POLICY: Inflammatory Conditions – Infliximab Products

- Avsola™ (infliximab-axxq for injection, for intravenous use – Amgen)
- Inflectra™ (infliximab-dyyb for injection, for intravenous use – Hospira/Pfizer)
- Remicade® (infliximab for intravenous infusion – Janssen Biotech, Inc./Johnson&Johnson)
- Renflexis® (infliximab-abda IV infusion – Samsung Bioepis/Merck)

DATE REVIEWED: 08/28/2019; selected revision 06/03/2020

OVERVIEW

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

1. **Rheumatoid arthritis** (RA), in combination with methotrexate (MTX) for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately to severely active RA.
2. **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 in the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adults with fistulizing Crohn's disease.
3. **Ankylosing spondylitis** (AS), for reducing signs and symptoms of active disease;
4. **Psoriatic arthritis** (PsA), for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function.
5. **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; AND
6. **Ulcerative colitis** (UC), for the following uses:
   - for 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
   - for reducing signs and symptoms and inducing and maintaining clinical remission 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.

- **Spondyloarthritis:** Guidelines from the Assessment of SpondyloArthritis International Society (ASAS)/EULAR (2016) recommend biologics (e.g., TNFis, Cosentyx) in patients with persistently high disease activity despite traditional conventional treatments (e.g., nonpharmacological management, NSAIDs).[4] Purely axial disease should not be treated with conventional synthetic DMARDs. Guidelines from the American College of Rheumatology (ACR) and the

Spondyloarthritis Research and Treatment Network (SPARTAN) [2015] recommend TNFis for patients with active disease despite treatment with an NSAID (includes patients with non-radiographic axial [nr-ax]SpA).[5] Predominantly axial manifestations are not recommended for a conventional synthetic DMARD prior to a TNFi. However, for symptomatic peripheral arthritis, a conventional synthetic DMARD is recommended (preferably sulfasalazine).

- **Crohn's Disease:** The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).[6] 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.
- **Plaque Psoriasis:** Guidelines from the American Academy of Dermatologists (AAD) and National Psoriasis Foundation (NPF) 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 PsA and in those who were previously treated with an oral therapy.[8]
- **Rheumatoid Arthritis:** Guidelines from the American College of Rheumatology (ACR) [2015] have TNF inhibitors and non-TNF biologics, administered with or without MTX, equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., MTX, leflunomide, hydroxychloroquine, sulfasalazine).[9]
- **Ulcerative Colitis:** Updated ACG guidelines for UC (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: Uceris tablets; Oral or intravenous systemic corticosteroids Entyvio, Xeljanz, or TNFis (adalimumab, Simponi SC, infliximab).[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). A retrospective, open-label, case series demonstrated some efficacy of Humira in patients with pouchitis previously treated with infliximab.[10]

Other Uses with Supportive Evidence

There are guidelines and/or published data supporting the use of infliximab products in the following conditions:

- **Behcet's Disease:** EULAR recommendations (2018) include TNFis for initial or recurrent sight-threatening uveitis.[12] 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] notes 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.[13]
- **Graft-Versus-Host Disease:** In retrospective analyses and case series, infliximab has been effective in treating some patients with steroid-refractory acute or chronic graft-versus-host disease.[19-24] In a prospective study in 19 patients, infliximab was not effective in the *prophylaxis* of acute GVHD, but may have delayed platelet engraftment and was associated with frequent infectious complications. In studies evaluating the role of infliximab for treatment of steroid-refractory acute GVHD, the overall response rates ranged from 15% to 100%, with the highest response rates in patients with GI and skin disease.
- **Hidradenitis Suppurativa:** In a Phase II double-blind, placebo-controlled crossover trial, adult patients with moderate to severe hidradenitis suppurativa were randomized to placebo (n = 23) or infliximab 5 mg/kg (n = 15) at Weeks 0, 2, and 6.[25] After Week 8, patients were unblinded, and placebo patients were offered induction with placebo. Maintenance was continued through 22

weeks of treatment. Following Week 8, more patients in the infliximab-treatment group experienced a 50% or greater decrease in the Hidradenitis Suppurativa Severity Index (HSSI) score (approximately 26% and 5% of patients receiving infliximab and placebo, respectively [data presented graphically]; P = 0.092). In post-hoc analysis, significantly more patients treated with infliximab responded with a 25% to < 50% response (60% and 5.6% for infliximab and placebo, respectively; P < 0.001). Improvement was noted through Week 30. In case series, inflximab has been effective in treating hidradenitis suppurativa that was refractory to other therapies.[26-28]

