09-J0000-46

Original Effective Date: 01/01/05

Reviewed: 03/08/23

Revised: 04/01/23

Subject: Adalimumab Products (Humira® and biosimilars)

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:

Adalimumab (Humira) is one of five commercially available tumor necrosis factor (TNF)-alpha inhibitors, not counting biosimilars as separate products, available in the United States, and was first approved in December 2002. 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.

Humira is approved by the US Food and Drug Administration (FDA) for the treatment of nine indications (the most of any TNF inhibitor): ankylosing spondylitis (2006), Crohn's disease (2007), hidradenitis suppurativa (2015), polyarticular juvenile idiopathic arthritis (2008), plaque psoriasis (2008), psoriatic arthritis (2005), rheumatoid arthritis (2002), ulcerative colitis (2012), and uveitis (2016). In October 2018, the indications for uveitis and hidradenitis suppurativa were expanded to include pediatric patients (2 years of age and older) and adolescent patients (12 years of age and older), respectively. In February 2021, the indication for ulcerative colitis was expanded to include pediatric patients (5 years of age and older). In 2019, AbbVie released a citrate-free formulation of Humira that includes a thinner needle and half the injection volume as compared the original Humira formulation. The changes are intended to reduce the amount of pain immediately following injection. As of January 2021, both formulations are available in the market. In January 2021, AbbVie released an 80 mg/0.8 mL citrate-free

pen as an every-other-week alternative dosing option to Humira 40 mg weekly. The only indications FDA-approved for 40 mg weekly dosing (and now 80 mg every-other-week dosing) are hidradenitis suppurativa, pediatric ulcerative colitis (40 kg or greater), and rheumatoid arthritis when used as monotherapy for patients with a suboptimal response to 40 mg every 2 weeks. In September 2016 the first biosimilar to adalimumab, adalimumab-atto (Amjevita), was FDA approved. Additional biosimilars have followed: adalimumab-adbm (Cyltezo) approved in August 2017, adalimumab-adaz (Hyrimoz) approved in October 2018, adalimumab-bwwd (Hadlima) approved in July 2019, adalimumab-afzb (Abrilada) approved in November 2019, adalimumab-fkjp (Hulio) approved in July 2020, adalimumab-aqvh (Yusimry) in December 2021, and adalimumab-aacf (Idacio) in December 2022. In October 2021, Cyltezo was approved by the FDA as the first interchangeable biosimilar product to treat certain inflammatory diseases. Cyltezo is now consider both biosimilar to, and interchangeable with (may be substituted for), its reference product Humira for Cyltezo's approved uses. Amjevita was the first biosimilar to launch on January 31, 2023. As of February 2023, Amjevita has the same indications as Humira except it does not include uveitis, hidradenitis suppurativa, or pediatric UC. Amjevita is currently only available as a low-concentration (40 mg/0.8 mL) formulation but it is citrate-free. It does not have interchangeability status and starter packs are not available. The other biosimilars will not launch until on or after July 1, 2023. The TNF-alpha inhibitors as a class are considered to have similar efficacy and safety for the majority of indications. Similar to other TNF-alpha inhibitors, the package labeling contains a Boxed Warning regarding potential increased risk of serious infections (e.g., tuberculosis) and certain malignancies during therapy.

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 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) 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, 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 (IBD) 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.[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

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 (great than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when is 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:

- Limited disease (less than 5% of BSA):
  - Topical corticosteroids are first line as either monotherapy or in conjunction with non-steroidal topical agents
  - Vitamin D analogs, calcipotriene, calcipotriol, and calcitriol, are other first line agents and are often used in combination with topical corticosteroids
  - Tazarotene is a corticosteroid sparing agent and can be used in combination with topical corticosteroids to produce a synergistic effect and longer durations of treatment benefit and remission
  - Phototherapy is another first line option for limited disease, and allows for selective targeting of localized lesions and resistant areas such as the scalp and skin folds, leaving surrounding, non-lesional skin unaffected
  - Calcineurin inhibitors (tacrolimus and pimecrolimus) may also be considered first line for intertriginous, inverse, face, and genital psoriasis
  - Systemic agents are considered second line and only for short term use
- Moderate to severe disease without PsA (more than 5% of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life):
  - UV-therapy is considered first line as monotherapy or in combination with acitretin or MTX
  - If UV-therapy is unavailable, first line therapies include MTX, cyclosporine, acitretin, and biologics
  - Second line systemic agents include leflunomide, sulfasalazine, and tacrolimus
- 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

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

Hidradenitis Suppurativa (HS)

Hidradenitis suppurativa (HS) is a chronic inflammatory disease causing painful, nodules to form in the folds of the skin and often secrete puss and blood. HS can be described as mild (single or few lesions in one area of the skin, Hurley Stage I), moderate (repeated cycles of enlarged lesions that break open and occur in more than one area of the skin, Hurley Stage II), and severe (widespread lesions, scarring, and chronic pain; Hurley Stage III).

Pharmacological treatment for mild HS includes topical clindamycin, oral tetracyclines, hormonal treatment, retinoids, intralesional corticosteroid injections (i.e., triamcinolone), and deroofing. Oral tetracyclines are recommended for mild to moderate HS for at least a 12 weeks course or as long-term maintenance. Combination clindamycin and rifampin is effective second-line therapy for mild to moderate HS, or as first-line or adjunct therapy for severe HS. Combination rifampin, moxifloxacin, and metronidazole are recommended as second or third-line therapy for moderate to severe disease. Dapsone may be effective for a minority of patients with mild to moderate HS as long-term maintenance therapy. Oral retinoids, such as acitretin and isotretinoin, have also been used for mild HS as second or third-line therapy. Hormonal therapy may be considered in female patients for mild to moderate disease as monotherapy, or as adjunct therapy for severe disease. such as hormonal contraceptives, metformin, finasteride, and spironolactone.

Treatment recommendations for moderate to severe and refractory HS include immunosuppressants (e.g., cyclosporine and low dose systemic corticosteroids) and biologic agents. The TNF-inhibitors that are recommended are adalimumab, at doses within FDA labeling, and infliximab, but optimal doses have not been established. Anakinra and ustekinumab may be effective, but require dose ranging studies to determine optimal doses for management.

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

Ulcerative Colitis (UC)

Ulcerative colitis (UC) is a chronic immune-mediated inflammatory condition affecting the large intestine associated with inflammation of the rectum, but that can extend to involve additional areas of the colon. The American College of Gastroenterology (ACG) recommends a treat-to-target approach and recommend therapeutic management should be guided by diagnosis (i.e., Montreal classification), assessment of disease activity (i.e., mild, moderate, and severe), and disease prognosis. The ACG treatment recommendations are further broken down into induction therapies and maintenance of

remission. The 2019 ACG treatment guidelines recommend the following for therapeutic management of UC[37]:

Induction of remission:

- Mildly active disease:
    - Rectal 5-ASA at a dose of 1 g/day with or without oral 5-ASA at a dose of at least 2 g/day for left-sided UC
    - Rectal 5-ASA at a dose of 1 g/day for ulcerative proctitis
    - Oral 5-ASA at a dose of at least 2 g/day for extensive UC
    - Add oral budesonide multi-matrix (MMX) 9 mg/day for patients that are intolerant or non-responsive to oral and/or rectal and oral 5-ASA at appropriate doses
- Moderately active disease:
    - Oral budesonide multi-matrix (MMX) 9 mg/day for induction of remission
- Moderately to severely active disease:
    - Oral systemic corticosteroids, TNF inhibitors (i.e., adalimumab, golimumab, or infliximab), tofacitinib, or vedolizumab to induce remission
    - Combination of infliximab with thiopurine therapy when using infliximab for induction
    - Switch to tofacitinib or vedolizumab for induction in patients that have failed TNF inhibitors
    - Patients with initial response to TNF inhibitors that lose response should have antibody levels and serum drug levels tested to assess reason for loss of response. If serum levels are adequate, use of another TNF inhibitor is not likely to be of benefit.

