Utilization Review Policy 215

POLICY: Biosimilars – Remicade, Renflexis & infliximab

- Remicade® (infliximab for intravenous infusion – Janssen Biotech, Inc./Johnson&Johnson)
- Renflexis® (infliximab-abda for intravenous infusion – Samsung Bioepis/Merck)
- Infliximab intravenous infusion – Janssen/Johnson & Johnson

EFFECTIVE DATE: 1/1/2021

LAST REVISION DATE: 05/07/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Infliximab products are tumor necrosis factor inhibitors (TNFis) approved for the following indications:[1-3]

- **Ankylosing spondylitis**, for reducing signs and symptoms of active disease.
- **Crohn's disease**, for the following uses:
  - Reducing the signs and symptoms and inducing and maintaining clinical remission in patients ≥ 6 years of age with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy; AND
  - Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adults with fistulizing Crohn's disease.
- **Plaque psoriasis**, for treatment of adults with chronic severe (i.e., extensive and/or disabling) disease who are candidates for systemic therapy and when other systemic therapies are less appropriate.
- **Psoriatic arthritis**, for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function.
- **Rheumatoid arthritis**, in combination with methotrexate for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately to severely active disease.
- **Ulcerative colitis**, for the following uses:
  - Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adults with moderately to severely active disease who have had an inadequate response to conventional therapy; AND
  - Reducing signs and symptoms and inducing and maintaining clinical remission in patients ≥ 6 years of age with moderately to severely active disease who have had an inadequate response to conventional therapy.

Avsola, Inflectra, and Renflexis were approved as biosimilar to Remicade, indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, dosage form, and strength as Remicade.[2-3] However, minor differences in clinically inactive components are allowed. At this time, only biosimilarity has been demonstrated (not interchangeability).

Guidelines

TNFis feature prominently in guidelines for treatment of many inflammatory conditions.

- **Ankylosing Spondylitis and Non-Radiographic Spondyloarthritis:** Guidelines for ankylosing spondylitis and non-radiographic axial spondyloarthritis are published by the American College of Rheumatology (ACR)/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (2019).[4] Following primary nonresponse to a TNFi, an interleukin (IL)-17 blocker is recommended; however, if the patient is a secondary nonresponder, a second TNFi is recommended over switching out of the class. In patients with a contraindication to a TNFi, use of an IL-17 blocker is recommended over traditional oral agents such as methotrexate or sulfasalazine.
- **Crohn's Disease:** The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).[5] TNFis are listed as an option for disease that is resistant to corticosteroids, severely active disease, perianal fistulizing disease, and maintenance of remission. In post-operative Crohn's disease, a TNFi should be started within 4 weeks of surgery to prevent recurrence. Guidelines from the American Gastroenterological Association (AGA) [2021] include infliximab among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.[6]
- **Plaque Psoriasis:** Guidelines from the American Academy of Dermatologists (AAD) and National Psoriasis Foundation (NPF) [2019] recommend infliximab as a monotherapy treatment option for adults with moderate to severe disease.[7]
- **Psoriatic Arthritis:** Guidelines from ACR (2019) recommend TNFis over other biologics for use in treatment-naïve patients with psoriatic arthritis, and in those who were previously treated with an oral therapy.[8]
- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic disease modifying anti-rheumatic drug (DMARD) for a patient taking the maximum tolerated dose of methotrexate who is not at target.[9]
- **Ulcerative Colitis:** Updated ACG guidelines for ulcerative colitis (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: budesonide extended-release tablets; oral or intravenous systemic corticosteroids, Entyvio® (vedolizumab intravenous infusion), Xeljanz®/XR (tofacitanib tablets/extended-release tablets), or TNFis.[10] In addition to the approved indication, clinical guidelines for the management of pouchitis, published in 2009 indicate that first-line therapy for pouchitis is antibiotic therapy (e.g. metronidazole, ciprofloxacin).[11] Other treatment options include maintenance probiotics, oral or topical budesonide, anti-inflammatory drugs (e.g., mesalamine), or immunosuppressive drugs (e.g., infliximab). Guidelines from the AGA (2020) recommend infliximab for moderate to severe ulcerative colitis.[12]
- **Behcet's Disease:** The European League Against Rheumatism (EULAR) recommendations (2018) include TNFis for initial or recurrent sight-threatening uveitis.[13] For patients refractory to first-line treatments (e.g., corticosteroids), TNFis are among the treatment options for mucocutaneous manifestations, venous thrombosis, severe or refractory gastrointestinal disease, and recurrent/chronic joint involvement. Recommendations for the use of TNFis in ocular inflammatory disorders from the American Academy of Ophthalmology (AAO) [2014] note that TNFis may be used first-line in patients with ophthalmic manifestations of Behcet's disease and for acute exacerbations of pre-existing Behcet's disease.[14]

