disease (IBD) or recurrent uveitis, TNF-inhibitors are recommended over other biologics
    - Glucocorticoids are not recommended

**Polyarticular Juvenile Idiopathic Arthritis (PJIA)**

Juvenile idiopathic arthritis (JIA) is arthritis that begins before the 16$^{th}$ 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

**Nonradiographic Axial Spondyloarthritis (nr-axSpA)**

Nonradiographic axial spondyloarthritis (nr-axSpA) falls under the same spondyloarthritis family as ankylosing spondylitis (AS). Nr-axSpA includes patients with chronic back pain and features suggestive of spondyloarthritis (SpA), but do not meet the classification of AS. The goals of treatment are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstay of treatment has been NSAIDs and exercise, with the additional use of DMARDs in patients with peripheral arthritis. The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommendation for nr-axSpA are the same as AS:

- Stable SpA: conditional recommendation for on-demand treatment with NSAIDs
- Active SpA:
    - First line therapy with continuous NSAIDs and physical therapy
    - TNF inhibitor conditionally recommended for patients with active SpA despite an adequate trial with NSAIDs
        - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
    - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
    - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
    - Recommendations for nonresponse to TNF therapy (all conditional):
        - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
        - Secondary nonresponse: switch to another TNF over a non-TNF biologic
        - Recommend against addition of sulfasalazine or MTX
        - Recommend against switching to a biosimilar of the failed TNF
    - DMARDs (i.e., methotrexate, sulfasalazine, leflunomide, pamidronate, thalidomide, apremilast) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
    - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
    - If patient has concomitant inflammatory bowel disease or recurrent uveitis, TNF-inhibitors are recommended over other biologics
    - Glucocorticoids are not recommended

**Rheumatoid arthritis (RA)**

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

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

- RA requires early evaluation, diagnosis, and management
- Treatment decisions should follow a shared decision-making process
- Treatment decisions should be reevaluated within a minimum of 3 months based on efficacy and tolerability of the DMARD(s) chosen

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

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

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

Early use of DMARD, particularly MTX, is recommended as soon as possible following diagnosis of RA. Dosing of MTX for RA is once weekly dosing with starting doses at 7.5 mg or 15 mg once weekly. MTX dose is increased as tolerated and as needed to control symptoms and signs of RA disease. The usual

target dose is at least 15 mg weekly and the usual maximum dose is 25 mg weekly. ACR defines optimal dosing for RA treatments as 1) dosing to achieve a therapeutic target derived from mutual patient-clinician consideration of patient priorities and 2) given for at least 3 months before therapy escalation or switching. For patients who are unable to take MTX, hydroxychloroquine, sulfasalazine, or leflunomide are other DMARD options. In patients resistant to initial MTX treatment, combination DMARD (e.g., MTX plus sulfasalazine or hydroxychloroquine or a TNF-inhibitor) is recommended.

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

**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

**DERMATOLOGICAL DISORDERS**

**Psoriasis (PS)**

Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful.

Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life.

The American Academy of Family Physicians (AAFP) categorizes psoriasis severity into mild to moderate (less than 5% of body surface area [BSA]) and moderate to severe (5% or more of BSA). The AAFP psoriasis treatment guidelines recommend basing treatment on disease severity:

- Mild to moderate (less than 5% of BSA and sparing the genitals, hands, feet, and face):
  - Candidate for intermittent therapy: topical corticosteroids, vitamin D analogs (calcipotriene and calcitriol), or tazarotene (Tazorac)
  - Candidate for continuous therapy: calcineurin inhibitors (tacrolimus and pimecrolimus)
- Severe (5% or more of BSA or involving the genitals, hands, feet, and face):
  - Less than 20% of BSA affected: vitamin D analogs (calcipotriene and calcitriol) with or without phototherapy. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids
  - 20% or more of BSA affected: systemic therapy with MTX, cyclosporine, acitretin, or biologics. Biologics are recommended for those with concomitant PsA
- Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin

The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as limited or mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (greater than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when it occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus. The AAD psoriasis treatment guidelines recommend the following:

- Mild to moderate disease (less than 5% of BSA):
  - Topical corticosteroids (strength of recommendation A)
  - Off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis (strength of recommendation B)
  - Long-term use (up to 52 weeks) of topical vitamin D analogs including calcipotriene, calcitriol, tacalcitol, and maxacalcitol (strength of recommendation A)
  - Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel for the treatment of mild to moderate scalp psoriasis (strength of recommendation A)
  - Use of tacalcitol ointment or calcipotriene combined with hydrocortisone for facial psoriasis (strength of recommendation B)
  - Vitamin D analogs in combination with topical corticosteroids (strength of recommendation A)
  - Topical tazarotene alone or in combination with narrowband ultraviolet B (NB-UVB) (strength of recommendation B), or topical corticosteroids (strength of recommendation A)
  - Topical salicylic acid alone or in combination with topical corticosteroids (strength of recommendation B)
  - Coal tar preparations (strength of evidence A)

