Health Care Provider Administered (HCPA) Biologic Immunomodulator Medical Drug Criteria Program Summary

For BCBS KS, this program only targets the following non-preferred infliximab agents: Infliximab, Remicade, Renflexis

For BCBS KS, the following preferred infliximab agents are **not** subject to prior authorization: Avsola, Inflectra

POLICY REVIEW CYCLE

Effective Date 06-01-2025 **Date of Origin**

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Avsola™ (infliximab-axxq) Intravenous infusion	Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Ulcerative Colitis (UC) who have had an inadequate response to conventional therapy Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in combination with methotrexate in adult patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS) Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis (PSA) Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PS) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.		20
Inflectra®	Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with		1

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Agent(s)	FDA Indication(s)	Notes	Ref#
(infliximab-dyyb) Intravenous infusion	moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Ulcerative Colitis (UC) who have had an inadequate response to conventional therapy Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in combination with methotrexate in adult patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS) Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis (PSA) Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PS) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.		
Remicade®, Infliximab Intravenous infusion	Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Ulcerative Colitis (UC) who have had an inadequate response to conventional therapy Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in combination with methotrexate in adult patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS)		2

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Agent(s)	FDA Indication(s)	Notes	Ref#
	Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis (PSA) Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PS) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.		
Renflexis® (infliximab-abda) Intravenous infusion	Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Ulcerative Colitis (UC) who have had an inadequate response to conventional therapy Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in combination with methotrexate in adult patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS) Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis (PSA) Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PS) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.		3

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

RHEUMATOID DISORDERS - Ankylosing Spondylitis (AS)	Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis, enthesitis, and a marked propensity for sacroiliac joint and spinal fusion. AS is distinguished by universal involvement with sacroiliac joint inflammation or fusion and more prevalent spinal ankylosis. Goals of treatment for AS are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstays of treatment have been nonsteroidal anti-inflammatory drugs (NSAIDs) and exercise/physical therapy.(4,28)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	NSAIDs are used as first line therapy for patients with active AS, with continuous treatment with NSAIDs being preferred. In patients with stable disease, NSAIDs may be used on-demand to decrease the risk of adverse effects with long term use.(12,13,28) No particular NSAID is recommended as a preferred option.(12) Biologics should be used in patients who continue to have persistently high disease activity despite NSAIDs. Failure of standard treatment with NSAIDs can be defined as a lack of response (or intolerance) to at least 2 NSAIDs after at least a 4-week duration of therapy in total.(13,28) Tumor necrosis factor (TNF) inhibitors or interleukin (IL)-17 inhibitors are recommended as initial biologic therapy.(12,13) Other present comorbidities (e.g., inflammatory bowel disease, psoriasis, uveitis) can help guide selection of the initial biologic agent/drug class.(12,13,28) Patients who have an inadequate response to a TNF inhibitor or IL-17 inhibitor may switch to a biologic of the other drug class, or switch to a Janus kinase (JAK) inhibitor.(12,13) Patients with secondary failure to a biologic (presence of antidrug antibodies) may switch to another biologic of the same or different mode of action.(12) Systemic glucocorticoids should generally not be used in the treatment of AS. Short-term glucocorticoid injections may be used in select patients with peripheral signs and symptoms. Conventional disease-modifying antirheumatic drugs (cDMARDs) (e.g., methotrexate, sulfasalazine, leflunomide) are not recommended as treatment due to their lack of efficacy. However, sulfasalazine may be considered in patients with peripheral arthritis.(12,13,28)
RHEUMATOID DISORDERS- Rheumatoid Arthritis (RA)	Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that primarily affects the joints but can also damage extra-articular organs. The main goal of therapy is to achieve remission, but additional goals include decreased disease activity, prevention of systemic complications, and improved physical functioning.(11) 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.(5) The American College of Rheumatology (ACR) guidelines (2021) list the following guiding principles in the treatment of RA:(5) • 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 disease-modifying antirheumatic drug(s) (DMARDs) chosen • Recommendations are limited to DMARDs approved by the US FDA for treatment of RA: o Conventional synthetic DMARDs (csDMARDs): hydroxychloroquine, sulfasalazine, methotrexate (MTX), leflunomide o Biologic DMARDs (bDMARDS): Tumor necrosis factor (TNF) inhibitors (e.g., etanercept, adalimumab, infliximab, golimumab, certolizumab), T cell costimulatory inhibitors (e.g., abatacept), Interleukin (IL)-6 inhibitors (e.g., tocilizumab, sarilumab), anti-CD20 antibody* (e.g., rituximab) ▪ *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