- **Graft-Versus-Host Disease (GVHD):** Guidelines for hematopoietic cell transplantation from the National Comprehensive Cancer network (NCCN) [version 2.2024 – August 30, 2024] list infliximab among the agents used for steroid-refractory acute GVHD.[15]
- **Hidradenitis Suppurativa:** Guidelines from the US and Canadian Hidradenitis Suppurativa Foundations make recommendations for topical, intralesional, and systemic medical management of disease.[16] For acute lesions of all stages, antiseptic washes, short-term oral steroids, and interlesional steroids are among the recommendations. Systemic antibiotics have been a mainstay of treatment. Infliximab is a recommended therapy for moderate to severe disease.
- **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors:** NCCN has guidelines (version 2.2024 – December 6, 2024) for Management of Immunotherapy-Related Toxicities.[17] Infliximab is recommended among the alternatives to manage steroid-refractory inflammatory arthritis, vision changes related to uveitis (steroid-refractory), myocarditis, pericarditis, stage 3 acute kidney injury, pneumonitis, and diarrhea/colitis. Additionally, the guidelines also note that infliximab has not been tested and is not recommended for hepatotoxicity due to concerns of liver toxicity.
- **Indeterminate Colitis:** Infliximab has been effective in some patients with refractory indeterminate colitis (retrospective reviews).[18,19] When patients who are refractory to standard therapy can be definitively classified as having ulcerative colitis, colectomy is considered an effective long-term surgical treatment. Patient's with Crohn's disease; however, have a high risk of complications after ileal pouch-anal anastomosis and are treated more aggressively with medical interventions since surgical options cannot offer the same likelihood of success as in ulcerative colitis.
- **Juvenile Idiopathic Arthritis (JIA):** There are guidelines from ACR and the Arthritis Foundation for the treatment of JIA (2021) which address oligoarthritis and temporomandibular joint (TMJ) arthritis.[20] For oligoarthritis, a biologic is recommended following a trial of a conventional synthetic DMARD. In patients with TMJ arthritis, scheduled nonsteroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids are recommended first-line. A biologic is a therapeutic option if there is an inadequate response or intolerance. Additionally, rapid escalation to a biologic ± conventional synthetic DMARD (methotrexate preferred) is often appropriate given the impact and destructive nature of TMJ arthritis. In these guidelines, there is not a preferred biologic that should be initiated for JIA. The ACR/Arthritis Foundation Guideline for the treatment of JIA (2019) provides updated recommendations for juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[21] Infliximab is among the TNFis recommended as subsequent therapy following treatment with a conventional synthetic DMARD such as methotrexate. TNF antagonists such as infliximab may also be used as second- or third-line treatment for systemic JIA.[22]
- **Ocular Inflammatory Disorders:** Recommendations for the use of TNFis in ocular inflammatory disorders from the AAO (2014) note that infliximab may be used as second-line corticosteroid-sparing therapy for chronic and severe scleritis.[14] Infliximab may be used in patients with uveitis due to various causes (e.g., spondyloarthropathy-associated or human leukocyte antigen [HLA]-B27-associated uveitis, juvenile idiopathic arthritis-associated uveitis, and other posterior uveitides and panuveitis syndromes). Infliximab should be considered second-line in vision-threatening JIA-associated uveitis when methotrexate has failed or is not tolerated (strong recommendation) and vision-threatening chronic uveitis from seronegative spondyloarthropathy (strong recommendation). Infliximab may also be considered in other

patients who have vision-threatening or corticosteroid-dependent disease who have failed first-line therapies. The recommendations point out that studies evaluating infliximab in uveitis included patients with birdshot chorioretinitis (BSCR), a bilateral posterior uveitis generally treated with systemic immunomodulation; these patients showed a good response to infliximab.