- Moderate to severe disease without PsA (5% or more of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life):
    - Methotrexate (adults) (strength of evidence A)
    - Methotrexate is less effective than TNF-inhibitors (strength of evidence B)
    - Combination therapy with methotrexate and NB-UVB (adult patients) (strength of evidence B)
    - Cyclosporine for patients with severe, recalcitrant (strength of recommendation A), erythrodermic, generalized pustular, and/or palmoplantar psoriasis (strength of recommendation B)
    - Acitretin as monotherapy or in combination with psoralen plus ultraviolet light (PUVA) or broad band ultraviolet light (BB-UVA [strength of evidence B])
    - If UV-therapy is unavailable, first line therapies include MTX, cyclosporine, acitretin, and biologics
    - Apremilast (strength of recommendation A)
    - TNF-α inhibiters monotherapy (strength of evidence A) or in combination with topical corticosteroids with or without a vitamin D analogue (strength of evidence B) or in combination with acitretin (strength of evidence C)
    - TNF-α inhibitors should be considered as a preferred treatment option for patients with concomitant PsA
    - Infliximab (strength of evidence A)
    - IL-12/IL-23 Inhibitors monotherapy (strength of evidence A) or in combination with topical corticosteroids with or without a vitamin D analogue (strength of evidence C) or in combination with acitretin or methotrexate (strength of evidence B)
    - IL-12/IL-23 inhibitors in combination with apremilast or cyclosporine (strength of evidence C)
    - IL-17 inhibitors monotherapy (strength of evidence A)
    - IL-23 inhibitors monotherapy for moderate to severe plaque psoriasis or as monotherapy for generalized pustular psoriasis (strength of evidence B)

*Strength of recommendation and descriptions

| Strength of recommendation | Description |
|---|---|
| A | Recommendation based on consistent and good-quality patient-oriented evidence |
| B | Recommendation based on inconsistent or limited-quantity patient-oriented evidence |
| C | Recommendation based on consensus, opinion, case studies, or disease-oriented evidence |

Biologics are routinely used when one or more traditional systemic agents fail to produce adequate response, but are considered first line in patients with moderate to severe psoriasis with concomitant severe PsA. Primary failure is defined as initial nonresponse to treatment. Primary failure to a TNF-α inhibitor does not preclude successful response to a different TNF-α inhibitor. Failure of another biologic therapy does not preclude successful response to ustekinumab.

The National Psoriasis Foundation (NPF) medical board recommend a treat-to-target approach to therapy for psoriasis that include the following:

- The preferred assessment instrument for determining disease severity is BSA
- Target response after treatment initiation should be BSA ≤1% after 3 months
- Acceptable response is either a BSA ≤3% or a BSA improvement ≥75% from baseline at 3 months after treatment initiation

**INFLAMMATORY BOWEL DISEASE**

**Crohn's Disease (CD)**

Crohn's Disease (CD) is an inflammatory condition that can affect any portion of the gastrointestinal tract from the mouth to the perianal area. Choice of therapy is dependent on the anatomic location of disease, the severity of disease, and whether the treatment goal is to induce remission or maintain remission. The American Gastroenterological Association (AGA) 2021 guideline recommends the following:

- Biologic therapy:
    - The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids
    - Anti-TNF (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission
    - Vedolizumab is suggested over no treatment for the induction and maintenance of remission
    - AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission
    - Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission
    - Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission
    - Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first line drug, there is indirect evidence to suggest using infliximab as a second-line agent)
- DMARD therapy:
    - Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
    - Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission
    - Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission

- The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission
- The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission
- The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission

- Combination therapy:
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of infliximab in combination with thiopurines over infliximab monotherapy for the induction and maintenance of remission (combination infliximab with methotrexate may be more effective over infliximab monotherapy)
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of adalimumab in combination with thiopurines over adalimumab monotherapy for the induction and maintenance of remission (combination adalimumab with methotrexate may be more effective over adalimumab monotherapy)
  - No recommendations are being made regarding the use of ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic monotherapy for induction or maintenance or remission

The 2018 American College of Gastroenterology (ACG) guidelines recommend the following:

- Mild to moderately severe disease/low risk disease:
  - Sulfasalazine (in doses of 3-6 grams daily) is effective in colonic and/or ileocolonic CD, but not those with isolated small bowel disease
  - 5-aminosalicylic (ASA) suppositories and enema preparations are effective for induction and maintenance of remission in rectal and sigmoid disease
  - Conventional corticosteroids are primarily used for the treatment of flares, and are often used as a bridge until immunomodulators and/or biologic agents become effective
  - Controlled ileal release budesonide is effective for induction of remission in ileocecal disease
- Moderate to severe disease/moderate to high risk disease
  - Corticosteroids are effective for short-term use in alleviating signs and symptoms of moderate to severely active CD, but do not induce mucosal healing and should be used sparingly
  - Azathioprine, 6-mercaptopurine, or MTX (15 mg once weekly) may be used in treatment of active disease and as adjunctive therapy for reducing immunogenicity against biologic therapy
  - TNF inhibitors should be used to treat CD that is resistant to treatment with corticosteroids and that is refractory to thiopurines or MTX
  - Vedolizumab with or without an immunomodulator should be considered for induction of symptomatic remission for patients with moderate to severely active CD and objective evidence of active disease

- Ustekinumab should be used in patients that have failed previous treatment with corticosteroids, thiopurines, MTX, or TNF inhibitors, or in patients with no prior TNF inhibitor exposure

- Severe/fulminant disease:
  - IV corticosteroids should be used
  - TNF inhibitors can be considered
- Maintenance therapy:
  - Thiopurines or methotrexate should be considered once remission is induced with corticosteroids
  - TNF inhibitors, specifically infliximab, adalimumab, and certolizumab pegol, should be used in combination with azathioprine, MTX, or 6-mercaptopurine to maintain remission of TNF induced remission
  - Vedolizumab should be used for maintenance of remission of vedolizumab induced remission
  - Ustekinumab should be used for maintenance of remission of ustekinumab induced remission

## POSITION STATEMENT:

**Site of Care**: If certolizumab pegol (Cimzia) 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) 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 list of self-administered products with prerequisites for certain indications can be found at Preferred Agents and Drug List.