Maintenance of remission:

- Previously mildly active disease:
    - Rectal 5-ASA at a dose of 1 g/day in patients with ulcerative proctitis
    - Oral 5-ASA at a dose of at least 2 g/day in patients with left-sided or extensive UC
- Previously moderately to severely active disease:
    - Thiopurines in patients that achieved remission due to corticosteroid induction
    - Continue TNF inhibitors (i.e., adalimumab, golimumab, or infliximab) for remission due to TNF induction
    - Continue vedolizumab for remission due to vedolizumab induction
    - Continue tofacitinib for remission due to tofacitinib induction

The American Gastroenterology Association (AGA) published recommendations for the management of mild to moderate UC:

- Use either standard-dose mesalamine (2-3 g/day) or diazo-bonded 5-ASA for patients with extensive UC for induction of remission and maintenance of remission

- May add rectal mesalamine to oral 5-ASA in patients with extensive or left-sided UC for induction of remission and maintenance of remission
- Use high dose mesalamine (>3 g/day) with rectal mesalamine in patients with suboptimal response to standard-dose mesalamine, diazo-bonded 5-ASA, or with moderate disease activity for induction of remission and maintenance of remission
- Add either oral prednisone or budesonide MMX in patients that are refractory to optimized oral and rectal 5-ASA regardless of disease extent

The American Gastroenterology Association (AGA) published recommendations for the management of moderate to severe UC.

- Standard of care is to continue agents initiated for induction therapy as maintenance therapy, if they are effective (excluding corticosteroids and cyclosporine)
- Adult outpatients with moderate to severe UC:
    - Infliximab, adalimumab, golimumab, vedolizumab, tofacitinib or ustekinumab are strongly recommended over no treatment
    - Biologic naïve patients:
        - infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission
        - Recommend tofacitinib only be used in the setting of a clinical or registry study
    - Previous exposure to infliximab, particularly those with primary non-response, ustekinumab or tofacitinib are conditionally recommended over vedolizumab or adalimumab for induction of remission
    - Conditionally recommend against use of thiopurine monotherapy for induction, but may be used for maintenance of remission over no treatment

OTHER DISORDERS

Uveitis

Uveitis is inflammation of the uvea, which is the middle layer of the eye, leading to tissue damage and vision loss. There are three types of uveitis: anterior, intermediate and posterior. Uveitis frequently occurs in association with other systemic medical conditions, especially infections and inflammatory disease, but may occur as an isolated process. Treatment of non-infectious uveitis depends on the location of inflammation. Anterior uveitis is generally treated with topical glucocorticoids, such as prednisolone ophthalmic drops. Uveitis that is primarily posterior to the lens is generally not responsive to topical medication, although some experts are increasingly using difluprednate. Oral corticosteroids continue to be the mainstay of treatment for noninfectious intermediate, posterior, and pan uveitis. Intraocular and periocular injections of triamcinolone or glucocorticoids are also options, although patients may decline the injections. Systemic treatment is generally reserved for resistant inflammation and may be indicated in patients with glaucoma who cannot be treated with local injection. If remission has been achieved for 6 to 12 months with systemic glucocorticoids, the maintenance dose may be gradually discontinued. The American Academy of Ophthalmology recommends the use of immunosuppressive agents, such as methotrexate, azathioprine, mycophenolate, cyclosporine, and

tacrolimus, for patients that are intolerant and/or resistant to systemic corticosteroids. TNF-inhibitors, such as adalimumab, are recommended if the patient is inadequately controlled by corticosteroids and non-corticosteroid systemic immunomodulatory therapies.

POSITION STATEMENT:

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

Table 1

Disease State	Step 1		Step 2 (Directed to ONE step 1 agent)	Step 3a (Directed to TWO step 1 agents)	Step 3b (Directed to TWO agents from step 1 and/or step 2)	Step 3c (Directed to THREE step 1 agents)
	Step 1a	Step 1b (Directed to ONE TNF inhibitor) NOTE: Please see Step 1a for preferred TNF inhibitors				
Rheumatoid Disorders						
Ankylosing Spondylitis (AS)	SQ: Cosentyx, Enbrel, **Humira**	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Simponi, Taltz	N/A	SQ: **Amjevita** (Humira is required Step 1 agent)
Nonradiographic Axial Spondyloarthritis (nr-axSpA)	SQ: Cimzia, Cosentyx	Oral: Rinvoq	N/A	SQ: Taltz	N/A	N/A
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	SQ: Enbrel, **Humira**	Oral: Xeljanz	SQ: Actemra (Humira is required Step 1 agent)	N/A	SQ: Orencia	SQ: **Amjevita** (Humira is required Step 1 agent)
Psoriatic Arthritis (PsA)	SQ: Cosentyx, Enbrel, **Humira**, Skyrizi, Stelara, Tremfya Oral: Otezla	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Orencia, Simponi, Taltz	N/A	SQ: **Amjevita** (Humira is required Step 1 agent)
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	SQ: **Amjevita** (Humira is required Step 1 agent)
Dermatological Disorders						

Hidradenitis Suppurativa (HS)	SQ: **Humira**	N/A	SQ: **Amjevita** (Humira is required Step 1 agent)	N/A	N/A	N/A
Psoriasis (PS)	SQ: Cosentyx, Enbrel, **Humira**, Skyrizi, Stelara, Tremfya Oral: Otezla	N/A	N/A	SQ: Cimzia, Ilumya	N/A	SQ: SQ: **Amjevita** (Humira is required Step 1 agent), Siliq, Taltz Oral: Sotyktu
Inflammatory Bowel Disease						
Crohn's Disease	SQ: **Humira**, Skyrizi, Stelara	N/A	N/A	SQ: Cimzia (Humira is a required Step 1 agent)	N/A	SQ: **Amjevita** (Humira is required Step 1 agent)
Ulcerative Colitis	SQ: **Humira**, Stelara	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Simponi (Humira is required Step 1 agent)	N/A	Zeposia (Humira, Rinvoq, Stelara, OR Xeljanz/Xeljanz XR are required Step agents)	SQ: **Amjevita** (Humira is required Step 1 agent)
Other						
Uveitis	SQ: **Humira**	N/A	SQ: **Amjevita** (Humira is required Step 1 agent)	N/A	N/A	N/A
Indications Without Prerequisite Biologic Immunomodulators						
Alopecia Areata (AA) Atopic Dermatitis Deficiency of IL-1 Receptor Antagonist (DIRA) Enthesitis Related Arthritis (ERA) Giant Cell Arteritis (GCA) Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Systemic Juvenile Idiopathic Arthritis (SJIA) Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)	N/A	N/A	N/A	N/A	N/A	N/A