- **Pyoderma Gangrenosum:** Although guidelines are not current, multiple topical and systemic therapies have been used for pyoderma gangrenosum. Oral prednisone is the most common initial immunosuppressant medication.[23] Other systemic therapies include cyclosporine, methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, and TNFis (i.e., infliximab, etanercept, and adalimumab products). In case reports, TNFis have been effective.
- **Sarcoidosis:** The European Respiratory Society Task Force has guidelines for treatment of pulmonary, cutaneous, cardiac, and neurologic sarcoidosis.[24] Infliximab is a recommended therapy after continued disease or relapse while taking systemic corticosteroids and immunosuppressants (e.g., methotrexate, azathioprine, leflunomide, mycophenolate mofetil, hydroxychloroquine).
- **Still's Disease:** Still's disease presents in adults with features similar to those of systemic onset JIA.[25,26] In case series, infliximab has been effective in patients with Still's disease that was refractory to therapy with corticosteroids, methotrexate, azathioprine, and cyclophosphamide.[27]

Dosing Information

The recommended dose of infliximab intravenous is weight-based and varies slightly by indication.[1-3] Dosing increase, interval shortening, or changing to another therapy is generally recommended for attenuation of response. Thus, published recommendations note that the dose and interval of infliximab may be adjusted, as needed, in patients who initially respond but then lose that response.[2] Additionally, data are emerging concerning tapering of infliximab dosage in patients with inflammatory conditions who are in remission or have low disease activity. When the dose of any RA therapy is tapered, it is recommended that there be a comprehensive plan to monitor disease activity and address possible flares.

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of infliximab products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of

Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Remicade, Renflexis, or infliximab (authorized generic to Remicade) is recommended for request meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Avsola and Inflectra
Non-Preferred Products(s): Remicade, Renflexis, or infliximab (authorized generic to Remicade)

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any *one* *of the items listed below (A, B, C, D or E)*. *Chart notes documenting* the issue must be provided at time of request:

A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR

B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established.

FDA-Approved Indications

1. Ankylosing Spondylitis (AS). ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient is ≥ 18 years of age. [IC-L]

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

a. Patient has been established on therapy for at least 6 months; [IC-ISGP] AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

b. Patient meets at least one of the following (a or b):

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondyloarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 6 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

2. Crohn's Disease. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following conditions (i and ii):

i. The patient is greater than or equal to 6 years of age; [IC-L] AND

ii. The patient meets one of the following conditions (a, b, c or d):

a. The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; [IC-L, IC-ISGP] OR
Note: Examples of corticosteroids are prednisone, methylprednisolone.

b. The patient has tried one other conventional systemic therapy for Crohn's disease; [IC-L, IC-ISGP] OR

Note: Examples of conventional systemic therapies for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate. An exception to the requirement for a trial of or contraindication to steroids or a trial of one other conventional systemic agent can be made if the patient has already tried at least one biologic other than the requested medication A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for Crohn's disease. A trial of mesalamine does not count as a systemic therapy for Crohn's disease.

c. The patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; IC-L OR

d. The patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence). IC-EC

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; IC-ISGP AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
Note: Examples of objective measures include fecal markers (e.g., fecal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging studies (magnetic resonance enterography [MRE], computed tomography enterography [CTE]), endoscopic assessment, and/or reduced dose of corticosteroids.

b. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or blood in stool. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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3. Plaque Psoriasis. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):

i. Patient is ≥ 18 years of age; IC-L AND

ii. The patient meets ONE of the following conditions (a or b):

i. The patient has tried at least one traditional systemic agent for psoriasis for at least 3 months, unless other systemic therapies are medically less appropriate; IC-L OR
Note: Examples include methotrexate (MTX), cyclosporine, or acitretin (Soriatane®, generics). A 3-month trial of psoralen plus ultraviolet A light (PUVA)

also counts. An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already has a 3-month trial or previous intolerance to at least one biologic other than the requested medication. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for psoriasis. A patient who has already tried a biologic for psoriasis is not required to "step back" and try a traditional systemic agent for psoriasis.

ii. The patient has a contraindication to methotrexate (MTX), as determined by the prescriber. IC-EC

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has been established on therapy for at least 3 months; IC-ISGP AND
Note: A patient who has received < 3 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating an infliximab product) in at least one of the following: estimated body surface area affected, erythema, induration/thickness, and/or scale of areas affected by psoriasis; IC-ISGP AND

iii. Compared with baseline (prior to receiving an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, itching, and/or burning. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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4. Psoriatic Arthritis (PsA). ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient is ≥ 18 years of age. IC-L

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

a. Patient has been established on therapy for at least 6 months; IC-ISGP AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

b. Patient meets at least one of the following (a or b):

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
Note: Examples of objective measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace

Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; or decreased soft tissue swelling in joints or tendon sheaths. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving Infliximab. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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5. Rheumatoid Arthritis (RA). ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 8 months[29] if patient meets BOTH of the following (i and ii):

i. Patient is ≥ 18 years of age; IC-L AND

ii. Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months. IC-ISGP

Note: Examples include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already had a 3-month trial of at least one biologic other than the requested medication. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for rheumatoid arthritis. A patient who has already tried a biologic is not required to "step back" and try a conventional synthetic DMARD.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; IC-ISGP AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