Initiation of certolizumab pegol (Cimzia) meets the definition of medical necessity when **ALL** of the following are met ("1" to "5"):

1. **ONE** of the following ("a", "b", or "c"):
   a. The member has been treated with certolizumab pegol (starting on samples is not approvable) within the past 90 days
   b. The prescriber states the member has been treated with certolizumab pegol (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. Certolizumab pegol will be used for the treatment of an indication listed in Table 1, and **ALL** of the indication-specific criteria are met

ii. **EITHER** of the following if the member has an FDA-approved indication ("I" or "II")

I. The member's age is within FDA labeling for the requested indication for certolizumab pegol

II. The prescriber has provided information in support of using certolizumab pegol for the member's age for the requested indication

2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, PJIA, RA; gastroenterologist for CD; dermatologist for PS) 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 certolizumab pegol

4. Member will **NOT** be using certolizumab pegol in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

5. **ANY** of the following ("a", "b", "c", or "d"):

   a. The dosage does not exceed:

      - Loading dose:
        - AS, nr-axSpA: Initial dose of 400 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 or 4 weeks later
          - QL: 6 X 200 mg/mL syringe, starter kit - 1 starter kit (3 doses)/180 days
        - CD: Initial dosing of 400 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 4 weeks later
          - QL: 6 X 200 mg/mL syringe, starter kit - 1 starter kit (3 doses)/180 days
        - PJIA:
          - 10 kg (22 lbs) to less than 20 kg (44 lbs): Initial dose of 100 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 weeks later
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
          - 20 kg (44 lbs) to less than 40 kg (88 lbs): Initial dose of 200 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 weeks later
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
          - Greater than or equal to 40 kg (88 lbs): Initial dose of 400 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 weeks later
            - QL: 6 X 200 mg/mL syringe, starter kit – 1 starter kit (3 doses)/180 days
        - PsA and RA: Initial dosing of 400 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 or 4 weeks later

        - QL: 6 X 200 mg/mL syringe, starter kit – 1 starter kit (3 doses)/180 days
    - PS: member's body weight ≤90 kg – initial dose of 400 mg on day 1 and at week 2 and week 4, followed by maintenance doses starting 2 weeks later
        - QL: 6 X 200 mg/mL syringe, starter kit – 1 starter kit (3 doses)/180 days
- Maintenance dose:
    - AS, CD, nr-axSpA, PsA and RA: 200 mg every 2 weeks (14 days) or 400 mg every 4 weeks (28 days)
        - QL: 2 x 200 mg/mL syringe, kit - 1 kit/28 days
        - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
    - PJIA:
        - 10 kg (22 lbs) to less than 20 kg (44 lbs): 50 mg every 2 weeks
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
        - 20 kg (44 lbs) to less than 40 kg (88 lbs): 100 mg every 2 weeks
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
        - Greater than or equal to 40 kg (88 lbs): 200 mg every 2 weeks
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
            - QL: 2 x 200 mg/mL syringe, kit - 1 kit/28 days
    - PS and other indications: 400 mg every 2 weeks (14 days)
        - QL: 2 x 200 mg/mL syringe, kit - 2 kits/28 days
        - QL: 400 mg vial kit (two 200 mg vials) – 2 kits/28 days

b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

    i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose 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

    ii. **ALL** of the following ("1", "2", and "3"):

        1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication

        2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)

        3. **EITHER** of the following ("a" or "b"):

            a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose 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

b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

   i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose 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

   ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

d. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

   i. 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

   ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

**Approval duration**: Loading dose (doses on day 1, 15, and 29) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]

**Table 1**

| Diagnosis | Criteria |
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| Moderately to severely active rheumatoid arthritis (RA) | **BOTH** of the following:<br>1. **ONE** of the following:<br>a. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) after at least a 3-month duration of therapy<br>**OR**<br>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 after at least a 3-month duration of therapy<br>**OR** |

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| | 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<br><br>**OR**<br><br>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<br><br>**OR**<br><br>e. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA<br><br>**AND**<br><br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br><br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br><br>**OR**<br><br>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 at least **TWO** of the following:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd) |

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| | • Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>**OR**<br>d. **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:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib) |
| Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) | **ALL** of the following:<br>1. **ONE** of the following:<br>a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA after at least a 3-month duration of therapy<br>**OR** |

