Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 12/14/2023

Infliximab Policy

Avsola™ (infliximab-axxq)
Inflectra® (infliximab-dyyb)
Ixifi™ (infliximab-qbtx)
Infliximab (Remicade®)
Renflexis® (infliximab-abda)

HCPCS: Avsola Q5121; Inflectra Q5103; Ixifi Q5109; Remicade J1745; Renflexis Q5104

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
    a. FDA approved indication
    b. FDA approved age
    c. Diagnosis of Crohn's disease
        i. Active Crohn's disease:
            1. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated
        ii. Fistulizing Crohn's disease
    d. Diagnosis of ulcerative colitis:
        i. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated
    e. Diagnosis of rheumatoid arthritis:
        i. Trial and failure of at least 3 months of one disease-modifying anti-rheumatic drug (DMARD) unless contraindicated or not tolerated. Examples include methotrexate, hydroxychloroquine, leflunomide, sulfasalazine
        ii. Administered in combination with methotrexate
    f. Diagnosis of psoriatic arthritis
    g. Diagnosis of plaque psoriasis
        i. Trial and failure, contraindication, or intolerance to one topical corticosteroid
    h. Diagnosis of ankylosing spondylitis

i. Diagnosis of generalized pustular psoriasis as defined by the European Rare and Severe Psoriasis Expert Network
j. Not to be used in combination with other biologics or targeted DMARDs
k. Trial and failure of the preferred product despite dose optimization
l. A credible explanation must be provided as to why the requested product is expected to work when the preferred product did not
m. Trial and failure, contraindication, OR intolerance to the preferred products as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Infliximab is a tumor necrosis factor inhibitor (TNFi) approved for the following indications:
  - Induction and maintenance treatment of adults 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
  - Adults with fistulizing CD
  - Induction and maintenance treatment of adults with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy
  - Induction and maintenance treatment of pediatric patients 6 years of age and older with moderately to severely active UC who have had an inadequate response to conventional therapy
  - Treatment of adults with moderately to severely active rheumatoid arthritis (RA) when used in combination with methotrexate
  - Adults with active ankylosing spondylitis (AS)
  - Adults with psoriatic arthritis (PsA)
  - Treatment of adults with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate
- Remicade by Janssen was the first infliximab product approved by the FDA. Since its introduction to market, four infliximab biosimilar products have also been approved: Inflectra, Renflexis, Avsola and Ixifi. In addition, Janssen released an "unbranded" formulation of infliximab in November 2021. This "unbranded biologic" is not a biosimilar but rather the same drug re-labeled, similar to authorized generics for non-biologics.

- There is a large body of literature, punctuated by the NOR-SWITCH trial, evaluating the impact of switching from reference infliximab (Remicade) to a biosimilar. The great majority of studies do not report differences in safety, efficacy, or immunogenicity after a single switch. Data suggests a low risk of safety concerns or loss of efficacy after switching to biosimilar infliximab. There are no studies showing that if a biosimilar does not work, a patient will respond to the innovator product or another biosimilar.

- There is insufficient information regarding the concurrent use of infliximab products with other biologic agents or targeted DMARDs. Due to the lack of robust clinical evidence and the possibility of an increased risk of infection, infliximab products are not recommended for use in combination with other biologics or targeted DMARDs.

- Crohn's Disease

    - The 2018 American College of Gastroenterology (ACG) guidelines establish therapeutic recommendations for patients with Crohn's disease based upon disease location, disease severity, disease-associated complications, and future disease prognosis. Therapeutic approaches are individualized according to the symptomatic response and tolerance to medical intervention. Current therapeutic approaches should be considered a sequential continuum to treat acute disease or induce clinical remission and then to maintain response/remission. In general, clinical evidence of improvement should be evident within 2 – 4 weeks and the maximal improvement should occur within 12 – 16 weeks. Those with continued symptoms should be treated with an alternative therapy for mild to moderate disease, have their medication dose adjusted in order to attempt to optimize therapy, or advance to treatment for moderate to severe disease according to their clinical status.