1. Patient experienced a beneficial clinical response when assessed by at least one objective measure; IC-ISGP OR

   Note: Examples of objective measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate or C-reactive protein, Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).
2. Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or

activities of daily living; or decreased soft tissue swelling in joints or tendon sheaths. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 3 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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6. Ulcerative Colitis. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i and ii):

i. The patient is greater than or equal to 6 years of age; [IC-L] AND

ii. The patient meets ONE of the following conditions (a or b):

a. Patient had a trial of one systemic agent or was intolerant to one of these agents for ulcerative colitis; [IC-L, IC-ISGP] OR

Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis. A previous trial of one biologic other than the requested medication also counts as a trial of one systemic agent for ulcerative colitis. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for ulcerative colitis.

b. Patient meets BOTH of the following [(1) and (2)]:

1. The patient has pouchitis; [IC-EC] AND
2. The patient has tried therapy with an antibiotic, probiotic, corticosteroid enema, or Rowasa® (mesalamine) enema. [IC-EC]

Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema (Cortenema, generics).

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; [IC-ISGP] AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR

Note: Examples of objective measures include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.

b. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or rectal bleeding. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

Other Uses with Supportive Evidence

7. Behcet's Disease. ^

Criteria. Approve for the duration noted if the patient meets the following criteria (A or B):

A) Initial Approval. Approve for 3 months if the patient meets one of the following conditions (i or ii):

- **i.** The patient has tried at least ONE conventional therapy; OR
  Note: Examples include systemic corticosteroids (e.g., methylprednisolone), immunosuppressants (azathioprine, methotrexate [MTX], mycophenolate mofetil, cyclosporine, tacrolimus, Leukeran® [chlorambucil], cyclophosphamide], interferon alfa). An exception to the requirement for a trial of one conventional therapy can be made if the patient has already had a trial of at least one tumor necrosis factor inhibitor (e.g., an adalimumab product [e.g., Humira], an etanercept product [e.g., Enbrel]). A patient who has already tried one biologic other than the requested drug for Behcet's disease is not required to "step back" and try a conventional therapy. A biosimilar of the requested biologic does not count.
- **ii.** The patient has ophthalmic manifestations of Behcet's disease. IC-EC

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- **i.** Patient has been established on therapy for at least 3 months; IC-ISGP AND
  Note: A patient who has received < 3 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP AND
  Note: Examples of objective measures are dependent upon organ involvement but may include best-corrected visual acuity (if ophthalmic manifestations); serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate); or ulcer depth, number, and/or lesion size.
- **iii.** Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain or improved visual acuity (if ophthalmic manifestations). IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then no more frequently than once every 6 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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8. Graft-Versus-Host Disease (GVHD). ^

Criteria. Approve for the duration noted if the patient meets the following criteria (A or B):

A) Initial Approval. Approve for 1 month if the patient has tried at least one conventional systemic treatment for graft-versus-host disease. [IC-ISGP]
Note: Examples of conventional treatments corticosteroids (e.g., methylprednisolone), antithymocyte globulin, cyclosporine, tacrolimus, and mycophenolate mofetil.

B) Patient is Currently Receiving an Infliximab Product. Approve for 3 months if the patient meets BOTH of the following (i and ii):

- **i.** Patient has been established on an infliximab product for at least 1 month; [IC-ISGP] AND
  Note: A patient who has received < 1 month of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
- **ii.** Patient meets at least one of the following (a or b):
  i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR
  Note: An example of objective measures is normalization of liver function tests, red blood cell count, or platelet count, or resolution of fever or rash.
  ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as improvement in skin, oral mucosal, ocular, or gastrointestinal symptoms (e.g., nausea, vomiting, anorexia). [IC-ISGP]

Dosing. Approve the following regimens (A and B):

A) The dose is up to 10 mg per kg given intravenously; AND

B) Doses are administered no more frequently than once weekly.

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9. Hidradenitis Suppurativa. ^

Criteria. Approve for the duration noted if the patient meets the following criteria (A or B):

A) Initial Therapy. Approve for 3 months if the patient has tried one other therapy. [IC-ISGP]
Note: Examples include intralesional or oral corticosteroids (e.g., triamcinolone, prednisone), systemic antibiotics (e.g., clindamycin, dicloxacillin, erythromycin), and isotretinoin).