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| | b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PJIA<br><br>**OR**<br><br>c. The member has a labeled contraindication to **ALL** of the conventional agents used in the treatment of PJIA<br><br>**OR**<br><br>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 or AHFS for the treatment of PJIA<br><br>**AND**<br><br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br><br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz (tofacitinib)<br><br>**OR**<br><br>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 at least **TWO** of the following:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Simlandi (adalimumab-ryvk) |

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| | • Xeljanz (tofacitinib)<br><br>**OR**<br><br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz (tofacitinib)<br><br>**OR**<br><br>d. **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:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz (tofacitinib)<br><br>**AND**<br><br>3. If the product is being self-administered, the member weighs at least 40 kg (88 lbs) |
| Active psoriatic arthritis (PsA) | **BOTH** of the following:<br><br>1. **ONE** of the following:<br>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 after at least a 3-month duration of therapy |

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| | **OR**<br><br>b. The member has an intolerance or hypersensitivity to **ONE** of the conventional agents used in the treatment of PsA<br><br>**OR**<br><br>c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of PsA<br><br>**OR**<br><br>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)<br><br>**OR**<br><br>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)<br><br>**OR**<br><br>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 or AHFS for the treatment of PsA<br><br>**AND**<br><br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br><br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Selarsdi (ustekinumab-aekn) |

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| | • Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab-rzaa)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>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 at least **TWO** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab-rzaa)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz |

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| | • Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab-rzaa)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>d. **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:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Rinvoq/Rinvoq LQ (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab-rzaa)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab) |

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| | • Xeljanz/Xeljanz XR (tofacitinib)<br>• Yesintek (ustekinumab-kfce) |
| Moderate to severe plaque psoriasis (PS) | **BOTH** of the following:<br>1. **ONE** of the following:<br>a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS after at least a 3-month duration of therapy<br>**OR**<br>b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PS<br>**OR**<br>c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS<br>**OR**<br>d. The member has severe active 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)<br>**OR**<br>e. The member has concomitant severe psoriatic arthritis (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)<br>**OR**<br>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 or AHFS for the treatment of PS<br>AND<br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product: |

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| | • Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Sotyktu (deucravacitinib)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>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 at least **TWO** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Sotyktu (deucravacitinib)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba) |

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| | • Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Sotyktu (deucravacitinib)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>d. **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:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Otezla (apremilast)<br>• Selarsdi (ustekinumab-aekn) |

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| | • Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Sotyktu (deucravacitinib)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce) |
| Moderately to severely active Crohn's disease (CD) | **BOTH** of the following:<br>1. **ONE** of the following:<br>a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy<br>**OR**<br>b. The member has an intolerance or hypersensitivity to **ONE** of the conventional agents used in the treatment of CD<br>**OR**<br>c. The member has an FDA labeled contraindication **ALL** of the conventional agents used in the treatment of CD<br>**OR**<br>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 or AHFS for the treatment of CD<br>**AND**<br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Entyvio (vedolizumab) subcutaneous injection<br>• Hadlima (adalimumab-bwwd) |

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| | • Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>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 at least **TWO** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Entyvio (vedolizumab) subcutaneous injection<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Entyvio (vedolizumab) subcutaneous injection |

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| | • Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce)<br>**OR**<br>d. **ALL** of the following 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<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Entyvio (vedolizumab) subcutaneous injection<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Selarsdi (ustekinumab-aekn)<br>• Simlandi (adalimumab-ryvk)<br>• Skyrizi (risankizumab)<br>• Stelara (ustekinumab)<br>• Steqeyma (ustekinumab-stba)<br>• Tremfya (guselkumab)<br>• Yesintek (ustekinumab-kfce) |
| Active ankylosing spondylitis (AS) | **BOTH** of the following:<br>1. **ONE** of the following:<br>a. The member has tried and had an inadequate response to **TWO** different NSAIDs used in the treatment of AS after at least a 4-week total trial |

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| | **OR**<br><br>b. The member has an intolerance or hypersensitivity to **TWO** different NSAIDs used in the treatment of AS<br><br>**OR**<br><br>c. The member has an FDA labeled contraindication to **ALL** NSAIDs used in the treatment of AS<br><br>**OR**<br><br>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 or AHFS for the treatment of AS<br><br>**AND**<br><br>2. **ANY** of the following* (submitted medical records/chart notes are required for confirmation):<br><br>a. The member has tried and had an inadequate response to at least **TWO** of the following preferred products after at least a 3-month trial per product:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br><br>**OR**<br><br>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 at least **TWO** of the following:<br><br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept) |

| | |
|---|---|
| | • Hadlima (adalimumab-bwwd)<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>**OR**<br>c. The member has an FDA labeled contraindication to **ALL** of the following:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib)<br>**OR**<br>d. **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:<br>• Adalimumab-aaty<br>• Adalimumab-adaz<br>• Cosentyx (secukinumab)<br>• Enbrel (etanercept)<br>• Hadlima (adalimumab-bwwd<br>• Humira (adalimumab)<br>• Rinvoq (upadacitinib)<br>• Simlandi (adalimumab-ryvk)<br>• Xeljanz/Xeljanz XR (tofacitinib) |

| | |
|---|---|
| Active non-radiographic axial spondyloarthritis (nr-axSpA) | **ONE** of the following:<br>1. The member has tried and had an inadequate response to **TWO** different NSAIDs used in the treatment of nr-axSpA after at least a 4-week total trial<br>**OR**<br>2. The member has an intolerance or hypersensitivity to **TWO** different NSAIDs used in the treatment of nr-axSpA<br>**OR**<br>3. The member has an FDA labeled contraindication to **ALL** NSAIDs used in the treatment of nr-axSpA<br>**OR**<br>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 or AHFS for the treatment of nr-axSpA |
| 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 |
| *Members initiating provider-administered (i.e., submitted as a medical claim with J0717) certolizumab therapy are **NOT** required to have had an inadequate response to the preferred self-administered (i.e., subcutaneous) products. However, members transitioning to self-administered treatment after a single provider-administered first dose must still meet the preferred self-administered biologic product requirement. | |