    - Corticosteroids are used primarily for the treatment of flares of CD. Conventional corticosteroids are effective for reducing the signs and symptoms of active CD and induction of remission in patients with moderately to severely active CD. Oral corticosteroids are effective and can be used for short-term use in alleviating signs and symptoms of moderate to severely active disease. The ACG guidelines recommend prednisone equivalent doses ranging from 40 to 60 mg per day. These doses are typically maintained for 1 –2 weeks and tapered at 5 mg weekly until 20 mg and then 2.5 –5 mg weekly. Once begun, care should be taken to ensure that corticosteroids are successfully discontinued, and steroid-sparing agents should be used.

    - In patients with moderate-to-severe CD who remain symptomatic despite current or prior corticosteroid therapy, mercaptopurine, azathioprine, and intramuscular or subcutaneous methotrexate are effective as steroid-sparing agents and are recommended by the guidelines. Maximum effectiveness of these agents can be seen between 8 to 12 weeks from therapy initiation. Methotrexate is also recommended in combination with steroids as effective for treatment of moderately active steroid-dependent/resistant CD. Cyclosporine, tacrolimus, and mycophenolate are not recommended for treatment of CD.

    - TNFi biologics including infliximab, adalimumab, and certolizumab pegol are effective for treatment of patients with CD who inadequately respond to treatment with corticosteroids, thiopurines, and methotrexate. These agents are rapid in onset of effect, with benefit often noted within 2 weeks of initiating therapy. Treatment guidelines do not recommend the use of one agent over another. The ACG guidelines also recommend the use of biologics in combination with immunosuppressants to help decrease the formation of antibodies against the biologic therapy. There are no robust, published studies to support use of biologic agents in combination.

    - The 2021 American Gastroenterological Association (AGA) guidelines include similar recommendations for the management of moderate-to-severe CD compared to the recommendations cited in the 2018 ACG guidelines. Both guidelines recommend corticosteroids over no treatment for induction of remission.

Additionally, both guidelines recommend thiopurines, such as azathioprine or 6-mercaptopurine, as steroid-sparing agents for maintenance of remission. The AGA guidelines also recommend the same biologic agents cited in the ACG guidelines for treatment of CD, with the exception of Tysabri® (natalizumab), which the ACG suggests against use of due to its associated risk of progressive multifocal leukoencephalopathy (PML).

- Of note, the AGA guidelines conditionally recommend earlier introduction of biologic therapy prior to failure of corticosteroids; however, this recommendation is supported by a low level of clincial evidence. To date, no blinded randomized controlled trials (RCTs) have demonstrated the superiority of early introduction of biologic therapy compared to conventional induction therapy with corticosteroids followed by steroid-sparing therapy. The 2021 AGA guideline authors also acknowledge that earlier therapy with either combination immunomodulotor plus biologic therapy or biologic monotherapy may result in over-treating some patients and potentially exposing them to treatment-related risks and costs with limited benefit.

- Ulcerative Colitis

  - The 2019 American College of Gastroenterology guidelines and the 2020 American Gastroenterology Association guidelines state therapeutic management in ulcerative colitis should be guided by the specific diagnosis, an assessment of disease activity, and disease prognosis. Treatment selection should be based not only on inflammatory activity but also on disease prognosis.

  - Remission can be induced using a variety of medications, including, oral 5-aminosalicylates (5-ASA), corticosteroids, or biologic agents. In patients with mild to moderately active disease, treatment with 5-ASA therapy has proven to be safe and efficacious for induction. Recommended dosing is 2 grams per day of oral 5-ASA or at least 1 gram per day of rectal 5-ASA with improvement usually seen within 4 weeks. A typical treatment course may last up to 8 weeks.

  - Oral steroids are recommended for induction for patients with severe disease or those who did not respond to 5-ASA therapy. The typical starting doses of oral prednisone are 40 – 60 mg per day, and clinical response is expected within 5 – 7 days of treatment. A typical treatment course with oral prednisone is 14 days. The duration of systemic corticosteroids should be as short as possible with early initiation of steroid-sparing therapy. The speed of the taper should be guided by clinical symptoms, cumulative steroid exposure, and onset of action of alternate therapies. Those unable to taper off of 10-20 mg of prednisone per day without relapsing are considered steroid dependent. Use systemic corticosteroids for maintenance of remission is not recommended.

  - Thiopurines, such as azathioprine and mercaptopurine, can be used to maintain remission. Thiopurines are slow acting with their maximum effectiveness seen between 8 to 12 weeks from therapy initiation. They do not induce remission in moderately to severely active ulcerative colitis. Similarly, methotrexate is not an effective induction agent for induction or maintenance of remission.