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	o Targeted synthetic DMARDs (tsDMARDs): Janus kinase (JAK) inhibitors (e.g., tofacitinib, baricitinib, upadacitinib) • Triple therapy refers to hydroxychloroquine, sulfasalazine, and either methotrexate or leflunomide • Biosimilars are considered equivalent to FDA-approved originator bDMARDs • 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 guideline (2021) treatment recommendations are broken down by previous treatment and disease activity:(5) • DMARD-naïve patients with moderate-to-high disease activity initial treatment: o MTX monotherapy is strongly recommended over hydroxychloroquine, sulfasalazine, bDMARDs monotherapy, tsDMARD monotherapy, or combination of MTX plus a non-TNF bDMARD or tsDMARD o 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: o Hydroxychloroquine is conditionally recommended over other csDMARDs o Sulfasalazine is conditionally recommended over MTX o MTX is conditionally recommended over leflunomide • Initial therapy in csDMARD-treated patients, but MTX naïve, with moderate-to high disease activity: o MTX monotherapy is conditionally recommended over combination MTX plus a bDMARD or tsDMARD • Treatment modifications in patients treated with DMARDs who are not at target: o 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 o 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 The European Alliance of Associations for Rheumatology (EULAR) guidelines for RA (2022 update) also recommend a treat-to-target approach in therapy. MTX is recommended as first line therapy and should be initiated as soon as the diagnosis of RA is made. If MTX is not clinically appropriate, then an alternative csDMARD should be used as part of the (first) treatment strategy. If initial csDMARD therapy does not produce adequate improvement after 3 months, another csDMARD may be added or switched to as long as poor prognosis factors are absent. In the presence of poor prognosis factors, a bDMARD or JAK inhibitor should be added to csDMARD therapy. If treatment failure occurs with the initial bDMARD or JAK inhibitor, another bDMARD or JAK inhibitor should be considered. If a TNF- or IL-6 receptor inhibitor therapy was initially failed, patients may receive an agent with another mode of action or a second TNF- or IL-6 receptor inhibitor.(10)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	Initial dosing of MTX for RA should optimally be 15 mg once weekly, with the dose increased as tolerated and as needed to control signs and symptoms. A fast dose escalation of 5 mg/month to 25-30 mg/week has been associated with higher efficacy, but toxicity with this dosing regimen is a limiting factor.(15) In the presence of sufficient folic acid supplementation, the MTX dose can be rapidly escalated to 25 mg once weekly.(10) The MTX target dose is 25 mg weekly, or the highest tolerable dose.(10,15)
RHEUMATOID DISORDERS - Psoriatic Arthritis (PsA)	Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis (PS), most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient due to one of the following: actively inflamed joints, dactylitis, enthesitis, axial disease, active skin and/or nail involvement, and/or extraarticular manifestations such as uveitis or inflammatory bowel disease (IBD).(19) Disease severity is based on the assessment of the level of disease activity at a given point in time, and the presence/absence of poor prognostic factors and long-term damage. Severe PsA is defined in the American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA and includes the presence of one or more of the following:(19) • Erosive disease • Elevated markers of inflammation (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) attributable to PsA • Long-term damage that interferes with function (e.g., joint deformities, vision loss) • Highly active disease that causes a major impairment in quality of life, such as: o Active PsA at many sites including dactylitis and enthesitis o Function-limiting PsA at a few sites • Rapidly progressive disease Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis disorders, particularly spondyloarthritis and rheumatoid arthritis, and other management strategies of the cutaneous manifestations of psoriasis. Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and local glucocorticoid injections.(19) Only patients with very mild peripheral disease may sufficiently benefit from NSAIDs as monotherapy, and instead patients are typically treated with disease-modifying antirheumatic drugs (DMARDs) and/or biologics. Efficacy of DMARD and biologic therapies should be assessed 3 months after initiation, and if adequate improvement is not seen then the treatment regimen should be updated or changed.(9) The ACR-NPF guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and treatment recommendations for active disease are as follows:(19) • Treatment naïve patients: o First line options include oral small molecules (OSM), tumor necrosis factor (TNF) inhibitors, interleukin (IL)-17 inhibitors, and IL-12/23 inhibitors ▪ OSM (i.e., methotrexate [MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe PS, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitors ▪ Biologics (e.g., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe PS