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- **i.** Patient has been established on therapy for at least 3 months; [IC-ISGP] AND
  Note: A patient who has received < 3 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] AND

Note: Examples of objective measures include Hurley staging, Sartorius score, Physician Global Assessment, and Hidradenitis Suppurativa Severity Index.

iii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain or drainage of lesions, nodules, or cysts. IC-ISGP

Dosing. Approve the following regimens (A and B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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10. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy. ^
Note: This includes severe immune-related colitis

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. The patient developed an immunotherapy-related toxicity other than hepatitis; IC-ISGP AND
Note: For example, gastrointestinal system toxicity (e.g., colitis), ocular toxicity (e.g., uveitis/iritis, episcleritis, and blepharitis). myocarditis, pericarditis, inflammatory arthritis, acute kidney injury (e.g., azotemia, creatinine elevation, inability to maintain acid/base or electrolyte balance, urine output change), or pneumonitis.

ii. The patient developed this immune-related toxicity while receiving a checkpoint inhibitor; IC-ISGP AND
Note: Examples of checkpoint inhibitors include Keytruda (pembrolizumab IV infusion), Opdivo (nivolumab IV infusion), Yervoy (ipilimumab IV infusion), Tecentriq (atezolizumab IV infusion), Bavancio (avelumab IV infusion), or Imfinzi (durvalumab IV infusion).

iii. The patient has tried one systemic corticosteroid.
Note: Examples include methylprednisolone and prednisone.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; IC-ISGP AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
Note: Examples of objective measures are dependent upon organ involvement but may include clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), fecal markers (e.g., fecal calprotectin), and/or reduced dosage of corticosteroids.

ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness or swelling (if joint symptoms), stool frequency and/or rectal bleeding (if gastrointestinal symptoms), and/or improved function or activities of daily living. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 10 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then no more frequently than once every 4 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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11. Indeterminate Colitis. ^

Note: Indeterminate colitis is defined as colitis that cannot be classified with certainty as either ulcerative colitis or Crohn's disease.

Criteria. Approve for the duration noted if the patient meets one of the following criteria (A or B):

A) Initial Therapy. Approve for 6 months if the patient has tried at least one conventional therapy. IC-ISGP

Note: Examples include a systemic corticosteroid (for example, prednisone, methylprednisolone), mesalamine, azathioprine, 6-mercaptopurine.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; IC-ISGP AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b)

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
Note: Examples of objective measures include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.

ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or rectal bleeding. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

12. Juvenile Idiopathic Arthritis (JIA). ^

Note: This includes JIA regardless of type of onset, including a patient with juvenile spondyloarthropathy/active sacroiliac arthritis. JIA is also referred to as Juvenile Rheumatoid Arthritis.

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ONE of the following criteria (i or ii):

- **i.** Patient has tried one other systemic medication for this condition. [IC-ISGP]
  Note: Examples of other medications for JIA include methotrexate (MTX), sulfasalazine, or leflunomide, a nonsteroidal anti-inflammatory drug (NSAID) [e.g., ibuprofen, naproxen]. A previous trial of one biologic other than the requested medication also counts as a trial of one medication. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for JIA.
- **ii.** The patient has aggressive disease, as determined by the prescriber. [IC-ISGP]

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- **i.** Patient has been established on therapy for at least 6 months; [IC-ISGP] AND
  Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** Patient meets at least one of the following (a or b):
  - **i.** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR
    Note: Examples of objective measures include Physician Global Assessment (MD global), Parent/Patient Global Assessment of Overall Well-Being (PGA), Parent/Patient Global Assessment of Disease Activity (PDA), Juvenile Arthritis Disease Activity Score (JDAS), Clinical Juvenile Arthritis Disease Activity Score (cJDAS), Juvenile Spondyloarthritis Disease Activity Index (JSpADA), serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
  - **ii.** Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, or improved function or activities of daily living. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 6 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

13. Pyoderma Gangrenosum. ^

Note: This includes pyoderma gangrenosum with co-existing inflammatory bowel disease

Criteria. Approve for the duration noted if the patient meets the following criteria (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets ONE of the following conditions (i or ii):

- **i.** The patient has tried one systemic corticosteroid; [IC-ISGP] OR
  Note: An example is prednisone.
- **ii.** The patient has tried one other immunosuppressant for at least 2 months or was intolerant to one of these medications. [IC-ISGP]
  Note: Examples include mycophenolate mofetil and cyclosporine.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- **i.** Patient has been established on therapy for at least 4 months; [IC-ISGP] AND
  Note: A patient who has received < 4 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating an infliximab product) in at least one of the following: size, depth, and/or number of lesions; [IC-ISGP] AND
- **iii.** Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain and/or tenderness of affected lesions. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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14. Sarcoidosis. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Approval. Approve for 3 months if the patient meets BOTH of the following conditions (i and ii):