  - In patients with moderate to severe disease, TNFi, Entyvio® (vedolizumab), and Stelara® (ustekinumab) may be recommended for the induction and maintenance of remission. For patients with moderate to severe disease in remission, guidelines do not recommend biologic monotherapy over thiopurine monotherapy. Thiopurines can be used as adjunctive therapy for reducing immunogenicity against biologic therapy and are guideline recommended.

  - TNFi (infliximab, adalimumab, and golimumab) are effective for treatment of patients with ulcerative colitis. These agents are rapid in onset of effect, with benefit often noted within 2 weeks of initiating therapy. Treatment guidelines do not recommend the use of one agent over another as there have been no head-to-head trials comparing the agents. For patients who had an initial response to aTNFi but lost efficacy, it is

recommended that patients switch to an alternative TNFi therapy. For patients who are primary non-responders to therapy with a TNFi, it is recommended to consider an agent with a different mechanism.

- Rheumatoid Arthritis

  - The 2021 American College of Rheumatology (ACR) Guidelines for the Treatment of Rheumatoid Arthritis (RA) established recommendations for the care of adult RA patients. The guidelines state that treatment decisions should follow a shared decision-making process and should be reevaluated within a minimum of 3 months based on the efficacy and tolerability of the DMARD(s) chosen.

  - For the initial treatment of symptomatic RA, the guidelines strongly recommend the use of conventional synthetic DMARD (csDMARD) monotherapy in those who are DMARD-naive. csDMARD monotherapy is a less costly first line treatment option with an extensive safety record accompanied by well-documented clinical efficacy and a large body of clinical experience and familiarity among prescribers. csDMARDs in the guidelines refer to methotrexate (MTX), hydroxychloroquine, leflunomide (LEF), and sulfasalazine. Azathioprine, cyclosporine, minocycline, and gold were not included due to their infrequent use in RA and lack of new data since the prior guidelines were published. Oral MTX is recommended as the preferred initial DMARD for patients with moderate-to-high disease activity, and hydroxychloroquine is recommended as the preferred initial DMARD for patients with low disease activity.

  - If disease activity remains moderate or high despite optimal dosing of methotrexate monotherapy, the use of dual therapy with methotrexate plus biologic DMARD (bDMARD; etanercept, adalimumab, infliximab, golimumab, certolizumab pegol, abatacept, tocilizumab, sarilumab, rituximab) or targeted synthetic DMARD (tsDMARD; tofacitinib, baricitinib, upadacitinib) therapy is conditionally recommended over the use of triple therapy (i.e., addition of sulfasalazine and hydroxychloroquine). The guidelines do not inform preference of bDMARD over tsDMARD therapy (or vice-versa) for use in combination with MTX. No one agent has been shown to be superior to another. The guidelines do acknowledge the emergence of safety signals for the JAK inhibitor class (tsDMARD), and state that further modification of this recommendation may be necessary as additional data are published.

  - A treat-to-target approach is conditionally recommended over usual care for patients who have had an inadequate response to bDMARDs or tsDMARDs. Treat-to-target refers to a systematic approach involving frequent monitoring of disease activity using validated instruments and modification of treatment to minimize disease activity with the goal of reaching a pre-defined target (low disease activity or remission).

- Ankylosing Spondylitis

  - Axial spondyloarthritis, comprising ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (NRAS), is the main form of chronic inflammatory arthritis affecting the axial skeleton. Non-radiographic means that damage to the joints is not visible on X-ray. When changes to the vertebrae (the bones of the spine) or sacroiliac joints don't show any changes on an X-ray, that's known as NRAS. Once the joints are clearly affected on an X-ray, a person can be diagnosed with AS.

  - The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. In adult patients who have active disease despite treatment with nonsteroidal anti-inflammatory drugs (NSAIDS), treatment with TNFi are recommended. They do not recommend any particular TNFi as the preferred choice for the typical patient. Secukinumab or ixekizumab is recommended over the use of a second TNFi in patients with primary nonresponse to the first TNFi, whereas for patients with a secondary nonresponse (i.e. those who relapse after an initial response) it may be beneficial to switch to a different TNFi rather than immediately switch to a different biologic class. In the case of nonresponse (primary or secondary), the

guidelines recommend against switching to treatment with a biosimilar since clinical response would not be expected to be different.