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

Initiation of adalimumab (Humira) 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 Humira (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with Humira (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"):
        a. Humira will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific criteria are met
        b. **EITHER** of the following ("I" or "II")
            i. The member's age is within FDA labeling for the requested indication for Humira
            ii. The prescriber has provided information in support of using Humira for the member's age
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; 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 Humira
4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the member has begun therapy for latent TB
5. Member will **NOT** be using Humira in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following ("a", "b", or "c"):
    a. The dosage does not exceed:
        - Loading dose
            - Adult AS, PsA, and RA: no loading dose required
            - PJIA and pediatric uveitis: no loading dose required
            - Adult CD and UC: Initial dose of 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
                - QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.8 mL pen] - 1 kit (6 pens)/180 days
                - QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.4 mL pen (citrate-free)] - 1 kit (6 pens)/180 days
                - QL: Crohn's disease, Ulcerative colitis, or Hidradenitis suppurativa Starter kit [80 mg/0.8 mL pen] - 1 kit (3 pens)/180 days
            - Pediatric CD:

- 17 kg to <40 kg: Initial dose of 80 mg on day 1, 40 mg on day 15, then maintenance dose starting on day 29
    - QL: Pediatric Crohn's Starter Kit [40 mg/0.8mL (3 syringe pack)] - 1 kit (3 syringes)/180 day
    - QL: Pediatric Crohn's Disease Starter kit [40 mg/0.4 mL and 80 mg/0.8 mL syringe (citrate-free)]- 1 kit (2 syringes)/180 days
- ≥40 kg: 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
    - QL: Pediatric Crohn's Starter Kit [40 mg/0.8mL (6 syringe pack)] - 1 kit (6 syringes)/180 days
    - QL: Pediatric Crohn's Disease Starter kit [80 mg/0.8 mL syringe (citrate-free)]- 1 kit (3 syringes)/180 days

o Pediatric UC:

- 20 kg to <40 kg: Initial dose of 80 mg on day 1, 40 mg on days 8 and 15, and then maintenance dose starting on day 29
    - QL: Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter kit [80 mg/0.8 mL and 40 mg/0.4 mL pen] - 1 kit (3 pens)/180 days
- ≥40 kg: Initial dose of 160 mg (single dose or split over two consecutive days) on day 1, 80 mg on days 8 and 15, and then maintenance dose starting on day 29
    - QL: Pediatric Ulcerative Colitis Starter kit [80 mg/0.8 mL pen (citrate-free)] - 1 kit (4 pens)/180 day

o PS and adult uveitis: Initial dose of 80 mg, then maintenance dose starting one week after the initial dose

- QL: Psoriasis, Uveitis, or Adolescent Hidradenitis Suppurativa Starter kit [40 mg/0.8 mL pen] - 1 kit (4 pens)/180 days
- QL: Psoriasis, Uveitis, or Adolescent Hidradenitis Suppurativa Starter kit [40 mg/0.4 mL pen (citrate-free)] - 1 kit (4 pens)/180 days
- QL: Psoriasis, Uveitis, or Adolescent Hidradenitis Suppurativa Starter kit [80 mg/0.8 mL and 40 mg/0.4 mL pen] - 1 kit (3 pens)/180 days

o Adult HS: Initial dose of 160 mg day 1, 80 mg on day 15, then maintenance dose starting on day 29

- QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.8 mL pen] - 1 kit (6 pens)/180 days
- QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.4 mL pen (citrate-free)] - 1 kit (6 pens)/180 days
- QL: Crohn's disease, Ulcerative Colitis, or Hidradenitis Suppurativa Starter kit [80 mg/0.8 mL pen (citrate-free)] - 1 kit (3 pens)/180 days

o Adolescent HS:

- 30 kg to <60 kg: Initial dose of 80 mg on day 1, then maintenance dose starting on day 8
    - QL: Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter kit [40 mg/0.8 mL pen] - 1 kit (4 pens)/180 days
    - QL: Psoriasis, Uveitis, or Adolescent Hidradenitis Suppurativa Starter kit [40 mg/0.4 mL pen (citrate-free)] - 1 kit (4 pens)/180 days
    - QL: Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter kit [80 mg/0.8 mL and 40 mg/0.4 mL pen] - 1 kit (3 pens)/180 days
- ≥60 kg: 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
    - QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.8 mL pen] - 1 kit (6 pens)/180 days
    - QL: Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit [40 mg/0.4 mL pen (citrate-free)] - 1 kit (6 pens)/180 days
    - QL: Crohn's disease, Ulcerative Colitis, or Hidradenitis Suppurativa Starter kit [80 mg/0.8 mL pen (citrate-free)] - 1 kit (3 pens)/180 days

- Maintenance dose - 40 mg every 2 weeks (14 days) [for HS, pediatric UC (greater than 40 kg), and RA monotherapy ONLY - 40 mg once a week (every 7 days) or 80 mg every 2 weeks (14 days)]
    - QL: 10 mg/0.1 mL syringe - 2 syringes/28 days
    - QL: 10 mg/0.2 mL syringe - 2 syringes/28 days
    - QL: 20 mg/0.2 mL syringe - 2 syringes/28 days
    - QL: 20 mg/0.4 mL syringe, kit - 2 syringes/28 days
    - QL: 40 mg/0.8 mL syringe, kit - 2 syringes/28 days
    - QL: 40 mg/0.4 mL syringe - 2 syringes/28 days
    - QL: 40 mg/0.8 mL pen - 2 pens/28 days
    - QL: 40 mg/0.4 mL pen - 2 pens/28 days
    - QL: 80 mg/0.4 mL pen - 2 pens/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:

- Adult AS, PsA, and RA - 12 months
- PJIA and adolescent uveitis - 12 months
- UC - Loading dose (doses on day 1 and 15 for adults or days 1, 8, and 15 for pediatrics) for 4 weeks, then maintenance dose for 8 additional weeks [12 weeks for total duration of approval]
- CD - Loading dose (doses on day 1 and 15) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- PS and adult uveitis - Loading dose (doses on day 1, 8, 22) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Adult HS and pediatric HS (≥60 kg) - Loading dose (doses on day 1 and 15) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Pediatric HS (30 kg to <60 kg) - Loading dose (doses on day 1, 8, 22) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Other indications - 12 months

Table 2

Diagnosis	Criteria
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 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 or AHFS for the treatment of RA
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 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
Moderate to severe plaque psoriasis (PS)	**ONE** of the following: 1. 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 for at least 3 months **OR**

	2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PS **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS **OR** 4. 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) **OR** 5. 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) **OR** 6. 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
Moderately to severely active Crohn's disease (CD)	**ONE** of the following: 1. 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 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 CD **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of CD **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 or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with adalimumab is deemed

	clinically necessary - provider must include additional details regarding disease severity and/or risk factors
Moderately to severely active ulcerative colitis (UC)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC 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 UC **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **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 or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with adalimumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors
Non-infectious intermediate uveitis, posterior uveitis, or panuveitis	**ONE** of the following: 1. **BOTH** of the following: i. **ONE** of the following: i. The member has tried and had an inadequate response to oral corticosteroids used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for a minimum of 2 weeks **OR** ii. The member has tried and had an inadequate response to periocular or intravitreal corticosteroid injections in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR**

	iii. The member has an intolerance or hypersensitivity to oral corticosteroids OR periocular or intravitreal corticosteroid injections used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** iv. The member has an FDA labeled contraindication to **BOTH** oral corticosteroids and periocular/intravitreal corticosteroids **AND** ii. **ONE** of the following: i. The member has tried and had an inadequate response to **ONE** conventional systemic agent (i.e., azathioprine, mycophenolate, methotrexate, cyclosporine, tacrolimus) used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for at least 3 months **OR** ii. The member has an intolerance or hypersensitivity to **ONE** conventional systemic agent used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** iii. The member has an FDA labeled contraindication to **ALL** conventional systemic agents used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** 2. 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 non-infectious intermediate uveitis, posterior uveitis, or panuveitis
Active ankylosing spondylitis (AS)	**ONE** of the following: 1. The member has tried and had an inadequate response to **TWO** different NSAIDs used in the treatment of AS for at least a 4-week total trial **OR** 2. The member has an intolerance or hypersensitivity to TWO different NSAIDs used in the treatment of AS **OR**