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	• Previous treatment with OSM and continued active disease: o Switch to a biologic (i.e., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor); recommended over switching to a different OSM ▪ Biologic monotherapy is conditionally recommended over biologic plus MTX combination therapy o Switch to a different OSM (except apremilast) OR add on apremilast to current OSM therapy; recommended over adding another OSM o Add another OSM (except apremilast) to current OSM therapy; may consider for patients that have exhibited partial response to current OSM o Switch to apremilast monotherapy; may be considered instead of adding apremilast to current OSM therapy if the patient has intolerable side effects with the current OSM • Previous treatment with a biologic and continued active disease: o Switch to another biologic (e.g., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) as monotherapy o Add MTX to the current biologic; may consider adding MTX in patients with a partial response to current biologic therapy The European Alliance of Associations for Rheumatology (EULAR) guidelines for PsA (2023 update) also recommend a treat-to-target approach in therapy. MTX (preferred) or another conventional synthetic disease-modifying antirheumatic drug (csDMARD) (e.g., sulfasalazine, leflunomide) should be used for initial therapy. If the treatment target is not achieved with a csDMARD, a biologic should be initiated with preference of product being based on patient specific disease characteristics. Biologics include TNF inhibitors, IL-12/23 inhibitors, IL-17A inhibitors, IL-17A/F inhibitors, IL-23 inhibitors, and cytotoxic T-lymphocyte–associated antigen 4 (CTLA4) analogs. No order of preference of biologics is provided since none have demonstrated superiority for joint involvement, however, CTLA4 analogs are least preferred due to limited efficacy in clinical trials. The use of a Janus kinase (JAK) inhibitor (e.g., tofacitinib, upadacitinib) may be used after failure of a biologic or if biologics are not clinically appropriate for the patient. However, careful consideration should be applied prior to using a JAK inhibitor due to the increased risk of cardiovascular and malignancy events in older patients with RA and cardiovascular risk factors. A phosphodiesterase-4 (PDE4) inhibitor (i.e., apremilast) may be considered in patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a biologic nor a JAK inhibitor is appropriate. Patients with an inadequate response to a biologic or JAK inhibitor may switch to a different drug within the same class or switch to a different mode of action. Adding MTX to a biologic may increase drug survival by limiting the development of antidrug antibodies, especially for TNF inhibitors.(9)
DERMATOLOGICAL DISORDERS - Psoriasis (PS)	Psoriasis (PS) is a chronic inflammatory skin and systemic disorder. It is a complex disease that affects the skin and joints and is associated with numerous comorbidities, including obesity and inflammatory bowel disease. Psoriasis vulgaris, or plaque psoriasis, is a cutaneous form that often presents with pink plaques with silvery scale on the scalp, elbows, knees, or presacral region, but any area of the skin may be involved.(21,23) Plaque psoriasis is the most common form (affecting 90% of adults with psoriasis), but others include guttate, erythrodermic, pustular, inverse, nail, and psoriatic arthritis (PsA). PS is clinically diagnosed based on the presence of cutaneous and systemic symptoms, and treatment is similar for most forms but is guided by the body surface area (BSA) involved.(7) The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (greater than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when it causes serious emotional consequences, occurs in select locations (e.g., hands, feet, scalp, face, or genital area), or when it causes intractable pruritus.(21) Topical therapies are most commonly used to treat mild to moderate PS, but they may be used in combination with phototherapy, systemic, or biologic therapies for the treatment of moderate to severe PS.(14) Topical therapies alone can be sufficient for managing limited disease and also have fewer significant adverse effects compared to

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	systemic treatment options. However, topical therapies may be inadequate to obtain and maintain skin clearance, and systemic therapies may be warranted. Conventional systemic agents are widely used as monotherapy or in combination with biologics for moderate to severe disease, and they are beneficial for widespread disease and ease of administration.(23) Biologics are routinely used when one or more conventional agents fail to produce an adequate response, but are considered first line in patients with severe PS or patients with concomitant severe PsA.(19) The NPF medical board recommends a treat-to-target approach to therapy for psoriasis that includes the following:(22) • The preferred assessment instrument for determining treatment response is BSA • The preferred time to perform initial evaluation of treatment response is after 3 months • Target response after treatment initiation should be BSA less than or equal to 1% after 3 months • Acceptable response is either a BSA less than or equal to 3% or a BSA improvement greater than or equal to 75% from baseline at 3 months after treatment initiation Selection of treatment is based on several factors including benefit-risk assessment, clinical presentation, disease severity, and comorbidities.(22) The AAD/NPF psoriasis treatment guidelines support the following treatment options: • Topical therapies:(14) o Topical corticosteroids (TCS) o Topical calcineurin inhibitors (TCIs), such as tacrolimus and pimecrolimus o Vitamin D analogues (e.g., calcipotriene and calcitriol) o Tazarotene (topical retinoid) o Coal tar preparations o Topical anthralin • Psoralen plus ultraviolet light (PUVA) phototherapy(16) • Systemic non-biologic therapies:(32) o Methotrexate (MTX) o Cyclosporine o Acitretin o Apremilast • Biologic therapies:(21) o Tumor necrosis factor (TNF)-α inhibitors (e.g., adalimumab, certolizumab, etanercept, infliximab) o Interleukin (IL)-17 inhibitors (e.g., brodalumab, ixekizumab, secukinumab) o IL-23 inhibitors (e.g., guselkumab, risankizumab, tildrakizumab) o IL-12/IL-23 Inhibitors (e.g., ustekinumab) o *Note: Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics was published in 2019. No specific biologic drug/class is recommended as first-line for all patients with psoriasis, and instead choice of therapy should be individualized based on patient specific factors. Additional biologic drugs have since received FDA approval for psoriasis that are not discussed. Primary failure for biologics is defined as initial nonresponse to treatment. Primary failure to a tumor necrosis factor (TNF)-α inhibitor does not preclude successful response to a different TNF-α inhibitor, and failure of another biologic therapy does not preclude successful response to ustekinumab. All biologics may lose efficacy in a patient who initially responds favorably to the medication (secondary failure), and loss of efficacy may be attributed to the presence of antidrug antibodies. The concomitant