- Psoriasis

  - Psoriasis is a chronic, painful and life-altering immune-mediated disease which predominantly manifests with skin and joint involvement. Patients may also experience significant cardiovascular and psychological comorbidities. Approximately 2% of U.S. adults are affected by psoriasis (men and women equally), and it can occur at any age. Approximately 90% of psoriasis-affected patients have plaque psoriasis, which is characterized by well-defined round or oval plaques that vary in size and often coalesce. The severity of psoriasis is defined as: mild = less than 3% of body affected; moderate = 3-10% of body affected; and severe being more than 10% of the body affected.

  - Per the 2020 Joint American Academy of Dermatology (AAD) - National Psoriasis Foundation (NPF) guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures: topical corticosteroids provide a high efficacy and good safety option for patients with localized disease. They are generally recommended as first-line therapy. Choice of steroid potency may depend on severity, location, patient preference, and patient age, while the duration of treatment may vary with steroid potency, location and severity of disease often ranging from 2-12 weeks. Therapeutic regimens may include 2-4 weeks with a topical steroid applied twice daily, followed by a maintenance regimen where topical steroids are alternated with a steroid-sparing topical agent. Treatment with topical steroids for over 12 weeks is recommended under careful supervision by a physician.

  - Per the 2019 Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with phototherapy: phototherapy serves as a reasonable and effective treatment option for patients requiring more than topical medications and/or those wishing to avoid systemic medications or simply seeking an adjunct to a failing regimen. Guidelines also state that the majority of patients with mild-to-moderate disease have adequate disease control with topical therapies and phototherapy alone.

  - Per the 2020 Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with systemic nonbiologic therapies: many oral medications, including methotrexate, cyclosporine, and acitretin, have been used for decades to treat psoriasis, each with its own benefits and risks. Most work by targeting the immune system, whereas others, such as acitretin, work predominantly by decreasing keratinocyte hyperproliferation, thus restoring the normal epidermal differentiation. Both methotrexate and cyclosporine are category A guideline recommendations for the treatment of moderate to severe psoriasis in adults and for severe, recalcitrant psoriasis, respectively. Studies examining the use of methotrexate and cyclosporine in psoriasis showed the primary efficacy endpoints met within 12-16 weeks. Acitretin is a category B guideline recommendation as monotherapy for plaque psoriasis, with full treatment response expected within 3-6 months.

  - Per the 2019 Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics: biologic agents, as monotherapy or combined with other topical or systemic medications, have a high benefit-to-risk ration. TNFi, interleukin-12/23 inhibitor (IL-12/IL-23i), IL-23i, and IL-17i biologics have a category "A" recommendation as a monotherapy treatment option for adult patients with moderate-to-severe plaque psoriasis. TNFi biosimilars approved by the FDA should be considered similar to the reference branded version of the drug and therefore interchangeable. Guidelines do not recommend one product over another and note the similar efficacy seen across biologics within the same class.

- Psoriatic Arthritis

- Psoriatic Arthritis (PsA) is a chronic inflammatory disease often associated with psoriasis. PsA occurs in up to 30% of patients with psoriasis, most commonly appearing between the ages of 30 and 50, and causes pain, stiffness, and swelling in and around the joints. If not properly treated, progressive joint damage may occur.

- Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guideline for the treatment of psoriatic arthritis: all recommendations for treatment-naive patients with active PsA are conditional based on low- to very-low quality evidence.

- In treatment-naïve patients, oral systemic medications (OSMs), such as methotrexate, sulfasalazine, cyclosporine, and leflunomide, may be used in patients without severe psoriatic arthritis and without severe psoriasis. OSMs have robust longitudinal safety and efficacy data in patients with PsA. Maximal response to OSMs are most commonly achieved within 3 months of therapy.

- If PsA remains active despite OSM therapy, switching to a TNFi, an IL-17i, or an IL-12/23i biologic is recommended over switching to a different OSM; switching to a TNFi biologic over an IL-17i or IL-12/23i biologic is conditionally recommended in this scenario based on moderate quality evidence. The detailed recommendations for subsequent therapies can be found in the 2018 ACR/NPF guideline for the treatment of psoriatic arthritis.