	3. The member has an FDA labeled contraindication to **ALL** NSAIDs used in the treatment of AS **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 or AHFS for the treatment of AS
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 or AHFS for the treatment of PJIA
Moderate to severe hidradenitis suppurative (HS)	**ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., oral tetracyclines [doxycycline, minocycline, tetracycline]; oral contraceptives [females only]; metformin [females only]; finasteride [females only]; spironolactone [females only]; intralesional corticosteroids [triamcinolone]; clindamycin in combination with rifampin; combination of rifampin, moxifloxacin, and metronidazole; cyclosporine, oral retinoids) used in the treatment of HS for at least 3 months **OR** b. The member has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of HS **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of HS **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 or AHFS for the treatment of HS
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 adalimumab (Humira) meets the definition of medical necessity when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for Humira has been previously approved by Florida Blue
2. Member has had clinical benefit with Humira therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, RA; gastroenterologist for CD, UC; 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 Humira
5. Member will **NOT** be using Humira in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following ("a", "b", or "c"):
    a. The dosage does not exceed 40 mg every 2 weeks (14 days) [for HS, pediatric UC (greater than 40 kg), and RA monotherapy **ONLY** - 40 mg once a week (every 7 days) or 80 mg every 2 weeks (14 days)]
        - QL: 10 mg/0.1 mL syringe - 2 syringes/28 days
        - QL: 10 mg/0.2 mL syringe - 2 syringes/28 days
        - QL: 20 mg/0.2 mL syringe - 2 syringes/28 days
        - QL: 20 mg/0.4 mL syringe, kit - 2 syringes/28 days
        - QL: 40 mg/0.8 mL syringe, kit - 2 syringes/28 days
        - QL: 40 mg/0.4 mL syringe - 2 syringes/28 days
        - QL: 40 mg/0.8 mL pen - 2 pens/28 days
        - QL: 40 mg/0.4 mL pen - 2 pens/28 days
        - QL: 80 mg/0.4 mL pen - 2 pens/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

Initiation of Amjevita (adalimumab-atto) meets the definition of medical necessity when **ALL** of the following are met ("1" to "6"):

1. **BOTH** of the following ('i" and "ii"):
   a. Amjevita will be used for the treatment of an indication listed in Table 3, and **ALL** of the indication-specific criteria are met
   b. **EITHER** of the following ("I" or "II")
      i. The member's age is within FDA labeling for the requested indication for Amjevita
      ii. The prescriber has provided information in support of using Amjevita for the member's age
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; 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 Amjevita
4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the member has begun therapy for latent TB
5. Member will **NOT** be using Amjevita in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following ("a", "b", or "c"):
   a. The dosage does not exceed:
      - Loading dose
        - Adult AS, PsA, and RA: no loading dose required
        - PJIA and pediatric uveitis: no loading dose required
        - Adult CD and UC: Initial dose of 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
          - QL: Six 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
        - Pediatric CD:
          - 17 kg to <40 kg: Initial dose of 80 mg on day 1, 40 mg on day 15, then maintenance dose starting on day 29
            - QL: Three 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)

        - ≥40 kg: 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
            - QL: Six 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
    - Pediatric UC:
        - 20 kg to <40 kg: Initial dose of 80 mg on day 1, 40 mg on days 8 and 15, and then maintenance dose starting on day 29
            - QL: Four 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
        - ≥40 kg: Initial dose of 160 mg (single dose or split over two consecutive days) on day 1, 80 mg on days 8 and 15, and then maintenance dose starting on day 29
            - QL: Eight 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
    - PS and adult uveitis: Initial dose of 80 mg, then maintenance dose starting one week after the initial dose
        - QL: Four 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
    - Adult HS: Initial dose of 160 mg day 1, 80 mg on day 15, then maintenance dose starting on day 29
        - QL: Six 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
    - Adolescent HS:
        - 30 kg to <60 kg: Initial dose of 80 mg on day 1, then maintenance dose starting on day 8
            - QL: Five 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
        - ≥60 kg: 160 mg on day 1, 80 mg on day 15, then maintenance dose starting on day 29
            - QL: Six 40 mg/0.8 mL syringes or pens/autoinjectors (28-day supply)
- Maintenance dose - 40 mg every 2 weeks (14 days) [for HS, pediatric UC (greater than 40 kg), and RA monotherapy **ONLY** - 40 mg once a week (every 7 days) or 80 mg every 2 weeks (14 days)]
    - QL: 20 mg/0.4 mL syringe - 2 syringes/28 days
    - QL: 40 mg/0.8 mL syringe - 2 syringes/28 days
    - QL: 40 mg/0.8 mL pen/autoinjector - 2 pens/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:

- Adult AS, PsA, and RA - 12 months

- PJIA and adolescent uveitis - 12 months
- UC - Loading dose (doses on day 1 and 15 for adults or days 1, 8, and 15 for pediatrics) for 4 weeks, then maintenance dose for 8 additional weeks [12 weeks for total duration of approval]
- CD - Loading dose (doses on day 1 and 15) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- PS and adult uveitis - Loading dose (doses on day 1, 8, 22) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Adult HS and pediatric HS (≥60 kg) - Loading dose (doses on day 1 and 15) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Pediatric HS (30 kg to <60 kg) - Loading dose (doses on day 1, 8, 22) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Other indications - 12 months

Table 3

Diagnosis	Criteria
Moderately to severely active rheumatoid arthritis (RA)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3 months **OR** b. The member has tried and had an inadequate response to another conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA for at least 3 months **OR** c. The member has an intolerance or hypersensitivity to **ONE** of the following conventional agents (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** d. The member has an FDA labeled contraindication to **ALL** of the following conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** e. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA **AND** 2. **ANY** of the following:

	a. The member has tried and had an inadequate response to Humira (adalimumab) **AND** at least **TWO** of the following for at least 3 months: • Enbrel (etanercept) • 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 Humira (adalimumab) **AND** at least **TWO** of the following: • Enbrel (etanercept) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib) 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" and "2"): 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 or AHFS for the treatment of PsA **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Humira (adalimumab) **AND** at least **TWO** of the following for at least 3 months: • Cosentyx (secukinumab) • Enbrel (etanercept) • Otezla (apremilast) • Rinvoq (upadacitinib) • Skyrizi (risankizumab-rzaa) • 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 Humira (adalimumab) **AND TWO** of the following: • Cosentyx (secukinumab) • Enbrel (etanercept) • Otezla (apremilast) • Rinvoq (upadacitinib) • Skyrizi (risankizumab-rzaa) • 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) • Rinvoq (upadacitinib) • Skyrizi (risankizumab-rzaa) • 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) • Rinvoq (upadacitinib) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) • Tremfya (guselkumab) • Xeljanz/Xeljanz XR (tofacitinib)
Moderate to severe plaque psoriasis (PS)	**BOTH** of the following ("1" and "2"): 1. ONE of the following: 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 for at least 3 months **OR**

	b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PS **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS **OR** 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) **OR** 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) **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 or AHFS for the treatment of PS **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Humira (adalimumab) **AND** at least **TWO** of the following for at least 3 months: • Cosentyx (secukinumab) • Enbrel (etanercept) • Otezla (apremilast) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) • Tremfya (guselkumab) **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 Humira (adalimumab) **AND TWO** of the following: • Cosentyx (secukinumab) • Enbrel (etanercept) • Otezla (apremilast) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab)