Continuation of certolizumab pegol (Cimzia) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for certolizumab pegol has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
2. Member has had clinical benefit with certolizumab pegol therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PJIA, PsA, RA; gastroenterologist for CD; dermatologist for PS) 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 certolizumab pegol
5. Member will **NOT** be using certolizumab pegol in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended

release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

6. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed the following:
        - AS, CD, nr-axSpA, PsA and RA: 200 mg every 2 weeks (14 days) or 400 mg every 4 weeks (28 days)
            - QL: 2 x 200 mg/mL syringe, kit - 1 kit/28 days
            - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
        - PJIA:
            - 10 kg (22 lbs) to less than 20 kg (44 lbs): 50 mg every 2 weeks
                - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
            - 20 kg (44 lbs) to less than 40 kg (88 lbs): 100 mg every 2 weeks
                - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
            - Greater than or equal to 40 kg (88 lbs): 200 mg every 2 weeks
                - QL: 400 mg vial kit (two 200 mg vials) – 1 kit/28 days
                - QL: 2 x 200 mg/mL syringe, kit - 1 kit/28 days
        - PS and other indications: 400 mg every 2 weeks (14 days)
            - QL: 2 x 200 mg/mL syringe, kit - 2 kits/28 days
            - QL: 400 mg vial kit (two 200 mg vials) – 2 kits/28 days
    b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose 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
        ii. **ALL** of the following ("1", "2", and "3"):
            1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
            2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
            3. **EITHER** of the following ("a" or "b"):
                a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose 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
                b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is

support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
    i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose 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
    ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)
d. The member does **NOT** have an FDA labeled indication NOR a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):
    i. 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
    ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

**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 indications:**

Certolizumab pegol is indication for:

- Reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Treatment of adults with moderately to severely active rheumatoid arthritis
- Treatment of active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older
- Treatment of adult patients with active psoriatic arthritis
- Treatment of adults with active ankylosing spondylitis
- Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation

- Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

Crohn's Disease:

- Initial Dose: 400 mg (given as 2 subcutaneous injections of 200 mg) initially, and at weeks 2 and 4.
- Maintenance Dose: In members who obtain a clinical response, the recommended maintenance regimen is 400 mg every 4 weeks (starting at week 8).

Plaque Psoriasis:

- 400 mg (given as 2 subcutaneous injections of 200 mg) every other week
- For some patients (with body weight ≤90 kg), 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at Weeks 2 and 4, followed by 200 mg every other week can be considered.

Polyarticular Juvenile Idiopathic Arthritis:

- 10 kg (22 lbs) to less than 20 kg (44 lbs)
  - Initial Dose: 100 mg at Week 0, 2 and 4
  - Maintenance Dose: 50 mg every 2 weeks
- 20 kg (44 lbs) to less than 40 kg (88 lbs)
  - Initial Dose: 200 mg at Week 0, 2 and 4
  - Maintenance Dose: 100 mg every 2 weeks
- Greater than or equal to 40 kg (88 lbs)
  - Initial Dose: 400 mg at Week 0, 2 and 4
  - Maintenance Dose: 200 mg every 2 weeks
- There is no dosage form for Cimzia that allows for patient self-administration for doses below 200 mg. Doses less than 200 mg require administration by a health care professional using the vial kit.

Rheumatoid Arthritis, Active Psoriatic Arthritis, Ankylosing Spondylitis, and Non-radiographic Axial Spondyloarthritis:

- Initial Dose: 400 mg (given as 2 subcutaneous injections of 200 mg) initially, and at weeks 2 and 4.
- Maintenance Dose: 200 mg every other week (starting at week 6). 400 mg every 4 weeks can be considered (starting at week 8).

Administration: Certolizumab is administered by subcutaneous injection. Rotate injection sites and do not give injections into areas where the skin is tender, bruised, red, or hard. When a 400 mg dose is needed (given as 2 subcutaneous injections of 200 mg), injections should occur at separate sites in the thigh or abdomen

Powder for solution: Prepare the lyophilized powder and administer by a health care provider.

Prefilled syringe: A member may self-inject certolizumab if a health care provider determines that it is appropriate, with medical follow-up, as necessary, after proper training in subcutaneous injection technique. Instruct members using certolizumab to inject the full amount in the syringe (1 mL).

**Drug Availability**: certolizumab is available as:

- Lyophilized powder for reconstitution – contains two 200 mg vials of lyophilized powder for reconstitution and supplies needed for reconstitution
- Prefilled syringe for injection – contains two 200 mg/mL syringes
- Starter kit – contains six 200 mg/mL prefilled syringes to provide for the three 400 mg inial induction doses on week 0, 2, and 4

Refrigerate intact carton between 2 to 8 °C (36 to 46 °F). Do not freeze. Do not separate contents of carton prior to use. Protect solution from light.