- **Indeterminate Colitis:** Infliximab has been effective in some patients with refractory indeterminate colitis (retrospective reviews).[29,30] 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.
- **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.[13] Infliximab may be used in patients with uveitis due to various causes (e.g., spondyloarthropathy-associated or human leukocyte antigen [HLA]-B27-associated uveitis, JIA-associated uveitis, and other posterior uveitides and panuveitis syndromes).[13] Infliximab should be considered second-line in vision-threatening JIA-associated uveitis when MTX 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.
- **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors:** NCCN has guidelines in partnership with the American Society of Clinical Oncology (ASCO) [version 1.2019 – November 14, 2018] for Management of Immunotherapy-Related Toxicities.[14] Recommended therapies include use of infliximab to manage many toxicities. Some severe toxicities (e.g., pneumonitis, cardiac toxicity, renal failure) may also be treated with infliximab but are more likely to be administered in the hospital setting.
- **Juvenile Idiopathic Arthritis (JIA):** The 2011 ACR recommendations for the treatment of JIA propose initial DMARD treatment with MTX in most patients; however, sulfasalazine is recommended for patients with enthesitis-related arthritis and may also be used in certain patients with sacroiliac arthritis.[15] Leflunomide may be an appropriate initial DMARD in those with high disease activity and/or a poor prognosis. Kineret may be used in systemic arthritis and Actemra may be used in systemic and polyarticular juvenile arthritis.[15-16] TNF antagonists such as infliximab may also be used as second- or third-line treatment for systemic JIA.[15]
- **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.[17] Other systemic therapies include cyclosporine, MTX, azathioprine, cyclophosphamide, mycophenolate mofetil, and TNFis (i.e., infliximab, etanercept, and adalimumab products). In case reports, TNFis have been effective.
- **Still's Disease:** Still's disease presents in adults with features similar to those of systemic onset JIA.[31-32] In case series, infliximab has been effective in patients with Still's disease that was refractory to therapy with corticosteroids, MTX, azathioprine, and cyclophosphamide.[33]

- **Sarcoidosis:** Recommendations for best practice in the management of pulmonary and systemic sarcoidosis recommend glucocorticoids as first-line therapy.[18] Patients who cannot be weaned to a prednisone-equivalent dose of < 10 mg/day are appropriate candidates for steroid-sparing treatment with cytotoxic agents (e.g., MTX, azathioprine, leflunomide). If these agents fail or cause toxicity, adalimumab, infliximab, cyclophosphamide, or mycophenolate mofetil are proposed.

Dosing Information

The recommended dose of infliximab 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.[110-113] At this time, there is not a consensus regarding tapering. The 2015 ACR guidelines for RA mention tapering, defined as scaling back therapy (reducing dose or frequency) as a treatment option for patients who are in remission.[18] Although specific tapering schedules are not recommended, it is noted that minimizing therapy may decrease toxicity and lowers the risk of treating patients unnecessarily. 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.

Safety

Infliximab has Boxed Warnings concerning risks of serious infection and the risk of malignancy.[1] Prior to initiating therapy with infliximab, patients should be evaluated for active tuberculosis (TB) infection, and periodically during therapy patients should be assessed for latent TB infection. Patients should also be monitored for signs and symptoms of infection during and after treatment with infliximab, and if a serious infection or sepsis develops, infliximab should be discontinued. It is also recommended that patients treated with any TNF antagonist should be monitored for malignancies.

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. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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. Because of the specialized skills required for evaluation and diagnosis of patients treated with infliximab products as well as the monitoring required for adverse events and long-term efficacy, initial approval requires infliximab products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Ankylosing Spondylitis (AS).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if prescribed by or in consultation with a rheumatologist.
   - **B)** Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.