	• Tremfya (guselkumab) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Otezla (apremilast) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) • Tremfya (guselkumab) **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) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) • Tremfya (guselkumab)
Moderately to severely active Crohn's disease (CD)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: 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 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 CD **OR** c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of CD **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 or AHFS for the treatment of CD **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with adalimumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to **ALL** of the following for at least 3 months: • Humira (adalimumab) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) **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 **ALL** of the following: • Humira (adalimumab) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Humira (adalimumab) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) **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: • Humira (adalimumab) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab)
Moderately to severely active ulcerative colitis (UC)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine,

	balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC 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 UC **OR** c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **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 or AHFS for the treatment of UC **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with adalimumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Humira (adalimumab) **AND** at least **TWO** of the following for at least 3 months: • Rinvoq (upadacitinib) • Stelara (ustekinumab) • 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 Humira (adalimumab) **AND** at least **TWO** of the following: • Rinvoq (upadacitinib) • Stelara (ustekinumab) • Xeljanz/Xeljanz XR (tofacitinib) c. The member has an FDA labeled contraindication to **ALL** of the following: • Humira (adalimumab) • Rinvoq (upadacitinib) • Stelara (ustekinumab) • 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: • Humira (adalimumab) • Rinvoq (upadacitinib) • Stelara (ustekinumab) • Xeljanz/Xeljanz XR (tofacitinib)
Non-infectious intermediate uveitis, posterior uveitis, or panuveitis	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. **BOTH** of the following: i. **ONE** of the following: • The member has tried and had an inadequate response to oral corticosteroids used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for a minimum of 2 weeks **OR** • The member has tried and had an inadequate response to periocular or intravitreal corticosteroid injections in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** • The member has an intolerance or hypersensitivity to oral corticosteroids **OR** periocular or intravitreal corticosteroid injections used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** • The member has an FDA labeled contraindication to **BOTH** oral corticosteroids and periocular/intravitreal corticosteroids **AND** ii. **ONE** of the following: • The member has tried and had an inadequate response to **ONE** conventional systemic agent (i.e., azathioprine, mycophenolate, methotrexate, cyclosporine, tacrolimus) used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for at least 3 months **OR** • The member has an intolerance or hypersensitivity to **ONE** conventional systemic agent used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

	OR • The member has an FDA labeled contraindication to **ALL** conventional systemic agents used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis **OR** 1. 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 non-infectious intermediate uveitis, posterior uveitis, or panuveitis **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Humira (adalimumab) at least 3 months: **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to Humira (adalimumab) **OR** c. The prescriber has provided information indicating why Humira (adalimumab) is not clinically appropriate for the member, AND the prescriber has provided a complete list of previously tried agents for the requested indication
Active ankylosing spondylitis (AS)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **TWO** different NSAIDs used in the treatment of AS for at least a 4-week total trial **OR** b. The member has an intolerance or hypersensitivity to **TWO** different NSAIDs used in the treatment of AS **OR** c. The member has an FDA labeled contraindication to **ALL** NSAIDs used in the treatment of AS **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 or AHFS for the treatment of AS **AND** 2. **ANY** of the following:

	a. The member has tried and had an inadequate response to Humira (adalimumab) **AND** at least **TWO** of the following for at least 3 months: • Cosentyx (secukinumab) • Enbrel (etanercept) • 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 Humira (adalimumab) **AND TWO** of the following: • Cosentyx (secukinumab) • Enbrel (etanercept) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Cosentyx (secukinumab) • 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: • Cosentyx (secukinumab) • Enbrel (etanercept) • Humira (adalimumab) • Rinvoq (upadacitinib) • Xeljanz/Xeljanz XR (tofacitinib)
Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)	**BOTH** of the following ("1" and "2"): 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 FDA 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 or AHFS for the treatment of PJIA **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to **ALL** of the following for at least 3 months: • Enbrel (etanercept) • Humira (adalimumab) • Xeljanz (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 **ALL** of the following: • Enbrel (etanercept) • Humira (adalimumab) • Xeljanz (tofacitinib) **OR** c. The member has an FDA labeled contraindication to **ALL** of the following: • Enbrel (etanercept) • Humira (adalimumab) • Xeljanz (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) • Xeljanz (tofacitinib)

Moderate to severe hidradenitis suppurative (HS)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., oral tetracyclines [doxycycline, minocycline, tetracycline]; oral contraceptives [females only]; metformin [females only]; finasteride [females only]; spironolactone [females only]; intralesional corticosteroids [triamcinolone]; clindamycin in combination with rifampin; combination of rifampin, moxifloxacin, and metronidazole; cyclosporine, oral retinoids) used in the treatment of HS for at least 3 months **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of HS **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of HS **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 or AHFS for the treatment of HS **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Humira (adalimumab) at least 3 months: **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to Humira (adalimumab) **OR** c. The prescriber has provided information indicating why Humira (adalimumab) is not clinically appropriate for the member, AND the prescriber has provided a complete list of previously tried agents for the requested indication\
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 Amjevita (adalimumab-atto) meets the definition of medical necessity when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for Amjevita has been previously approved by Florida Blue
2. Member has had clinical benefit with Amjevita therapy

3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, RA; gastroenterologist for CD, UC; 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 Amjevita
5. Member will **NOT** be using Amjevita in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following ("a", "b", or "c"):
    a. The dosage does not exceed 40 mg every 2 weeks (14 days) [for HS, pediatric UC (greater than 40 kg), and RA monotherapy **ONLY** - 40 mg once a week (every 7 days) or 80 mg every 2 weeks (14 days)]
        - QL: 20 mg/0.4 mL syringe - 2 syringes/28 days
        - QL: 40 mg/0.8 mL syringe - 2 syringes/28 days
        - QL: 40 mg/0.8 mL pen/autoinjector - 2 pens/28 days
    b. The requested quantity (dose) is greater than program's quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
    c. The requested quantity (dose) is greater that the program's quantity limit and greater than the maximum FDA labeled dose **AND** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication, **AND** the prescriber has provided information in support of therapy with a higher dose for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

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

Table 3

Table 2: FDA-approved indications and recommended dosing	
Indication	**Dosage†**
Ankylosing Spondylitis	• 40 mg every other week
Crohn's Disease (CD)	Weight 17 kg to less than 40 kg: • Initial: 80 mg at week 0, and 40 mg at week 2 (day 15) • Maintenance: 20 mg every other week beginning at week 4