## PRECAUTIONS:

**Boxed Warning**

- **Infections:** Increased risk of serious infections leading to hospitalization or death including tuberculosis (TB), invasive fungal, and other opportunistic infections, some fatal, have occurred. Perform test for latent TB; if positive, start treatment for TB prior to starting therapy. Monitor all patients for active TB, even if initial tuberculin skin test is negative. Discontinue treatment if a patient develops a serious infection or sepsis.
- **Malignancy**: lymphoma and other malignancies, some fatal have been reported in children and adolescent individuals treated with TNF blockers including certolizumab. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescents and young adults with inflammatory bowel disease. Certolizumab pegol is not indicated for use in pediatric patients.

**Contraindications**

- Serious hypersensitivity reaction to certolizumab pegol or to any of the excipients

**Precautions/Warnings**

- **Serious Infections:** certolizumab should not be initiated in members during an active infection. If an infection develops, monitor carefully, and discontinue certolizumab if infection becomes serious.
- **Invasive fungal infections:** If a member develops a systemic infection while on certolizumab therapy, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic
- **Anaphylaxis:** anaphylaxis or serious allergic reactions may occur.
- **Hepatitis B virus reactivation:** members who are HBV caries should be monitored during and several months after therapy. If reactivation occurs during therapy, discontinue certolizumab and initiate anti-viral therapy.
- **Demyelinating disease:** exacerbation of new onset may occur

- **Cytopenia, pancytopenia:** advise members to seek immediate medical attention if symptoms develop and consider discontinuing certolizumab.
- **Heart failure:** worsening or new onset heart failure may occur.
- **Lupus-like syndrome:** discontinue certolizumab if syndrome develops.
- **Drug Interactions:** avoid concomitant use with abatacept (Orencia®) and anakinra (Kineret®), due to increased risk of serious infection.
- **Laboratory tests:** may interfere with certain aPTT tests
- **Immunizations:** Avoid administration of live vaccines during or immediately prior to initiation of therapy with certolizumab. Update immunizations in agreement with current immunization guidelines prior to initiating certolizumab therapy.
- **Pregnancy and Lactation**
    - Certolizumab is classified as pregnancy category B. Developmental toxicity studies performed in animals have revealed no evidence of harm to the fetus.
    - Because many immunoglobulins are secreted in milk and the potential for serious adverse reactions exists, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding:

| | |
|---|---|
| J0717 | Injection, certolizumab pegol, 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when self-administered) |

### ICD-10 Diagnosis Codes That Support Medical Necessity:

| | |
|---|---|
| K50.00 – K50.919 | Crohn's disease [regional enteritis] |
| L40.0 | Psoriasis vulgaris |
| L40.50 – L40.59 | Arthropathic psoriasis |
| 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 – M05.7A | Rheumatoid arthritis with rheumatoid factor without organ or systems involvement |
| M05.80 – M05.8A | Other rheumatoid arthritis with rheumatoid factor |
| M05.9 | Rheumatoid arthritis with rheumatoid factor, unspecified |

| | |
|---|---|
| M05.A | Abnormal rheumatoid factor and anti-citrullinated protein antibody with rheumatoid arthritis |
| M06.00 – M06.0A | Rheumatoid arthritis without rheumatoid factor |
| M06.20 – M06.29 | Rheumatoid bursitis |
| M06.30 – M06.39 | Rheumatoid nodule |
| M06.80 – M06.8A | 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 |
| M45.0 – M45.9 | Ankylosing spondylitis |
| M45.A0 – M45.AB | Non-radiographic axial spondyloarthritis |
| M46.81 – M46.89 | Other specified inflammatory spondylopathies |
| T45.AX5A | Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, initial encounter |
| T45.AX5D | Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, subsequent encounter |
| T45.AX5S | Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, sequela |

## 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. 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.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

## DEFINITIONS:

**Crohn's disease:** a chronic granulomatous inflammatory disease of unknown etiology, involving any part of the gastrointestinal tract from mouth to anus, but commonly involving the terminal ileum with

scarring and thickening of the bowel wall. It frequently leads to intestinal obstruction and fistula and abscess formation and has a high rate of recurrence after treatment.

**DMARDs:** An acronym for disease-modifying antirheumatic drugs. 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., baricitinib, tofacitinib, apremilast), and (3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

**Mild-Moderate Crohn's Disease**: Mild-moderate Crohn's disease applies to ambulatory members able to tolerate oral alimentation without manifestations of dehydration, toxicity (high fevers, rigors, prostration), abdominal tenderness, painful mass, obstruction, or >10% weight loss**.**

**Moderate to Severe Crohn's Disease:** Moderate to severe disease applies to patients who have failed to respond to treatment for mild to moderate disease or those with more prominent symptoms of fevers, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

**Monoclonal antibody:** derived from a single cell; pertaining to a single clone. Widely used to measure proteins and drugs in the serum, type tissue and blood, identify infectious agents, identify classification and follow-up therapy of leukemias and lymphomas, and identify tumor antibodies.