Note: Examples of a response to therapy include decreased pain or stiffness, improved function or activities of daily living. The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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2. Crohn's Disease. 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, ii, and iii):

i. The patient is greater than or equal to 6 years of age; 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; OR
Note: Examples of corticosteroids are prednisone and methylprednisolone.

b) The patient has tried one other agent for Crohn's disease; OR
Note: Examples of other agents for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate (MTX). A previous trial of a biologic (e.g., Cimzia [certolizumab pegol SC injection], an adalimumab product [e.g., Humira], Entyvio [vedolizumab IV infusion], or Stelara [ustekizumab IV infusion, ustekizumab SC injection]) also counts as a trial of one other agent for Crohn's disease).

c) The patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR

d) The patient has had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND

iii. The agent is prescribed by or in consultation with a gastroenterologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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3. Plaque Psoriasis. 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, ii, and iii):

i. The patient is an adult greater than or equal to 18 years of age; AND

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

a) The patient has tried at least at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant; OR

Note: Examples include methotrexate (MTX), cyclosporine, acitretin [Soriatane®, generics], or psoralen plus ultraviolet A light (PUVA). 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 (e.g., an adalimumab product [e.g., Humira], Cimzia [certolizumab pegol SC injection], an etanercept product [e.g., Enbrel], Cosentyx [secukinumab SC injection], Ilumya [tildrakizumab SC injection], Siliq [brodalumab SC injection], Skyrizi [risankizumab-rzaa SC injection], Stelara [ustekinumab for SC injection], Taltz [ixekizumab for SC injection), or Tremfya [guselkumab SC injection]). These patients who have already tried a biologic for psoriasis are not required to "step back" and try a traditional systemic agent for psoriasis).

b) The patient has a contraindication to methotrexate (MTX), as determined by the prescriber; AND

iii. The agent is prescribed by or in consultation with a dermatologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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4. Psoriatic Arthritis (PsA). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants [for example, C-reactive protein [CRP]). The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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5. Rheumatoid Arthritis (RA). 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 BOTH of the following criteria (i and ii):
- **i.** The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
  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 at least one biologic (e.g., Cimzia [certolizumab pegol SC injection], an etanercept product [e.g., Enbrel], an adalimumab product [e.g., Humira], Simponi/Aria [golimumab SC injection, golimumab IV infusion], Actemra [tocilizumab IV infusion, tocilizumab SC injection], Kevzara [sarilumab SC injection], Kineret [anakinra SC injection], Orencia [abatacept IV infusion, abatacept SC injection], and a rituximab product [Rituxan, Truxima]. These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD).
- **ii.** The agent is prescribed by or in consultation with a rheumatologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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6. Ulcerative Colitis. 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, ii, and iii):
- **i.** The patient is greater than or equal to 6 years of age; AND
- **ii.** The patient meets ONE of the following conditions (a or b):
  - **a)** Patient has had a trial of one systemic agent or was intolerant to one of these agents for ulcerative colitis; OR
    Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone. A previous trial of a biologic (e.g., an adalimumab product [e.g., Humira], Simponi SC [golimumab SC injection], or Entyvio [vedolizumab IV infusion] also counts as a trial of one systemic agent for UC).
  - **b)** The patient has pouchitis AND has tried therapy with an antibiotic, probiotic, corticosteroid enema, or Rowasa® (mesalamine) enema; AND
    Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema (Cortenema, generics).
- **iii.** The agent is prescribed by or in consultation with a gastroenterologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response include decreased stool frequency or rectal bleeding. The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

Other Uses with Supportive Evidence

7. Behcet's Disease. 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 meets BOTH of the following conditions (i and ii):
  - **i.** The patient meets ONE of the following (a or b):
    - **a)** 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]). These patients who have already tried a biologic for Behcet's disease are not required to "step back" and try a conventional therapy).
    - **b)** The patient has ophthalmic manifestations of Behcet's disease; AND
  - **ii.** The agent is prescribed by or in consultation with a rheumatologist, dermatologist, ophthalmologist, gastroenterologist, or neurologist.
- **B)** Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
  Note: The patient may not have a full response by Month 2 or 3, but there should be some response.