	Weight 40 kg or greater: • Initial: 160 mg at week 0, and 80 mg at week 2 (day 15) • Maintenance: 40 mg every other week beginning at week 4
Hidradenitis Suppurativa [Humira only]	≥60 kg (132 lbs.): • Initial: 160 mg at week 0, followed by 80 mg at week 2 (day 15) • Maintenance: 40 mg every week or 80 mg every other week beginning at week 4 (day 29) 30 kg (66 lbs.) to <60 kg (132 lbs.): • Initial: 80 mg at week 0, followed by 40 mg at week 1 (day 8) • Maintenance: 40 mg every 2 weeks beginning at week 3 (day 22)
Juvenile Idiopathic Arthritis (JIA)	Dose is based on weight: • 15 kg to 29.9 kg (33-66 lbs): 20 mg every other week • 30 kg or more: 40 mg every other week
Plaque Psoriasis	• Initial: 80 mg at week 0 • Maintenance: 40 mg every other week beginning at week 1
Psoriatic Arthritis (PsA)	• 40 mg every other week
Rheumatoid Arthritis (RA)	• Concomitant DMARD: 40 mg every other week • Monotherapy: 40 mg weekly or 80 mg every other week

Ulcerative Colitis (UC)
 	
[pediatric UC for Humira only]
	Adult (≥18 years old):
	• Initial: 160 mg at week 0, followed by 80 mg at week 2 (day 15)
	• Maintenance: 40 mg every other week beginning at week 4 (day 29)
	Pediatric:
	• 20 kg (44 lbs.) to <40 kg (88 lbs.):
	  ○ Initial: 80 mg on week 0 (day 1), followed by 40 mg on weeks 1 and 2 (days 8 and 15)
	  ○ Maintenance: 40 mg every other week or 20 mg weekly beginning at week 4 (day 29)
	• 40 kg (88 lbs.) or more:

	○ Initial: 160 mg (single dose or split over two consecutive days) on week 0 (day 1), followed by 80 mg on weeks 1 and 2 (days 8 and 15) ○ Maintenance: 80 mg every other week or 40 mg weekly beginning at week 4 (day 29)
Uveitis (non-infectious intermediate, posterior and panuveitis) [Humira only]	Adult (≥18 years old): • Initial: 80 mg at week 0 • Maintenance: 40 mg every other week beginning at week 1 Pediatric • ≥30 kg (66 lbs.): 40 mg every other week • 15 kg (33 lbs.) to <30 kg (66 lbs.): 20 mg every other week • 10 kg (22 lbs.) to <15 kg (33 lbs.): 10 mg every other week
[†]Administered as a subcutaneous injection	

- **Dose Adjustments:** dosage adjustments are not required for members with hepatic or renal impairment.
- **Drug Availability:**

  Humira

  - **Starter Packs**
    - Starter Pack for Psoriasis, Uveitis, and Adolescent Hidradenitis Suppurativa [four 40 mg/0.8 mL pens]
    - Starter Pack for Psoriasis, Uveitis, and Adolescent Hidradenitis Suppurativa (citrate-free) [four 40 mg/0.4 mL pens]
    - Starter Pack for Psoriasis, Uveitis, and Adolescent Hidradenitis Suppurativa (citrate-free) [one 80 mg/0.8 mL and two 40 mg/0.4 mL pens]
    - Starter Pack for Crohn's Disease, Ulcerative Colitis, and Hidradenitis Suppurativa [six 40 mg/0.8 mL pens]
    - Starter Pack for Crohn's Disease, Ulcerative Colitis, and Hidradenitis Suppurativa (citrate-free) [six 40 mg/0.4 mL pens]
    - Starter Pack for Crohn's Disease, Ulcerative Colitis, and Hidradenitis Suppurativa (citrate-free) [three 80 mg/0.8 mL pens]
    - Starter Pack for Pediatric Ulcerative Colitis (citrate-free) [four 80 mg/0.8 mL pens]
    - Starter Pack for Pediatric Crohn's Disease (<40 kg) [three 40 mg/0.8 mL syringes]
    - Starter Pack for Pediatric Crohn's Disease (<40 kg) (citrate-free) [one 80 mg/0.8 mL and one 40 mg/0.4 mL syringe]

- Starter Pack for Pediatric Crohn's Disease (≥40 kg) [six 40 mg/0.8 mL syringes]
- Starter Pack for Pediatric Crohn's Disease (≥40 kg) (citrate-free) [three 80 mg/0.8 mL syringes]

- **Pen**
  - 80 mg/0.8 mL single-use pen (citrate-free)
  - 40 mg/0.8 mL single-use pen - carton of two pens
  - 40 mg/0.4 mL single-use pen (citrate-free) - carton of two pens
- **Prefilled Syringe**
  - 80 mg/0.8 mL single-use syringe (citrate-free) – only available in starter packs
  - 40 mg/0.8 mL single-use syringe - carton of two syringes
  - 40 mg/0.4 mL single-use syringe (citrate-free) - carton of two syringes
  - 20 mg/0.4 mL single-use syringe - carton of two syringes
  - 20 mg/0.2 mL single-use syringe (citrate-free) - carton of two syringes
  - 10 mg/0.2 mL single-use syringe - carton of two syringes
  - 10 mg/0.1 mL single-use syringe (citrate-free) - carton of two syringes
- **Single-Use Institutional Use Vial**
  - 40 mg/0.8 mL single-use vial – carton of one vial

Amjevita

- **Autoinjector/Pen**
  - 40 mg/0.8 mL single-use pen (citrate-free) - carton of one or two pens
- **Prefilled Syringe**
  - 40 mg/0.8 mL single-use syringe (citrate-free) - carton of one or two syringes
  - 20 mg/0.4 mL single-use syringe (citrate-free) - carton of one syringe

PRECAUTIONS:

Boxed Warning

- **Infections:** 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.
- **Malignancy:** lymphoma and other malignancies, some fatal have been reported in children and adolescent individuals treated with TNF blockers including adalimumab. 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.

Contraindications

- None

Warnings/Precautions

Serious Infections: adalimumab products should not be initiated in members during an active infection. If an infection develops, monitor carefully, and discontinue adalimumab if infection becomes serious.

- **Invasive fungal infections:** If a member develops a systemic infection while on an adalimumab product, 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 the adalimumab product 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 the adalimumab product.
- **Heart failure:** worsening or new onset heart failure may occur.
- **Lupus-like syndrome:** discontinue the adalimumab product if syndrome develops.
- **Drug Interactions:** avoid concomitant use with abatacept (Orencia) and anakinra (Kineret), due to increased risk of serious infection.
- **Live vaccines:** Avoid administration of live vaccines (e.g., varicella and MMR) in members taking an adalimumab product.
- **Pregnancy and Lactation**
    - Available studies with use of adalimumab during pregnancy do not reliably establish an association between adalimumab and major birth defects.
    - 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:

HCPCS Coding:

J0135	Adalimumab (Humira) Injection 20 mg
J3590	Unclassified biologics [for Amjevita only]

ICD-10 Diagnosis Codes That Support Medical Necessity:

H20.00 – H20.9	Iridocyclitis
H44.111 – H44.119	Panuveitis
H44.131 - H44.139	Sympathetic uveitis
K50.00 – K50.919	Crohn’s disease [regional enteritis]
K51.00 – K51.919	Ulcerative colitis
K52.3	Indeterminate colitis
L40.0	Psoriasis vulgaris
L40.50 – L40.59	Arthropathic psoriasis

L73.2	Hidradenitis suppurativa
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
M08.1	Juvenile ankylosing spondylitis
M08.3	Juvenile Rheumatoid polyarthritis (seronegative)
M08.89	Other juvenile arthritis, multiple sites
M35.2	Behçet's disease
M45.0 – M45.9	Ankylosing spondylitis
M46.81 – M46.89	Other specified inflammatory spondylopathies

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.