- **i.** Patient has tried at least one corticosteroid; AND
  Note: An example is prednisone.
- **ii.** Patient has tried at least one other standard therapy.
  Note: Examples of other standard therapy include methotrexate, azathioprine, leflunomide, mycophenolate mofetil, hydroxychloroquine, or chloroquine.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- **i.** Patient has been established on therapy for at least 3 months; [IC-ISGP] AND
  Note: A patient who has received < 3 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] AND

Note: Examples of objective measures are dependent upon organ involvement but may include lung function (e.g., predicted forced vital capacity and/or 6-minute walk distance); serum markers (e.g., C-reactive protein, liver enzymes, N-terminal pro-brain natriuretic peptide [NT-proBNP]); improvement in rash or skin manifestations, neurologic symptoms, or rhythm control; or imaging (e.g., if indicated, chest radiograph, magnetic resonance imaging [MRI], or echocardiography).

iii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased cough, fatigue, pain, palpitations, neurologic symptoms, and/or shortness of breath. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then no more frequently than once every 6 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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15. Scleritis or Sterile Corneal Ulceration. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve for 6 months if the patient has tried one other therapy for this condition. [IC-ISGP]
Note: Examples include oral non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin; oral, topical (ophthalmic) or IV corticosteroids (such as prednisone, prednisolone, methylprednisolone); methotrexate (MTX); cyclosporine; or other immunosupressants.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; [IC-ISGP] AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR
Note: Examples of objective measures are serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased eye pain, redness, light sensitivity, tearing, and/or improvement in visual acuity. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 10 mg per kg as an IV infusion administered at baseline and followed by up to three additional similar doses (for example, up to three additional doses given 2, 6, and 8 weeks after the initial infusion).
B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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16. Still's Disease. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
A) Initial Therapy. Approve for 6 months if the patient has tried at least one conventional therapy. IC-ISGP

Note: Examples include a corticosteroid (for example, prednisone, methylprednisolone), conventional synthetic DMARD (for example, methotrexate). A previous trial of one biologic other than the requested drug (e.g., Actemra [tocilizumab intravenous injection, tocilizumab subcutaneous injection], Arcalyst [rilonacept subcutaneous injection], Ilaris [canakinumab subcutaneous injection]) also counts towards this requirement for previous therapy for Still's disease. A biosimilar of the requested biologic does not count.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
   a. Patient has been established on an this medication for at least 6 months; IC-ISGP AND
      Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
   b. Patient meets at least one of the following (a or b):
      i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
         Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
      ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living. IC-ISGP

Dosing.
A) Initial Therapy. Approve up to 6 mg per kg IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 8 weeks thereafter.
B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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17. Spondyloarthritis (SpA), Other Subtypes ^

Note: Examples of other subtypes include undifferentiated arthritis, non-radiographic axial SpA, Reactive Arthritis [Reiter's disease] [NOTE: For AS or PsA, refer to the respective criteria under FDA-approved indications].

Criteria. Approve for the duration noted if ONE of the following conditions are met (A or B):

A) Initial Approval. Approve for 6 months if the patient meets ONE of the following (i or ii):

- **i.** The patient has arthritis primarily in the knees, ankles, elbows, wrists, hands, and/or feet AND has tried at least ONE conventional synthetic disease-modifying antirheumatic drug (DMARD). IC-ISGP
  Note: Examples include methotrexate [MTX], leflunomide, sulfasalazine; OR
- **ii.** The patient has axial spondyloarthritis AND has objective signs of inflammation, defined as at least one of the following [(1) or (2)]: IC-ISGP
  a. C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory; IC-ISGP OR
  b. Sacroiliitis reported on magnetic resonance imaging (MRI). IC-ISGP

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- **i.** Patient has been established on therapy for at least 6 months; IC-ISGP AND
  Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** Patient meets at least one of the following (a or b):
  a. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); IC-ISGP OR
  Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS) and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
  b. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living. IC-ISGP

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 5 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, and then no more frequently than once every 6 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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18. Uveitis. ^

Note: This includes other posterior uveitides and panuveitis syndromes.

Criteria. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Approval. Approve for 6 months if the patient has tried one of the following therapies: periocular, intraocular, or systemic corticosteroids, or immunosuppressives. IC-ISGP

Note: Examples of corticosteroids include prednisolone, triamcinolone, betamethasone, methylprednisolone, prednisone. Examples of immunosuppressives include methotrexate (MTX), mycophenolate mofetil, and cyclosporine. An exception to the requirement for a trial of one of these therapies can be made if the patient has already had a trial of an etanercept product or an adalimumab product for uveitis. A patient who has already tried one biologic other than the requested medication also counts. A biosimilar of the requested biologic does not count.