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	use of MTX with a biologic may increase drug survival by limiting antibody formation.(21) For the treatment of PS in the pediatric patient population, topical corticosteroids are the mainstay option based on extensive clinical experience that supports efficacy. Topical calcineurin inhibitors are also a treatment option and may be preferred for psoriasis of the face, genitalia, and body folds. Vitamin D analogues are recommended as a treatment option for childhood plaque psoriasis and are considered safe, effective, and generally well tolerated. Other topical therapies that may be used for the treatment of pediatric psoriasis include tazarotene, anthralin, and coal tar. Phototherapy may be efficacious and well tolerated for pediatric patients with generalized psoriasis or localized psoriasis refractory to topical agents. Systemic non-biologic therapies, such as methotrexate, cyclosporine, and acitretin, are options for moderate to severe psoriasis. Biologic therapies (e.g., adalimumab, etanercept, infliximab, ustekinumab) have also shown efficacy in moderate to severe plaque psoriasis in this patient population.(27)
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.(8, 24) The American Gastroenterological Association (AGA) 2021 guideline recommends the following:(8) • Biologic therapy: o The AGA suggests early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids o Anti-tumor necrosis factor (TNF) (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission o Vedolizumab is suggested over no treatment for the induction and maintenance of remission o AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission o 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 o Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission o 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) • Disease modifying antirheumatic drug (DMARD) therapy: o Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission o Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission o Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission o The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission o 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 o The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission • Combination therapy:

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	o Patients that are naïve to biologics and immunomodulators, the AGA suggests 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) o Patients that are naïve to biologics and immunomodulators, the AGA suggests 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) o 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:(24) • Mild to moderately severe disease/low-risk disease: o Sulfasalazine (in doses of 3-6 grams daily) is effective in colonic and/or ileocolonic CD, but not those with isolated small bowel disease o 5-aminosalicylic (ASA) suppositories and enema preparations are effective for induction and maintenance of remission in rectal and sigmoid disease o 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 o Controlled ileal release budesonide is effective for induction of remission in ileocecal disease • Moderate to severe disease/moderate- to high-risk disease o 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 o Azathioprine, 6-mercaptopurine, or methotrexate (MTX) (15 mg once weekly) may be used in treatment of active disease and as adjunctive therapy for reducing immunogenicity against biologic therapy o TNF inhibitors should be used to treat CD that is resistant to treatment with corticosteroids and that is refractory to thiopurines or MTX o 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 o 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: o Intravenous (IV) corticosteroids should be used o TNF inhibitors can be considered • Maintenance therapy: o Thiopurines or methotrexate should be considered once remission is induced with corticosteroids o 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 o Vedolizumab should be used for maintenance of remission of vedolizumab induced remission o Ustekinumab should be used for maintenance of remission of ustekinumab induced remission