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:

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.

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).

Hidradenitis suppurativa (HS) (a.k.a., acne inversa): a chronic, inflammatory, recurrent, debilitating skin disease of the hair follicle that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillae, inguinal and anogenital regions. HS may have a large impact on quality of life, often causing depression, impaired sexual health, and embarrassment. Squamous cell carcinoma may arise from chronic (10-30 years of evolution) lesions. The main goals of treatment are to prevent the formation of new lesion, treat new lesions, and eliminate existing nodules and sinus tract to limit or prevent scar formation.

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.

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 which 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
Anakinra (Kineret), 09-J0000-45
Apremilast (Otezla) Tablet, 09-J2000-19
Baricitinib (Olumiant), 09-J3000-10
Brodalumab (Siliq) Injection, 09-J2000-74
Certolizumab Pegol (Cimzia), 09-J0000-77

Etanercept (Enbrel), 09-J0000-38
Golimumab (Simponi, Simponi Aria), 09-J1000-11
Guselkumab (Tremfya), 09-J2000-87
Infliximab Products [infliximab (Remicade), infliximab-dyyb (Inflectra), and infliximab-abda (Renflexis)], 09-J0000-39
Ixekizumab (Taltz), 09-J2000-62
Rituximab (Rituxan), 09-J0000-59
Risankizumab (Skyrizi), 09-J3000-45
Sarilumab (Kevzara), 09-J2000-87
Secukinumab (Cosentyx), 09-J2000-30
Tildrakizumab-asmn (Ilumya), 09-J3000-04
Tocilizumab (Actemra) Injection, 09-J1000-21
Tofacitinib (Xeljanz, Xeljanz XR) Tablets, 09-J1000-86
Upadacitinib (Rinvoq), 09-J3000-51
Ustekinumab (Stelara), 09-J1000-16
Vedolizumab (Entyvio) Injection, 09-J2000-18

OTHER:

Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy

Actemra (tocilizumab)

Adbry (tralokinumab-ldrm)

Amjevita (adalimumab-atto)

Arcalyst (rilonacept)

Avsola (infliximab-axxq)

Benlysta (belimumab)

Cimzia (certolizumab)

Cinqair (reslizumab)

Cosentyx (secukinumab)

Dupixent (dupilumab)

Enbrel (etanercept)

Entyvio (vedolizumab)

Fasenra (benralizumab)

Humira (adalimumab)

Ilaris (canakinumab)

Ilumya (tildrakizumab-asmn)

Inflectra (infliximab-dyyb)

Infliximab

Kevzara (sarilumab)

Kineret (anakinra)

Nucala (mepolizumab)

Orencia (abatacept)

Remicade (infliximab)

Renflexis (infliximab-abda)

Riabni (rituximab-arrx)

Rituxan (rituximab)

Rituxan Hycela (rituximab/hyaluronidase human)

Ruxience (rituximab-pvvr)

Siliq (brodalumab)

Simponi (golimumab)

Simponi Aria (golimumab)

Skyrizi (risankizumab-rzaa)

Stelara (ustekinumab)

Taltz (ixekizumab)

Tezspire (tezepelumab-ekko)

Tremfya (guselkumab)

Truxima (rituximab-abbs)

Tysabri (natalizumab)

Xolair (omalizumab)

Table 4: 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 5: 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. Alhusayen R, Shear NH. Pharmacologic interventions for hidradenitis suppurativa: what does the evidence say? Am J Clin Dermatol. 2012 Oct 1;13(5):283-91.
2. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part II: Topical, intralesional, and systemic medical management. J Am Acad Dermatol. 2019 Jul;81(1):91-101. Epub 2019 Mar 11.
3. Amjevita (adalimumab-atto injection) [package insert]. Amgen Inc. Thousand Oaks (CA): July 2022.
4. Angeles-Han ST, Ringold S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis. Arthritis Rheumatol. 2019 Jun;71(6):864-877. Epub 2019 Apr 25.
5. Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. J Am Acad Dermatol. 2017 Feb;76(2):290-298.
6. 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.
7. Barry RJ, Nguyen QD, Lee RW, et al. Pharmacotherapy for uveitis: current management and emerging therapy. Clin Ophthalmol. 2014 Sep 22; 8:1891-911. doi: 10.2147/OPTH.S47778.
8. Blok JL, van Hattem S, Jonkman MF, et al. Systemic therapy with immunosuppressive agents and retinoids in hidradenitis suppurativa: a systematic review. Br J Dermatol. 2013;168(2):243.
9. Callhoff J, Sieper J, Weiß A, et al. Efficacy of TNFα blockers in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Ann Rheum Dis. 2015 Jun;74(6):1241-8.
10. Canadian Psoriasis Guidelines Addendum Committee. 2016 Addendum to the Canadian Guidelines for the Management of Plaque Psoriasis 2009. J Cutan Med Surg. 2016 Sep;20(5):375-431.
11. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 10/25/22.
12. 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.

13. Dogra S, Jain A, Kanwar AJ. Efficacy and safety of acitretin in three fixed doses of 25, 35 and 50 mg in adult patients with severe plaque type psoriasis: a randomized, double blind, parallel group, dose ranging study. J Eur Acad Dermatol Venereol. 2013 Mar;27(3):e305-11.
14. Dogra S, Krishna V, Kanwar AJ. Efficacy and safety of systemic methotrexate in two fixed doses of 10 mg or 25 mg orally once weekly in adult patients with severe plaque-type psoriasis: a prospective, randomized, double-blind, dose-ranging study. Clin Exp Dermatol. 2012 Oct;37(7):729-34.
15. Elmets CA, Leonardi CL, Davis DM, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. J Am Acad Dermatol. 2019 Apr;80(4):1073-1113. Epub 2019 Feb 13.
16. Elmets CA, Lim HW, Stoff H, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. J Am Acad Dermatol. Epub 2019 July 25.
17. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. [cited 2022 October 25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/.
18. Feuerstein JD, Ho EY, Shmidt E, Singh H, Falck-Ytter Y, Sultan S, Terdiman JP; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021 Jun;160(7):2496-2508.
19. Feuerstein JD, Isaacs KL, Schneider Y, et al.; AGA Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020 Apr;158(5):1450-1461. 2020 Jan 13.
20. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021 Jul;73(7):924-939.
21. Gener G, Canoui-Poitrine F, Revuz JE, et al. Combination therapy with clindamycin and rifampicin for hidradenitis suppurativa: a series of 116 consecutive patients. Dermatology. 2009;219(2):148-54.
22. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis. 2016 Mar;75(3):499-510.
23. 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.
24. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018 Jun;77(6):808-818. Epub 2018 Apr 6.
25. Heydendael VM, Spuls PI, Opmeer BC, et al. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis. N Engl J Med 2003; 349:658-65.
26. Humira (adalimumab) [package insert]. AbbVie Inc. North Chicago (IL): February 2021.
27. Ingram JR, Woo PN, Chua SL, et al. Interventions for hidradenitis suppurativa. Cochrane Database Syst Rev. 2015 Oct 7;(10):CD010081.
28. Jemec GB. Clinical practice. Hidradenitis suppurativa. N Engl J Med. 2012 Jan;366(2):158-64.
29. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. J Am Acad Dermatol 2009; 60:824-37.
30. Levy-Clarke G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. Ophthalmology. 2014 Mar;121(3):785-96. e3.