B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- **i.** Patient has been established on therapy for at least 6 months; [IC-ISGP] AND
  Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
- **ii.** Patient meets at least one of the following (a or b):
  - i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); [IC-ISGP] OR
    Note: Examples of objective measures include best-corrected visual acuity, assessment of chorioretinal and/or inflammatory retinal vascular lesions, or anterior chamber cell grade or vitreous haze grade.
  - ii. Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased eye pain, redness, light sensitivity, and/or blurred vision; or improvement in visual acuity. [IC-ISGP]

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 10 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then no more frequently than once every 4 weeks thereafter.

B) Patient is Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered intravenously no more frequently than once every 4 weeks.

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19. Microscopic Colitis, Refractory. [#]

Criteria. Approve for 6 months if the patient has had a lack of response to standard pharmacologic therapy.
Note: Some examples of standard pharmacologic therapy are budesonide, cholestyramine, loperamide, bismuth salicylate.

Dosing. Approve up to 10 mg per kg as an IV infusion followed by additional similar doses at 2 and 6 weeks after the first infusion, then no more frequently than once every 4 weeks thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of infliximab products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52423 and Inflammatory Conditions – Infliximab Products Utilization Review Policy.	08/28/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52423, and Inflammatory Conditions – Infliximab Products Utilization Review Policy.	12/11/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Avsola (infliximab-axxq for injection, for intravenous use) [biosimilar to Remicade] was added to the policy. Criteria are the same as for the other infliximab products. *Throughout the policy, examples of infliximab products were replaced with a general reference to infliximab products. *Crohn's disease and UC– added "A previous trial of a biologic also counts as a trial" *Plaque psoriasis – added "An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already has a 3-month trial or previous intolerance to at least one biologic." *Plaque psoriasis – added or psoralen plus ultraviolet A light (PUVA) as a traditional systemic therapy *RA – removed specific requirements that define a response, changed to a response as determined by the prescriber	06/18/2020

	*Behcet's disease – changed requirement to try and have inadequate response to one other therapy to only a requirement to try one other conventional therapy. Also added An exception to the requirement for a trial of one conventional therapy can be made if the patient has already had a trial of at least one tumor necrosis factor inhibitor *Sarcoidosis – Patient has tried and was refractory to a corticosteroid and one other therapy, removed "refractory to" requirement *Conditions not recommended for approval – removed inflammatory myopathies	
Policy revision	**Crohn's Disease:** Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section). For the criterion applying to previous therapy, wording was changed to specify this must have been a conventional systemic therapy (criteria previously required a trial of one other agent, with conventional systemic agents listed among the examples). **Plaque Psoriasis:** Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section). **Rheumatoid Arthritis:** Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section). **Ulcerative Colitis:** Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section). **Graft Versus Host Disease (GVHD):** To align with updated guidelines and other policies, criteria were changed to require at least one conventional systemic treatment prior to an infliximab product. Previously, criteria required that the patient had tried at least one other immunosuprressant or be concurrently receiving an immunosuppressant in combination with an infliximab product. **Juvenile Idiopathic Arthritis:** Examples of biologics were moved to be included in the Appendix (previously listed in a Note in the criteria section).	10/01/2020
Policy revision	**Juvenile Idiopathic Arthritis:** The approval condition was reworded to as listed. Previously the indication also included Juvenile Rheumatoid Arthritis (regardless of type of onset), which was moved into a Note. **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy:** The requirement that the patient has an immunotherapy-related toxicity was reworded to generally refer to an immunotherapy-related toxicity other than hepatitis. Specific toxicities related to the gastrointestinal system, inflammatory arthritis, and ocular toxicity were moved from the criteria into a note representing examples of various immunotherapy-related toxicities. **Uveitis:** The approval condition was reworded to as listed. Previously, the indication included other posterior uveitides and panuveitis syndromes, which was moved into a note.	10/22/2021
Policy revision	Infliximab intravenous infusion (authorized generic to Remicade) was added to the policy. Criteria are the same as the other infliximab products addressed in the policy.	12/29/2021
Policy revision	**Ankylosing Spondylitis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Crohn's Disease:** Initial approval duration was changed to 6 months (previously was 3 months). Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. A note was	11/15/2022

	added to clarify that a trial of mesalamine does not count as a systemic agent for Crohn's disease. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Plaque Psoriasis:** Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 90 days. Requirements were added that for a patient who is currently receiving an infliximab product, the patient must have at least one objective and at least one subjective response to therapy. Previously, response was more general and according to the prescriber. **Psoriatic Arthritis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Rheumatoid Arthritis:** Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Ulcerative Colitis:** Initial approval duration was changed to 6 months (previously was 3 months). Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Behcet's Disease:** Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 90 days. Requirements were added that for a patient who is currently receiving an infliximab product, the patient must have at least one objective and at least one subjective response to therapy. Previously, response was more general and according to the prescriber. **Graft-Versus-Host Disease:** For a patient currently receiving, it was clarified that this applies to a patient who is receiving an infliximab product for ≥ 1 month. Requirements were added for a patient who is currently receiving, that there has been at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber.	