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

8. Graft-Versus-Host Disease (GVHD). Approve for the duration noted if the patient meets the following criteria (A or B):
- **A)** Initial Therapy. Approve for 1 month if the patient meets BOTH of the following (i and ii):
  - **i.** The patient meets ONE of the following conditions (a or b):
    - **a)** Patient has tried one conventional treatment for graft-versus-host disease (GVHD); OR
    - **b)** Patient is concurrently receiving at least one of these medications in combination with an infliximab product; AND
      Note: Examples of conventional treatments the patient may have tried or may be receiving include a high-dose corticosteroid (e.g., methylprednisolone), antithymocyte globulin, cyclosporine, Thalomid (thalidomide tablets), tacrolimus, and mycophenolate mofetil.
  - **ii.** The agent is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; OR
- **B)** Patients Currently Receiving an Infliximab Product. Approve for 3 months if the patient has had a response, as determined by the prescriber.

Dosing. Approve the following regimens (A and B):
- **A)** The dose is up to 10 mg per kg IV infusion; AND
- **B)** Doses are administered no more frequently than once weekly.

9. Hidradenitis Suppurativa. 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 meets BOTH of the following (i and ii):

i. The patient has tried one other therapy; AND
Note: Examples include intralesional or oral corticosteroids (e.g., triamcinolone, prednisone), systemic antibiotics (e.g., clindamycin, dicloxacillin, erythromycin), and isotretinoin).

ii. The agent is prescribed by or in consultation with a dermatologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.

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.[47]

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

10. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy. 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 ALL of the following (i, ii, iii, and iv):

i. The patient developed an immunotherapy-related toxicity involving the gastrointestinal system, inflammatory arthritis, or ocular toxicity; AND
Note: An example of a gastrointestinal system toxicity is colitis. Examples of ocular toxicities include uveitis/iritis, episcleritis, and blepharitis.

ii. The patient developed this immune-related toxicity while receiving a checkpoint inhibitor; 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 a systemic corticosteroid; AND
Note: Examples include methyprednisone and prednisone.

iv. The agent is prescribed by or in consultation with an oncologist, gastroenterologist, rheumatologist, or ophthalmologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has responded and needs continued treatment, as determined by the prescriber.

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

11. Indeterminate Colitis (defined as colitis that cannot be classified with certainty as either ulcerative colitis or Crohn's disease). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. The patient is greater than or equal to 6 years of age; AND
ii. The patient has tried one systemic corticosteroid; AND
Note: Examples include prednisone and methylprednisolone.
iii. The patient has tried mesalamine; AND
iv. The patient has tried either azathioprine or 6-mercaptopurine; AND
v. The agent is prescribed by or in consultation with a gastroenterologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.

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

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12. Juvenile Idiopathic Arthritis (JIA) [or Juvenile Rheumatoid Arthritis {JRA}] (regardless of type of onset) [Note: This includes patients with juvenile spondyloarthropathy/active sacroiliac arthritis]. 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 meets ONE of the following conditions (a or b):
a) Patient has tried one other agent for this condition; OR
Note: Examples of other agents for JIA include methotrexate (MTX), sulfasalazine, or leflunomide, a nonsteroidal anti-inflammatory drug (NSAID) [e.g., ibuprofen, naproxen]. A previous trial of a biologic (e.g., an adalimumab product [e.g, Humira], an etanercept product [e.g., Enbrel], Orencia [abatacept IV infusion, abatacept SC injection], Kineret [anakinra SC injection], and Actemra [tocilizumab IV infusion, tocilizumab SC injection] also counts as a trial of one agent for JIA).
b) The patient has aggressive disease, as determined by the prescriber; AND
ii. The agent is prescribed by or in consultation with a rheumatologist.

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response include improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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13. Pyoderma Gangrenosum. 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 BOTH of the following conditions (i and ii):
- **i.** The patient meets ONE of the following conditions (a or b):
  - **A)** The patient has tried one systemic corticosteroid; OR
    Note: An example is prednisone.
  - **B)** The patient has tried one other immunosuppressant for at least 2 months or was intolerant to one of these agents; AND
    Note: Examples include mycophenolate mofetil and cyclosporine.
- **ii.** The agent is prescribed by or in consultation with a dermatologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response by Month 4 or 5 (after 4 doses), but there should be some response.

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.[86]

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

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

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following conditions (i, ii, and iii):
- **i.** The patient has tried at least one corticosteroid; AND
  Note: An example is prednisone.
- **ii.** The patient has tried at least one immunosuppressive agent; AND
  Note: Examples include methotrexate (MTX), azathioprine, cyclosporine, Leukeran, Thalomid® (thalidomide capsules), or chloroquine.
- **iii.** The agent is prescribed by or in consultation with a pulmonologist, ophthalmologist, or dermatologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response by Month 3, but there should be some response.