31. 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.
32. Kimball AB, Kerdel F, Adams D, et al. Adalimumab for the treatment of moderate to severe Hidradenitis suppurativa: a parallel randomized trial. Ann Intern Med 2012; 157:846-855.
33. 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.
34. Kroon FP, van der Burg LR, Ramiro S, et al. non-steroidal anti-inflammatory drugs (NSAIDs) for axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis). Cochrane Database Syst Rev. 2015 Jul 17;7:CD010952.
35. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
36. Maz M, Chung SA, Abril A, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. Arthritis Care Res (Hoboken). 2021 Aug;73(8):1071-1087.
37. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65:137-74.
38. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 2009 Sep;61(3):451-85
39. 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.
40. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/25/22.
41. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Oligoarthritis, Temporomandibular Joint Arthritis, and Systemic Juvenile Idiopathic Arthritis. Arthritis Care Res (Hoboken). 2022 Apr;74(4):521-537. Epub 2022 Mar 1.
42. 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.
43. 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.
44. Rambhatla PV, Lim HW, Hamzavi I. A systematic review of treatments for hidradenitis suppurativa. Arch Dermatol. 2012 Apr;148(4):439-46.
45. Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2022 Oct 19:ard-2022-223297. Epub ahead of print.
46. 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.

47. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 Mar;114(3):384-413.
48. Rudwaleit M, van der Heijde D, Landewé R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011 Jan;70(1):25-31.
49. Sbidian E, Chaimani A, Garcia-Doval, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2021 Apr 19;4(4):CD011535. Update in: Cochrane Database Syst Rev. 2022 May 23;5:CD011535.
50. 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.
51. Scott DL, Kinglsey GH. Tumor necrosis factor inhibitors in rheumatoid arthritis. N Engl J Med 2006; 355:704-12.
52. 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.
53. Smith CH, Jabbar-Lopez JK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. Br J Dermatol 2017; 177: 628-136.
54. 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.
55. Suhler EB, Lowder CY, Goldstein DA, et al. Adalimumab therapy for refractory uveitis: results of a multicentre, open-label, prospective trial. Br J Ophthalmol. 2013 Apr;97(4):481-6.
56. Tracey D, Klareskog L, Sasso EH, et al. Tumor necrosis factor antagonist mechanism of action: a comprehensive review. Pharmacol Ther 2008; 117:244-79.
57. van der Zee HH, Boer J, Prens EP, et al. The effect of combined treatment with oral clindamycin and oral rifampicin in patients with hidradenitis suppurativa. Dermatology. 2009;219(2):143-7. Epub 2009 Jul 08
58. 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.
59. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1285-1299. Epub 2019 Aug 21.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/08/23.

GUIDELINE UPDATE INFORMATION:

01/01/05	New Medical Coverage Guideline.
08/15/05	Revised and Updated: Updated description, dosage/administration. Deleted precautions, updated when services are not covered, billing/coding information, and definitions, table 1, references.
11/15/05	Updated when services are covered for psoriatic arthritis, updated ICD-9 codes, definitions, and references.
11/15/06	Scheduled review: added indication of ankylosing spondylitis, added ICD-9 code, corrected CPT-4 coding and updated references.
01/01/07	MCG revised to include Medicare Part D as program exception.
04/15/07	Revision; consisting of adding Crohn's disease indication and ICD-9 code, related guidelines and definitions.
06/15/07	Review and revision; consisting of reformatting, updating related guidelines and references.
03/15/08	Revision; consisting of adding plaque psoriasis and juvenile idiopathic arthritis (JIA) as covered indications, rewording coverage criteria for Crohn's disease, updated dosage and administration section, added ICD-9 codes and updated references.
05/15/08	Review and revision; consisting of reformatting, adding a black box warning under "PRECAUTIONS", adding related guideline and updating references.
09/15/08	Revision of guideline; consisting of adding 3 ICD-9 codes.
01/01/09	Annual HCPCS coding update: deleted code 90772; added code 96372.
09/15/09	Review and revision; consisting of updating references, boxed warning and ICD-9 coding.
04/15/10	Revision; consisting of adding specific continuation criteria.
08/15/10	Review and revision; consisting of adding age criteria to all indications, updated precautions and references.
01/15/11	Revision; consisting of adding ICD-10 codes.
04/01/11	Revision; consisting of adding dosage limitations.
08/15/11	Review and revision to guideline; consisting of updating the precautions section, coding and references.
08/15/12	Review and revision to guideline; consisting of reformatting position statement, updating precautions and references.
09/15/12	Revision to guideline consisting of modifying plaque psoriasis criteria and continuation criteria.
11/15/12	Revision to guideline consisting of adding new indication of ulcerative colitis.
01/15/13	Revision to guideline; consisting of revising/reformatting/updating position statement, description, dosage/administration sections; reformatting precautions section; updating references.
04/15/13	Revision to guideline; consisting of revising position statement to include Orphan Drug indications and duration of approval
09/15/13	Review and revision to guideline; consisting of reformatting position statement, updating program exceptions section and references.
01/01/14	Revision to guideline; consisting of updating position statement.

04/15/14	Revision to guideline; consisting of reformatting and revising position statement to include clarifying language.
09/15/14	Review and revision to guideline; consisting of updating position statement, references, coding and related guidelines.
12/15/14	Revision to guideline; consisting of position statement, dosage/administration, references
09/15/15	Review and revision to guideline; consisting of consisting of updating description section, position statement, billing/coding, related guidelines, and references.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/15	Revision to guideline; consisting of updating description section, position statement, dosage/administration, and references based on a new FDA-approved indication.
02/15/16	Revision to guideline consisting of updating maximum dosages for pediatric patients in the position statement.
09/15/16	Review and revision to guideline consisting of consisting of updating description section, position statement, billing/coding, definitions, related guidelines, and references.
10/01/16	Revision: ICD-10 code updates
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.
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, related guidelines, and references.
12/15/18	Revision to guideline consisting of updating the description, position statement, dosage/administration, and references based on new pediatric/adolescent indications.
10/15/19	Review and revision to guideline consisting of updating the description, position statement, billing/coding, related guidelines, and references.
01/01/20	Revision to guideline consisting of updating the position statement “Note” due to changes in preferred products.
03/15/20	Revision to guideline consisting of updating the description section.
07/01/20	Review and revision to guideline consisting of consisting of updating the description section, position statement, definitions, billing/coding, and other.
01/01/21	Review and revision to guideline consisting of updating the description, position statement and references.
02/15/21	Revision to guideline consisting of updating the description, position statement, dosage/administration, and references.
05/15/21	Revision to guideline consisting of updating the description, position statement, dosage/administration, other section, and references.
09/15/21	Update to Table 1 in Position Statement.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the description, position statement and references.
02/15/22	Revision to guideline consisting of updating the description and position statement.
03/15/22	Revision to guideline consisting of updating the position statement and other sections.

05/15/22	Update to Table 1 in Position Statement.
07/15/22	Update to Table 1 in Position Statement.
09/15/22	Update to Table 1 in Position Statement.
01/01/23	Review and revision to guideline consisting of updating the description section (biosimilar information), position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination. For UC, added allowance for Humira to be used first line for members with severe disease and/or risk factors for disease complications.
04/01/23	Revision to guideline consisting of updating the title, description section, position statement, dosage/administration, billing/coding, other section, and references. MCG renamed Adalimumab Products (Humira and biosimilars). Amjevita added to the policy as a Step 3c agent with Humira always a required prerequisite.