- Generalized Pustular Psoriasis

  - Generalized pustular psoriasis (GPP) is a rare and potentially life-threatening neutrophilic skin disease characterized by flares consisting of widespread eruptions of painful, sterile pustules. Patients with acute GPP may appear systemically ill and require hospital admission for adequate supportive care, and flares can be so disruptive to the system that they can trigger sepsis, cardiovascular complications, and renal failure. Flare frequency varies among patients and may be spontaneous or triggered by stress, infection, medication, or pregnancy. The clinical course of GPP varies and can be relapsing with recurrent flares or persistent with intermittent flares.

  - The European Rare and Severe Psoriasis Expert Network (ERASPEN) consensus statement on phenotypes of pustular psoriasis (2017) define GPP as macroscopically visible primary sterile pustules occurring on non-acral skin and not within psoriasis plaques. GPP may occur with or without systemic inflammation and with or without psoriasis vulgaris and should only be diagnosed when the condition has relapsed at least once or when it persists for more than 3 months.

  - The goals of treatment of GPP are to improve skin manifestations, alleviate systemic symptoms, and minimize the risk for life-threatening systemic complications. There are no standard US or international guidelines for the treatment of GPP as high-quality data on the efficacy of treatments is lacking. Japanese guidelines for the treatment of GPP (2018) and the National Psoriasis Foundation (NPF) Medical Board (2012) recommend an oral retinoid (e.g. acitretin), cyclosporine, methotrexate, and various biologics as potential systemic treatments for GPP. In the United States, these therapies are used off-label to treat GPP flares, and the choice of systemic agent is based on disease severity. Demonstration of efficacy with any of these agents is solely based on limited evidence from case reports and small, uncontrolled trials. No randomized controlled trials or other comparative studies have been done comparing treatment methods.

  - Infliximab has a long history of off-label use in GPP and use is supported by the NPF Medical Board and the Japanese guidelines. It is often used for more severe disease as marked improvement can be seen within the first few days of treatment. Japanese guidelines cite the effects of infliximab as apparent within 24-48 hours in many cases and a clear effect often seen after 1 to 3 administrations. Once the flare has resolved,

patients can be transitioned to alternative therapies like methotrexate or a retinoid or remain on infliximab for maintenance.

References:

1. Singh JA, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan; 71 (1): 5-32.
2. Elmets CA, Korman NJ, Prater EF, Wong EB, Rupani RN, Kivelevitch D 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 (2020), doi: https://doi.org/10.1016/j.jaad.2020.07.087.
3. Elmets CA, Lim HW, 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 2019; 81: 775-804. https://doi.org/10.1016/j.jaad.2019.04.042
4. Menter A, Strober BE, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol 2019; 80: 1029-1072. https://doi.org/10.1016/j.jaad.2018.11.057
5. Menter A, Gelfand JM, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol 2020; 82: 1445-1486. https://doi.org/10.1016/j.jaad.2020.02.044.
6. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of crohn's disease in adults. AJG. 2018 April; 113 (4): 481-517
7. Jørgensen KK, Olsen IC, Goll GL et al. Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet. 2017; 389: 2304–16.
8. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 – 6.
9. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019; 114: 384–413.
10. Fraenkel L, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021 Jul; 73 (7):924-939.
11. Ward, MM, Deodhar, A, Akl, EA, 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):1599-1613.
12. Actemra (tocilizumab) [prescribing information]. South San Francisco, CA: Genentech Inc; May 2020.
13. Cimzia (certolizumab pegol) [prescribing information]. Smyrna, GA: UCB, Inc. September 2019.
14. Cosentyx (secukinumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; June 2020.
15. Enbrel (etanercept) [prescribing information]. Thousand Oaks, CA: Immunex Corporation; March 2020.
16. Entyvio (vedolizumab) [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America Inc; March 2020.
17. Humira (adalimumab) [prescribing information]. North Chicago, IL: AbbVie; March 2020.
18. Ilumya (tildrakizumab) [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc; July 2020.
19. Inflectra (infliximab-dyyb) [prescribing information].New York, NY: Pfizer; June 2019.
20. Kevzara (sarilumab) [prescribing information]. Bridgewater, NJ: Sanofi0Aventis; April 2018.
21. Kineret (anakinra) [prescribing information]. Stockholm, Sweden: Swedish Orphan Biovitrum AB; June 2018.
22. Olumiant (baricitinib) [prescribing information]. Indianapolis, IN: Eli Lilly; July 2020.
23. Orencia (abatacept) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; June 2020.
24. Otezla (apremilast) [prescribing information]. Thousand Oaks, CA: Amgen Inc; April 2020.
25. Remicade (infliximab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; May 2020.
26. Renflexis (infliximab-abda) [prescribing information]. Whitehouse Station, NJ: Merc Sharp & Dohme Corp; February 2020.
27. Rinvoq (upadacitinib) [prescribing information]. North Chicago, IL: AbbVie Inc; July 2020.

28. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech Inc; August 2020.
29. Siliq (brodalumab) [prescribing information]. Bridgewater, NL: Valeant Pharmaceuticals North America LLC; May 2018.
30. Simponi (golimumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; September 2019.
31. Simponi Aria (golimumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; September 2019.
32. Skyrizi (risankizumab-rzaa) [prescribing information]. North Chicago, IL: AbbVie Inc; March 2020.
33. Stelara (ustekinumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; July 2020.
34. Taltz (ixekizumab) [prescribing information]. Indianapolis, IN: Eli Lilly and Co; May 2020.
35. Tremfya (guselkumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; July 2020.
36. Xeljanz (tofacitinib) [prescribing information]. New York, NY: Pfizer; December 2019
37. Avsola (infliximab-axxq) [prescribing information]. Thousand Oaks, CA: Amgen Inc; December 2019.
38. Ixifi (infliximab-qbtx) [prescribing information]. New York, NY: Pfizer; December 2017.
39. Navarini AA, Burden AD, et al. European consensus statement on phenotypes of pustular psoriasis. J Eur Acad Dermatol Venerel. 2017 Nov;32(11):1792-1799. doi: 10.1111/jdv.14386.
40. Fujita H, Terui T, et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: The new pathogenesis and treatment of GPP. Journal of Dermatology 2018; 45: 1235-1270.
41. Robinson A, Van Voorhees, AS, et al. Treatment of pustular psoriasis: From the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol 2012;67:279-88.
42. Kalb RE. Pustular psoriasis: Pathogenesis, clinical manifestations, and diagnosis. In: UpToDate, Shefner JM (Ed), UpToDate, Waltham, MA. (Accessed September 6, 2022).
43. Kalb RE. Pustular psoriasis: Management. In: UpToDate, Shefner JM (Ed), UpToDate, Waltham, MA. (Accessed September 6, 2022).
44. 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
45. IPD Analytics. Payer & Provider Insights. Immunology: Tumor Necrosis Factor (TNF) Inhibitors. July 2023. Accessed August 24, 2023. https://www.ipdanalytics.com
46. Zymfentra (infliximab-dyyb) [prescribing information] Jersey City, NJ: Celltrion Inc. October 2023.

Policy History		
#	Date	Change Description
3.2	Effective Date: 12/14/2023	Updated to add FDA approved indications
3.1	Effective Date: 10/12/2023	Annual review of criteria performed, no changes were made
3.0	Effective Date: 10/06/2022	Added criteria for generalized pustular psoriasis
2.9	Effective Date: 12/09/2021	Removed FDA approved indication, phototherapy and oral DMARD criteria for psoriasis, and the oral DMARD criteria for psoriatic arthritis, and added trial of one topical corticosteroid for psoriasis indication.
2.8	Effective Date: 08/12/2021	Removal of criteria requiring documented negative TB test
2.7	Effective Date: 02/04/2021	Removal of the topical steroid criteria for psoriasis indication
2.6	Effective Date: 12/03/2020	Criteria updated to align management between pharmacy and medical benefit for all listed indications.
2.5	Effective Date: 08/21/2020	UM medical management system update for MAPPO and BCNA for Avsola
2.4	Effective Date: 04/16/2020	Updated criteria to include dose optimization of preferred product statement and updated pricing table