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

INFLAMMATORY BOWEL DISEASE - 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.(25) The American College of Gastroenterology (ACG) recommends a treat-to-target approach and recommends 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:(25) <u>Induction of remission</u>: • Mildly active disease: o Rectal 5-aminosalicylate (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 o Rectal 5-ASA at a dose of 1 g/day for ulcerative proctitis o Oral 5-ASA at a dose of at least 2 g/day for extensive UC o 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: o Oral budesonide MMX 9 mg/day for induction of remission • Moderately to severely active disease: o Oral systemic corticosteroids, tumor necrosis factor (TNF) inhibitors (i.e., adalimumab, golimumab, or infliximab), tofacitinib, or vedolizumab to induce remission o Combination of infliximab with thiopurine therapy when using infliximab for induction o Switch to tofacitinib or vedolizumab for induction in patients that have failed TNF inhibitors o 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. <u>Maintenance of remission</u>: • Previously mildly active disease: o Rectal 5-ASA at a dose of 1 g/day in patients with ulcerative proctitis o 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: o Thiopurines in patients that achieved remission due to corticosteroid induction o Continue TNF inhibitors (i.e., adalimumab, golimumab, or infliximab) for remission due to TNF induction o Continue vedolizumab for remission due to vedolizumab induction o Continue tofacitinib for remission due to tofacitinib induction The American Gastroenterology Association (AGA) published recommendations (2018) for the management of mild-to-moderate UC:(26)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	• Use either standard-dose mesalamine (2-3 g/day) or diazo-bonded 5-ASA (e.g., balsalazide) 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 (greater than 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 (2024) for the management of moderate-to-severe UC:(29) <u>General treatment information:</u> • Suggest *against* using thiopurine monotherapy for inducing remission o Suggest thiopurine monotherapy may be used for maintaining remission typically induced with corticosteroids • Suggest early use of advanced therapy (e.g., biologics, ozanimod, etrasimod), with or without immunomodulator therapy (e.g., thiopurines), rather than treatment with 5-ASA and a gradual step up to biologic/immunomodulator therapy after 5-ASA treatment failure o Patients with less severe disease or those who place a higher value on the safety of 5-ASA therapy over the efficacy of immunosuppressives may reasonably choose gradual step therapy with 5-ASA therapy • Recommend using one of the following advanced therapies over no treatment: o Infliximab, golimumab, vedolizumab, tofacitinib, upadacitinib, ustekinumab, ozanimod, etrasimod, risankizumab, guselkumab • Suggest using one of the following advanced therapies over no treatment: o Adalimumab, filgotinib*, mirikizumab (*not currently approved by the Food and Drug Administration) <u>Advanced therapy-naïve patients (first-line therapy):</u> • Suggest that a higher or intermediate efficacy medication be used rather than a lower efficacy medication o Higher efficacy: infliximab, vedolizumab, ozanimod, etrasimod, upadacitinib, risankizumab, guselkumab o Intermediate efficacy: golimumab, ustekinumab, tofacitinib, filgotinib, mirikizumab o Lower efficacy: adalimumab <u>Prior exposure to one or more advanced therapies, particularly TNF antagonists:</u> • Suggest that a higher or intermediate efficacy medication be used rather than a lower efficacy medication o Higher efficacy: tofacitinib, upadacitinib, ustekinumab o Intermediate efficacy: filgotinib, mirikizumab, risankizumab, guselkumab o Lower efficacy: adalimumab, vedolizumab, ozanimod, etrasimod

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Infliximab Dosing	The use of tumor necrosis factor (TNF)-inhibitors has been associated with the development of anti-drug antibodies in some patients. These antibodies can lead to increased clearance of the drug which results in lower serum drug levels and less duration of response. The formation of anti-drug antibodies is a concern with biologic TNF-inhibitors, including infliximab, and can lead to a loss of response (LOR) to the drug. Secondary LOR, or secondary non-response, describes patients who initially respond to treatment after induction therapy but subsequently lose response during maintenance treatment and experience clinical relapse. The timing when this occurs varies for each TNF-inhibitor, but it often requires dose intensification in order to re-achieve remission.(6) Data from the ACCENT1 trial estimates that the annual risk for LOR to infliximab is about 13% per patient-year of treatment. Using a regularly scheduled dosing regimen versus an episodic dosing regimen can decrease the risk of antibody formation and subsequent LOR. However, up to 15-29% of patients treated with infliximab are not compliant with infusions or injections. Patient specific factors may also contribute to LOR, including individual differences in bioavailability and pharmacokinetics of the drug.(6) In patients treated with a TNF-inhibitor who experience symptoms consistent with relapse, it must be determined whether the symptoms are due to active inflammation or if a different secondary cause is present. If it is determined that the relapse is due to active inflammation, this confirms LOR and a pharmacokinetic and immunogenic assessment should be performed.(6) The presence of anti-TNF antibodies suggests that immunogenicity against the drug has developed. Changing therapy to a different TNF-antagonist has generally been associated with a more prevalent outcome of complete or partial response versus increasing the dose of the current TNF-antagonist. Patients with high titers of anti-drug antibodies (greater than 9 micrograms/mL for infliximab) typically do not respond well to dose escalation. However, patients with low levels of antibodies have been shown to respond to dose intensification and can achieve increased anti-TNF drug levels. Adding an immunomodulator (e.g., thiopurine, methotrexate) as concurrent therapy is another option and can aid in reducing the risk of antibody formation and improving clinical outcomes. Studies have demonstrated that concomitant immunosuppressive therapy with infliximab resulted in higher trough levels and reduced anti-drug antibody formation.(6) If no anti-TNF antibodies are present, the presence of adequate drug levels should be assessed. Observational studies have shown that infliximab trough levels of greater than 3 mcg/mL are associated with an increased likelihood of maintaining response to the drug. However, patients who experience LOR and have adequate trough levels of the drug are unlikely to respond to dose intensification or switching to a different TNF-inhibitor. Instead, these patients may benefit from switching to a drug from a different class. Patients who are found to have sub-therapeutic drug levels often benefit from dose escalation in order to achieve clinical response, or they may benefit from the addition of an immunomodulator.(6) Dose intensification should occur by either increasing the dose or shortening the interval between doses, but not both at the same time. Increasing the dose may lead to less costs and less patient inconvenience compared to increasing the dosing frequency.(6) Infliximab infusion dosing above 10 mg/kg every 4 weeks is not supported for any indication per Food and Drug Administration (FDA) labeling, and higher doses or more frequent dosing of the drug can lead to an increased risk of serious infections.(2)
Safety	*Infliximab(1,2,3,20)* Infliximab products carry the following boxed warning:

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

	• Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative. • Lymphoma and other malignancies, some fatal have been reported in children and adolescent patients treated with TNF blockers. • Post marketing cases of hepatosplenic T-cell lymphoma have occurred in adolescents and young adults with inflammatory bowel disease treated with TNF blockers Infliximab products have the following contraindications for use: • Should not be administered at doses greater than 5 mg/kg in patients with moderate to severe heart failure • Should not be re-administered to patients who have experienced a severe hypersensitivity reaction to infliximab products, to the inactive components, or to murine proteins

REFERENCES

Number	Reference
1	Inflectra prescribing information. Celltrion, Inc. June 2021.
2	Remicade prescribing information. Centocor, Inc. October 2021.
3	Renflexis prescribing information. Samsung Bioepis Co. LTD. January 2022.
4	Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the treatment of ankylosing spondylitis and Nonradiographic axial spondyloarthritis. *Arthritis & Rheumatology*. 2015;68(2):282-298. doi:10.1002/art.39298298.
5	Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. 2021;73(7):924-939. doi:10.1002/acr.24596
6	Roda G, Jharap B, Neeraj N, Colombel JF. Loss of response to Anti-TNFs: Definition, Epidemiology, and management. *Clinical and Translational Gastroenterology*. 2016;7(1):e135. doi:10.1038/ctg.2015.63
7	Garner KK, Hoy KDS, Carpenter AM. Psoriasis: Recognition and Management Strategies. *Am Fam Physician*. 2023;108(6):562-573.
8	Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
9	Gossec L, Kerschbaumer A, Ferreira RJO, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update. *Annals of the Rheumatic Diseases*. 2024;83(6):706-719. doi:10.1136/ard-2024-225531
10	Smolen JS, Landewe RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Annals of the Rheumatic Diseases*. 2022;82(1):3-18. doi:10.1136/ard-2022-223356
11	Radu AF, Bungau SG. Management of Rheumatoid Arthritis: An Overview. *Cells*. 2021;10(11):2857. doi:10.3390/cells10112857
12	Bautista-Molano W, Fernández-Ávila DG, Brance ML, et al. Pan American League of Associations for Rheumatology recommendations for the management of axial spondyloarthritis. *Nature Reviews Rheumatology*. 2023;19(11):724-737. doi:10.1038/s41584-023-01034-z