**Plaque psoriasis:** It is the most common form of psoriasis. It affects 80 to 90% of people with psoriasis. Plaque psoriasis typically appears as raised areas of inflamed skin covered with silvery white scaly skin. These areas are called plaques.

**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:

**Abatacept (Orencia), 09-J0000-67**
**Adalimumab Products, 09-J0000-46**
**Anakinra (Kineret), 09-J0000-45**
**Apremilast (Otezla) Tablet, 09-J2000-19**

**Baricitinib (Olumiant), 09-J3000-10**
**Bimekizumab (Bimzelx), 09-J4000-70**
**Brodalumab (Siliq) Injection, 09-J2000-74**
**Deucravacitinib (Sotyktu), 09-J4000-37**
**Etanercept (Enbrel), 09-J0000-38**
**Golimumab (Simponi, Simponi Aria), 09-J1000-11**
**Guselkumab (Tremfya), 09-J2000-87**
**Infliximab Products, 09-J0000-39**
**Ixekizumab (Taltz), 09-J2000-62**
**Natalizumab (Tysabri) IV, 09-J0000-73**
**Psoralens with Ultraviolet A (PUVA), 02-10000-16**
**Risankizumab (Skyrizi), 09-J3000-45**
**Rituximab Products, 09-J0000-59**
**Sarilumab (Kevzara), 09-J2000-87**
**Secukinumab (Cosentyx), 09-J2000-30**
**Tildrakizumab-asmn (Ilumya), 09-J3000-04**
**Tocilizumab Products (Actemra, Tofidence, Tyenne), 09-J1000-21**
**Tofacitinib (Xeljanz, Xeljanz XR) Oral Solution, Tablet and Extended-Release Tablet, 09-J1000-86**
**Upadacitinib (Rinvoq), 09-J3000-51**
**Ustekinumab (Stelara), 09-J1000-16**
**Vedolizumab (Entyvio), 09-J2000-18**

## OTHER:

**NOTE**: The list of biologic immunomodulator agents not permitted as concomitant therapy can be found at Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

### Table 2: Xolair (omalizumab) - Conventional Synthetic DMARDs

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

### Table 3: Grading of Severity of Rheumatoid Arthritis

| Severity | Criteria |
|---|---|
| Mild | Joint pain<br>Inflammation of at least 3 joints<br>No inflammation in tissues other than the joints<br>Usually, a negative result on a rheumatoid factor test<br>An elevated erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) level<br>No evidence of bone or cartilage damage on x-rays |

| | |
|---|---|
| Moderate | Between 6 and 20 inflamed joints<br>Usually no inflammation in tissues other than the joints<br>An elevated ESR or CRP levels<br>A positive rheumatoid factor test or anti-cyclic citrullinated peptide (anti-CCP) antibodies<br>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<br>Elevated ESR or CRP levels<br>Anemia related to chronic illness<br>Low blood albumin level<br>A positive rheumatoid factor test, often with a high level<br>Evidence of bone and cartilage damage on x-ray<br>Inflammation in tissues other than joints |

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## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Committee on 02/12/25.

## GUIDELINE UPDATE INFORMATION:

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| 09/15/08 | New Medical Coverage Guideline. |
| 01/01/09 | Annual HCPCS coding update: deleted code 90772; added codes 96372. |
| 04/01/09 | Annual HCPCS coding update: added HCPCS code C9249 & deleted J3490. |

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| 04/15/09 | Revision; consisting of adding ICD-9 codes. |
| 06/15/09 | Revision; consisting of adding rheumatoid arthritis indication and updating boxed warning. |
| 10/15/09 | Review and revision; consisting of updating administration and dosage section and references. |
| 01/01/10 | Annual HCPCS coding update: added HCPCS code J0718 and deleted code C9249. |
| 04/15/10 | Revision; consisting of adding specific continuation criteria. |
| 08/15/10 | Review and revision; consisting of updating precautions and references. |
| 01/15/11 | Revision; consisting of adding ICD-10 codes. |
| 08/15/11 | Review and revision to guideline; consisting of updating precautions, coding and references. |
| 08/15/12 | Review and revision to guideline; consisting of reformatting position statement, updating precautions and references. |
| 10/15/12 | Revision to guideline; consisting of modifying continuation criteria. |
| 01/15/13 | Revision to guideline; consisting of reformatting position statement; revising and reformatting description, dosage/administration, and precautions sections. |
| 03/07/13 | Revision to guideline; additions to position statement. |
| 04/15/13 | Revision to guideline; consisting of revising position statement to include duration of approval. |
| 09/15/13 | Review and revision to guideline; consisting of reformatting position statement; updating related guidelines, references, program exceptions, and coding. |
| 01/01/14 | Revision to guideline; consisting of updating position statement, coding, and references. |
| 04/15/14 | Revision to guideline; consisting of updating position statement. |
| 09/15/14 | Review and revision to guideline; consisting of updating position statement, references, and coding. |
| 09/15/15 | Review and revision to guideline; consisting of updating description section, position statement, dosage/administration, warnings/precautions, billing/coding, related guidelines, and references. |
| 12/15/15 | Revision to guideline consisting of updating the position statement. |
| 09/15/16 | Review and revision to guideline consisting of updating description section, position statement, billing/coding, and references. |
| 11/15/16 | Revision to guideline consisting of updating position statement with ustekinumab prerequisite therapy requirement for Crohn's disease indication. |
| 10/15/17 | Review and revision to guideline consisting of updating description, position statement, 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 axial spondyloarthritis and use of three preferred products is required. Tofacitinib (Xeljanz, Xeljanz XR) added as prerequisite therapy for rheumatoid arthritis when certolizumab pegol is used as self-administered therapy. |
| 07/01/18 | Revision to guideline consisting of updating the position statement. |