	Hidradenitis Suppurativa: For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 90 days. Requirements were added that for a patient who is currently receiving an infliximab product, the patient must have at least one objective and at least one subjective response to therapy. Previously, response was more general and according to the prescriber. **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Indeterminate Colitis:** The definition of indeterminate colitis (colitis that cannot be classified with certainty as either ulcerative colitis or Crohn's disease) was moved to a note; previously this was included in the indication. Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Juvenile Idiopathic Arthritis:** Initial approval duration was changed to 6 months (previously was 3 months). Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years. **Pyoderma Gangrenosum:** For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 4 months. Requirements were added that for a patient who is currently receiving an infliximab product, the patient must have at least one objective and at least one subjective response to therapy. Previously, response was more general and according to the prescriber. **Sarcoidosis:** To align with guidelines, the note that includes examples of immunosuppressive medications was updated to add leflunomide, mycophenolate mofetil, and hydroxychloroquine; cyclosporine, chlorambucil, and thalidomide were removed from the examples. Cardiologist and neurologist were added to the list of specialists who must prescribe or be consulted for this indication. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 90 days. Requirements were added that for a patient who is currently receiving an infliximab product, the patient must have at least one objective and at least one subjective response to therapy. Previously, response was more general and according to the prescriber. **Scleritis or Sterile Corneal Ulceration:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently	

	receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Spondyloarthritis, Other Subtypes:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Still's Disease:** Initial approval duration was changed to 6 months (previously was 3 months). Note was updated to state that a previous trial of one biologic other than the requested drug counts towards a requirement for previous therapy. A biosimilar of the requested biologic does not count. For a patient currently receiving, it was clarified that this applies to a patient who is receiving an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Uveitis:** Initial approval duration was changed to 6 months (previously was 3 months). Note was clarified to state that a previous trial of a biologic applies to at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. For a patient currently receiving an infliximab product, it was clarified that this applies to a patient who has received an infliximab product for ≥ 6 months. A requirement was added for a patient who is currently receiving an infliximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber.	
Policy revision	**Ulcerative Colitis:** For a patient currently taking, a note was added to clarify that a mesalamine product does not count as a systemic therapy for ulcerative colitis.	12/13/2023
Policy revision	**Plaque Psoriasis:** For a patient currently taking an infliximab product, the timeframe for established on therapy was changed from 90 days to 3 months. **Behcet's Disease:** For a patient currently taking an infliximab product, the timeframe for established on therapy was changed from 90 days to 3 months. **Hidradenitis Suppurativa:** For a patient currently taking an infliximab product, the timeframe for established on therapy was changed from 90 days to 3 months. **Sarcoidosis:** For a patient currently taking an infliximab product, the timeframe for established on therapy was changed from 90 days to 3 months. Based on commercial policy revision	4/30/2024
Policy revision	**Microscopic Colitis, Refractory.** New indication added, criteria requires lack of response to standard pharmacologic therapy. Revision based on update to LCD.	07/17/2024, Effective 8/1/2024
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024

Policy revision	**Ankylosing Spondylitis:** For initial approvals, a requirement that the patient is ≥ 18 years of age was added. **Plaque Psoriasis:** In the Note, psoralen plus ultraviolet A light (PUVA) was removed from the examples of traditional systemic therapies. An additional Note was added that a 3-month trial of PUVA counts as a traditional systemic therapy. **Psoriatic Arthritis:** For initial approvals, a requirement that the patient is ≥ 18 years of age was added. **Rheumatoid Arthritis:** For initial approvals, a requirement that the patient is ≥ 18 years of age was added.	09/20/2024
Policy revision	**Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy:** Myalgia and myositis were removed from the examples of immunotherapy-related toxicities associated with checkpoint inhibitor therapy.	01/06/2025
Aspirus Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025
Policy review	No criteria changes. Based on review of LCD L33394 update.	09/08/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Simponi®, Simponi Aria® (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: PsA, PsO, UC
		IV formulation: UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.