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Number	Reference
13	Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Annals of the Rheumatic Diseases*. 2022;82(1):19-34. doi:10.1136/ard-2022-223296
14	Elmets CA, Korman NJ, Prater EF, et al. Joint AAD–NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *Journal of the American Academy of Dermatology*. 2021;84(2):432-470. doi:10.1016/j.jaad.2020.07.087
15	Visser K, Van Der Heijde D. Optimal dosage and route of administration of methotrexate in rheumatoid arthritis: a systematic review of the literature. *Annals of the Rheumatic Diseases*. 2008;68(7):1094-1099. doi:10.1136/ard.2008.092668
16	Elmets CA, Lim HW, Stoff B, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. *Journal of the American Academy of Dermatology*. 2019;81(3):775-804. doi:10.1016/j.jaad.2019.04.042
17	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 Care & Research*. 2019;71(6):717-734. doi:10.1002/acr.23870
18	Ringold S, Weiss PF, Colbert RA, et al. Childhood Arthritis and Rheumatology Research Alliance Consensus Treatment Plans for New-Onset Polyarticular Juvenile Idiopathic Arthritis. *Arthritis Care & Research*. 2013;66(7):1063-1072. doi:10.1002/acr.22259
19	Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Care & Research*. 2018;71(1):2-29. doi:10.1002/acr.23789
20	Avsola prescribing information. Amgen Inc. September 2021.
21	Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *Journal of the American Academy of Dermatology*. 2019;80(4):1029-1072. doi:10.1016/j.jaad.2018.11.057
22	Armstrong AW, Siegel MP, Bagel J, et al. From the medical board of the National Psoriasis Foundation: treatment targets for plaque psoriasis. *Journal of the American Academy of Dermatology*. 2017;76(2):290-298. doi: 10.1016/j.jaad.2016.10.017
23	Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *Journal of the American Academy of Dermatology*. 2020;82(6):1445-1486. doi:10.1016/j.jaad.2020.02.044
24	Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *The American Journal of Gastroenterology*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27
25	Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical guideline: Ulcerative colitis in adults. *The American Journal of Gastroenterology*. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152
26	Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology*. 2018;156(3):748-764. doi:10.1053/j.gastro.2018.12.009
27	Menter A, Cordoro KM, Davis DMR, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. *Journal of the American Academy of Dermatology*. 2020;82(1):161-201. doi:10.1016/j.jaad.2019.08.049
28	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 & Rheumatology*. 2019;71(10):1599-1613. doi:10.1002/art.41042
29	Singh S, Loftus EV, Limketkai BN, et al. AGA Living Clinical Practice Guideline on Pharmacological Management of Moderate-to-Severe Ulcerative Colitis. *Gastroenterology*. 2024;167(7):1307-1343. doi:10.1053/j.gastro.2024.10.001

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J1745	Infliximab	infliximab for iv inj	100 MG	M ; N ; O ; Y	N		2. Non-Preferred
J1745	Remicade	infliximab for iv inj	100 MG	M ; N ; O ; Y	N		2. Non-Preferred
Q5104	Renflexis	infliximab-abda for iv inj	100 MG	M ; N ; O ; Y	N		2. Non-Preferred

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Infliximab	infliximab for iv inj	100 MG	Commercial ; HIM ; ResultsRx
Remicade	infliximab for iv inj	100 MG	Commercial ; HIM ; ResultsRx
Renflexis	infliximab-abda for iv inj	100 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Infliximab and Infliximab Biosimilars	

Preferred Infliximab Agent(s)	Non-Preferred Infliximab Agent(s)
Avsola, Inflectra	Infliximab, Remicade, Renflexis

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
    1. BOTH of the following:
        A. ONE of the following:
            1. The patient has a diagnosis of moderately to severely active rheumatoid arthritis (RA) AND BOTH of the following:
                A. ONE of the following:
                    1. The patient has ONE of the following:
                        A. Has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) after at least a 3-month duration of therapy **OR**
                        B. Has tried and had an inadequate response to ONE conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA after at least a 3-month duration of therapy **OR**

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Module	Clinical Criteria for Approval
	C. Has an intolerance or hypersensitivity to ONE conventional agent (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** 2. The patient has an FDA labeled contraindication to ALL conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** 3. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of RA **AND** B. ONE of the following: 1. The patient will be using a conventional agent (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) in combination with the requested agent **OR** 2. The patient has an intolerance, hypersensitivity, or FDA labeled contraindication to ALL conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) **OR** 2. The patient has a diagnosis of active psoriatic arthritis (PsA) AND ONE of the following: A. The patient has ONE of the following: 1. Has tried and had an inadequate response to ONE conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA after at least a 3-month duration of therapy **OR** 2. Has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of PsA **OR** B. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of PsA **OR** C. The patient 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, vision loss], rapidly progressive) **OR** D. The patient 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** E. The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla that is FDA labeled or supported in compendia for the treatment of PsA **OR** 3. The patient has a diagnosis of chronic severe plaque psoriasis (PS) **OR** 4. The patient has a diagnosis of moderately to severely active Crohn's disease (CD) AND ONE of the following: A. The patient has ONE of the following: 1. Has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy **OR**