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| 07/15/18 | Revision to guideline consisting of updating the description section, position statement, dosage/administration, warnings/precautions, billing/coding, related guidelines, definitions, and references based on a new FDA-approved indication of plaque psoriasis. |
| 10/15/18 | Review and revision to guideline consisting of updating the position statement, related guidelines, and references. |
| 05/15/18 | Revision to guideline consisting of updating the description section and dosage/administration section based on the new FDA-approved indication of non-radiographic axial spondyloarthritis. |
| 07/15/19 | Revision to guideline consisting of updating the position statement. |
| 09/01/19 | Revision to guideline consisting of updating the position statement. |
| 10/15/19 | Review and revision to guideline consisting of updating the statement 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, and definitions. |
| 01/01/21 | Review and revision to guideline consisting of updating the position statement and references. |
| 03/15/21 | Revision to guideline consisting of updating Table 1 in the position statement. |
| 10/01/21 | Revision: Addition of new ICD-10 code range M45.A0 – M45.AB. |
| 11/15/21 | Revision to guideline consisting of updating the position statement. |
| 01/01/22 | Review and revision to guideline consisting of updating the description, position statement, related guidelines, other section, and references. |
| 2/15/22 | Update to Table 1 in Position Statement. |
| 03/15/22 | Revision to guideline consisting of updating the position statement and other section. |
| 05/15/22 | Update to Table 1 in Position Statement. |
| 07/15/22 | Revision to guideline consisting of updating the position statement. |
| 09/15/22 | Update to Table 1 in Position Statement. |
| 10/15/22 | Revision to guideline consisting of updating the position statement to include either Skyrizi or Stelara as a second preferred agent (in addition to Humira) prior to the use of self-administered Cimzia for the treatment of Crohn's disease. |
| 01/01/23 | Review and revision to guideline consisting of updating the position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination. |
| 04/15/23 | Revision to guideline consisting of updating the position statement and other section. |
| 07/01/23 | Revision to guideline consisting of updating the position statement and other section. Amjevita and Hadlima added as Step 1a agents. Rinvoq added as a Step 1b agent for CD. Humira biosimilar products added to list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy. |
| 01/01/24 | Review and revision to guideline consisting of updating the description (NCCN info), position statement, other section, billing/coding, and references. Amjevita low-concentration [10 mg/0.2 mL, 20 mg/0.4 mL, and 40 mg/0.8 mL concentrations only] |

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| | clarified as the preferred prerequisite product. Update to Table 1 in Position Statement. New drugs were added to the list of drugs that are not permitted for use in combination. |
| 07/01/24 | Revision to guideline consisting of updating the description, position statement, related guidelines, and other section. Amjevita low-concentration removed as a required prerequisite agent. Updates to the positioning of agents in Table 1. Removal of latent TB testing requirement. New drugs added to the list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy. |
| 10/01/24 | Revision to guideline consisting of updating the position statement and billing/coding. Updates to Table 1. Simlandi added among the required prerequisite agents for self-administered Cimzia for AS, RA, CD, PS, and PsA. Rinvoq LQ added among the required prerequisite agents for self-administered Cimzia for PsA. New ICD-10 codes. |
| 11/15/24 | Revision to guidelines consisting of updates to the description, position statement, dosage/administration, billing/coding, and references based on the new FDA-approved indication for the treatment of active PJIA in patients 2 years of age and older. |
| 01/01/25 | Review and revision to guideline consisting of updating the position statement, other section, and references. Adalimumab-aaty and Adalimumab-adaz added among the prerequisite therapies for AS, CD, PJIA, PsA, PS, and RA. Entyvio (vedolizumab) subcutaneous injection (now a step 1a agent) added among the prerequisite therapies for CD. Sotyktu (deucravacitinib) (now a step 1a agent) added among the prerequisite therapies for PS. Update to original Table 1 which is now a link out from the Position Statement. Table titles updated. Revised wording regarding maximum dosage exceptions. New drugs were added to the list of drugs that are not permitted for use in combination. |
| 04/01/25 | Revision to guidelines consisting of updates to the position statement. Self-administered Cimzia moved from a step 3c (triple step) to step 3a (double step) agent for PJIA. For the Crohn's disease indication, self-administered Cimzia is a 3a agent (double step), but the step no longer always requires an adalimumab product. |
| 05/15/25 | Revision. Tremfya added among the preferred agents for CD for self-administered Cimzia. |
| 07/01/25 | Revision: Added Selarsdi, Steqeyma and Yesintek among the preferred agents for CD, PS, and PsA for for self-administered Cimzia. |
| 10/01/25 | Revision: Added ICD-10 code M05.A. Updated ICD-10 code ranges for RA. |