2.3	Effective Date: 03/01/2020	UM medical management system update for BCBS for Avsola
2.2	Effective Date: 02/06/2020	Updated to include biosimilar Avsola (infliximab-axxq). UM medical management system update for BCN for Avsola
2.1	Effective Date: 08/15/2019	Updated to include a credible explanation statement
2.0	Effective Date: 06/03/2019	UM medical management system update for BCNA and MAPPO for Ixifi
1.9	Effective Date: 05/09/2019	Updated criteria to include trial of preferred products
1.8	Effective Date: 09/07/2018	The Treatments for RA Policy is being retired; all RA criteria was listed in this document.
1.7	Effective Date: 08/09/2018	Criteria update-Ixifi addition and Step Therapy
1.6	Effective Date: 02/08/2018	New criteria document; added drugs including biosimilars
1.5	Effective Date: 10/01/2017	UM medical management system update for BCBS for Renflexis
1.4	Effective Date: 07/05/2017	UM medical management system update for BCNA and MAPPO for Remicade, Renflexis, and Inflectra
1.3	Effective Date: 05/04/2017	Annual review of medical policy and template update
1.2	Effective Date: 04/01/2017	UM medical management system update for BCBS for Remicade and Inflectra
1.1	Effective Date: 10/01/2016	UM medical management system update for BCN for Remicade, Renflexis, and Inflectra
1.0	Effective Date: 05/05/2016	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Remicade® (infliximab) J1745, infliximab J1745, Inflectra™ (infliximab-dyyb) Q5103, Renflexis™ (infliximab-abda) Q5104, Avsola™ (infliximab-axxq) Q5121

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Remicade, Inflectra, Renflexis, and Avsola. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Initiation or Continuation of therapy? ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient administration:* _____
3. Please specify location of administration if hospital outpatient infusion: _____
4. Please provide the NPI number for the place of administration: _____
5. What is the Patient's weight in Kg? _____ Date recorded: _____
6. Primary Indication: ☐ Crohn's Disease **(See #7b)** ☐ Ulcerative Colitis **(See #7b)** ☐ Rheumatoid Arthritis **(See #7c)**
   ☐ Psoriatic Arthritis ☐ Plaque psoriasis **(See #7d)** ☐ Ankylosing spondylitis
   ☐ Generalized pustular psoriasis as defined by the European Rare and Severe Psoriasis Expert Network
   ☐ Other: _____
7. **Initiation AND Continuation of therapy**:
   a. Will the patient be receiving Remicade/Inflectra/Renflexis/Avsola with other biologic agents (for example: Humira, Kineret, Entyvio, or Tremfya, etc.) or with targeted DMARD medications (for example: Otezla)? ☐ Yes ☐ No, Comment:_____
   b. **Crohn's Disease AND Ulcerative colitis**
      i. Does the patient have Crohn's disease with fistula? ☐ Yes ☐ No
      ii. Which therapies has the patient tried and failed?
      ☐ Systemic corticosteroids (e.g. 40 to 60 mg prednisone, prednisolone) daily for 7 days
      ☐ Immunomodulatory therapy for at least 2 months (e.g. azathioprine, mercaptopurine, or methotrexate)
      ☐ None ☐ Other: _____
   c. **Rheumatoid Arthritis (RA:**
      iii. Has the patient had documented failure of at least 3 months of an oral DMARD? (e.g. hydroxychloroquine, methotrexate, leflunomide, or sulfasalazine)
      ☐ Yes, Length of therapy: _____ ☐ No
      iv. Will the patient be taking infliximab in combination with methotrexate? ☐ Yes ☐ No, Provide rationale: _____
   d. **Plaque Psoriasis**:
      i. Has the patient experienced treatment failure with one topical corticosteroid?
      ☐ Yes, Please list topical corticosteroids the patient has tried: _____
      ☐ No, Comment: _____
8. Which medication has the patient tried and failed at optimized dose? ☐ Inflectra ☐ Avsola ☐ Other: _____
   a. What was the maximum dose the patient received of Inflectra in mg/kg and frequency? _____
   b. What was the maximum dose the patient received of Avsola in mg/kg and frequency? _____
   c. How has the patient failed Inflectra and Avsola therapy?
   ☐ Hypersensitivity reaction (for example: hives during infusion), Please specify: _____
   ☐ Side effects, Please specify: _____
   ☐ Lack of efficacy (for example: abdominal pain, bloody stools, etc.), Please specify: _____
   ☐ Other, Please specify: _____
9. **Continuation Request:** Remicade/Inflectra/Renflexis/Avsola Start Date _____
   a. Has the patient's signs and symptoms improved with Remicade/Inflectra/Renflexis/Avsola? ☐ Yes ☐ No Comment: _____

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out	☐ Attached Chart Notes
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

1/31/2020; 7/1/2020; 2/4/2021; 12/9/2021; 10/7/2022