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Module	Clinical Criteria for Approval
	2. Has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of CD **OR** B. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of CD **OR** C. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of CD **OR** 5. The patient has a diagnosis of moderately to severely active ulcerative colitis (UC) AND ONE of the following: A. The patient has ONE of the following: 1. 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 after at least a 3-month duration of therapy **OR** 2. Has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of UC **OR** B. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of UC **OR** C. The patient has severely active ulcerative colitis **OR** D. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of UC **OR** 6. The patient has a diagnosis of active ankylosing spondylitis (AS) AND ONE of the following: A. The patient has ONE of the following: 1. Has tried and had an inadequate response to TWO different nonsteroidal anti-inflammatory drugs (NSAIDs) used in the treatment of AS after at least a 4-week TOTAL duration of therapy **OR** 2. Has tried and had an inadequate response to ONE NSAID used in the treatment of AS after at least a 4-week duration of therapy and an intolerance or hypersensitivity to ONE additional NSAID used in the treatment of AS **OR** 3. Has an intolerance or hypersensitivity to TWO different NSAIDs used in the treatment of AS **OR** B. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of AS **OR** C. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of AS **OR** 7. The patient has another FDA labeled indication for the requested agent and route of administration **AND** B. If the patient has an FDA labeled indication, then ONE of the following: 1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. There is support of using the requested agent for the patient's age for the requested indication **OR** 2. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. ONE of the following: A. The requested agent is a preferred agent **OR** B. The patient has ONE of the following (medical records required): 0. Has tried and had an inadequate response to TWO preferred agents after at least a 3-month duration of therapy per agent **OR**

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Module	Clinical Criteria for Approval
	1. Has tried and had an inadequate response to ONE preferred agent after at least a 3-month duration of therapy and an intolerance or hypersensitivity to ONE preferred agent that is not expected to occur with the requested agent **OR** 2. Has an intolerance or hypersensitivity to TWO preferred agents that is not expected to occur with the requested agent **OR** C. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested agent (medical records required) **AND** 3. The patient has been tested for latent tuberculosis (TB) AND if positive the patient has begun therapy for latent TB **AND** 4. The prescriber is a specialist in the area of the patient'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 patient's diagnosis **AND** 5. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 0. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 1. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. ONE of the following: A. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication **OR** B. The requested quantity (dose) exceeds the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication AND ALL of the following: 0. The patient has been titrated up to the requested dose due to ineffective symptom control at lower doses **AND** 1. ONE of the following: A. The request is either for a dose increase or shortening of the dosing interval, NOT both **OR** B. The patient is currently treated with the requested dose **AND** 2. The requested dose does NOT exceed 10 mg/kg every 4 weeks **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 12 months for all indications EXCEPT: • Crohn's disease: 14 weeks **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. ONE of the following: A. The requested agent is a preferred agent **OR** B. The patient has ONE of the following (medical records required): 1. Has tried and had an inadequate response to TWO preferred agents after at least a 3-month duration of therapy per agent **OR**

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Module	Clinical Criteria for Approval
	2. Has tried and had an inadequate response to ONE preferred agent after at least a 3-month duration of therapy and an intolerance or hypersensitivity to ONE preferred agent that is not expected to occur with the requested agent **OR** 3. Has an intolerance or hypersensitivity to TWO preferred agents that is not expected to occur with the requested agent **OR** C. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested agent (medical records required) **AND** 4. The prescriber is a specialist in the area of the patient'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 patient's diagnosis **AND** 5. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. ONE of the following: A. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication **OR** B. The requested quantity (dose) exceeds the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication AND ALL of the following: 1. The patient has been titrated up to the requested dose due to ineffective symptom control at lower doses **AND** 2. ONE of the following: A. The request is either for a dose increase or shortening of the dosing interval, NOT both **OR** B. The patient is currently treated with the requested dose **AND** 3. The requested dose does NOT exceed 10 mg/kg every 4 weeks **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 12 months

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Contraindicated as Concomitant Therapy
Cosentyx (secukinumab)
Cyltezo (adalimumab-adbm)
Dupixent (dupilumab)
Ebglyss (lebrikizumab-lbkz)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Imuldosa (ustekinumab-srlf)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Leqselvi (deuruxolitinib)
Litfulo (ritlecitinib)
Nemluvio (nemolizumab-ilto)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Otulfi (ustekinumab-aauz)
Pyzchiva (ustekinumab-ttwe)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Saphnelo (anifrolumab-fnia)
Selarsdi (ustekinumab-aekn)
Siliq (brodalumab)
Simlandi (adalimumab-ryvk)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Spevigo (spesolimab-sbzo) subcutaneous injection
Stelara (ustekinumab)
Steqeyma (ustekinumab-stba)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tofidence (tocilizumab-bavi)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tyenne (tocilizumab-aazg)
Tysabri (natalizumab)
Ustekinumab
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yesintek (ustekinumab-kfce)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved

Contraindicated as Concomitant Therapy
Yuflyma (adalimumab-aaty) Yusimry (adalimumab-aqvh) Zeposia (ozanimod) Zymfentra (infliximab-dyyb)

© Copyright Prime Therapeutics LLC. March 2025 All Rights Reserved