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.[1]

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

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15. Scleritis or Sterile Corneal Ulceration. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

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

i. The patient has tried one other therapy for this condition; AND
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.
ii. The agent is prescribed by or in consultation with an ophthalmologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response to therapy include decreased inflammation, reduced use of steroids or immunomodulators, decreased eye pain, redness, and/or photophobia. The patient may not have a full response by Month 2 or 3, but there should be some response.

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

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16. Still's Disease. Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following conditions (i, ii, and iii):
i. The patient has tried one corticosteroid; AND
Note: An example is prednisone.
ii. The patient has tried one conventional synthetic DMARD given for at least 2 months or was intolerant to a conventional synthetic DMARD; AND
Note: An example is methotrexate.
iii. The agent is prescribed by or in consultation with a rheumatologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response by Month 2 or 3, but there should be some response.

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

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) Patients Currently Receiving an Infliximab Product. Approve up to a maximum dose of 10 mg/kg administered 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]. For AS or PsA, refer to the respective criteria under FDA-approved indications). Approve for the duration noted if ONE of the following conditions are met (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following conditions (i and ii):
i. The patient meets ONE of the following (a or b):

a) 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) has been tried; OR
Note: Examples include methotrexate [MTX], leflunomide, and sulfasalazine.

b) The patient has axial spondyloarthritis AND has objective signs of inflammation, defined as at least one of the following [(1) or (2)]:

(1) C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory; OR

(2) Sacroiliitis reported on magnetic resonance imaging (MRI); AND

ii. The agent is prescribed by or in consultation with a rheumatologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the patient has had a response as determined by the prescriber.
Note: Examples of a response include decreased pain or stiffness, improved function or activities of daily living. The patient may not have a full response, but there should have been a recent or past response to an infliximab product.

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

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18. Uveitis (including other posterior uveitides and panuveitis syndromes). Approve for the duration noted if the patient meets ONE of the following criteria (A or B):

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

i. The patient has tried one of the following therapies: periocular, intraocular, or systemic corticosteroids, or immunosuppressives; AND
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 (e.g., Enbrel) or an adalimumab product (e.g., Humira) for uveitis. These patients who have already tried a biologic for uveitis are not required to try a another agent.

ii. The agent is prescribed by or in consultation with an ophthalmologist; OR

B) Patients Currently Receiving an Infliximab Product. Approve for 1 year if the has had a response as determined by the prescriber.
Note: Examples of a response include decreased inflammation, reduced use of steroids or immunomodulators, and improvement in visual acuity. The patient may not have a full response by Month 2 or 3, but there should be some response.

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Infliximab products have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD.** Data are lacking evaluating concomitant use of an infliximab product in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see APPENDIX for examples). Combination therapy with biologics and/or biologics + targeted synthetic DMARDs has a potential for a higher rate of AEs with combinations and lack controlled trial data in supportof additive efficacy.[34-35] Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with an infliximab product.

2. **Inflammatory Myopathies (Polymyositis, Dermatomyositis, Inclusion Body Myositis).** Exceptions are not recommended. In an open-label pilot study in 13 patients, four infliximab 5 mg/kg infusions given over 14 weeks were not effective in refractory inflammatory myopathies.[36] Infliximab could worsen muscle inflammation in these patients.

3. **Large Vessel Vasculitis (e.g., Giant Cell Arteritis, Takayasu's Arteritis).** Guidelines from EULAR for the management of large vessel vasculitis (e.g., giant cell arteritis, Takayasu's arteritis) do not mention the use of TNF blockers.[37] Additionally, a meta-analysis of RCTs did not find evidence supporting remission or reduction of corticosteroid dose with the use of TNF blockers in large vessel vasculitis.[38] In a controlled trial, 44 patients with newly diagnosed giant cell arteritis that was in glucocorticoid-induced remission were randomized to Infliximab 5 mg/kg plus glucocorticoid (n = 28) or placebo plus glucocorticoid (n = 16).[39] Infliximab did not increase the percentage of patients without relapse at Week 22 nor did it increase the percentage of patients whose glucocorticoid dose was decreased to 10 mg/day without relapse. Use of TNF blockers such as infliximab for Takayasu's arteritis is limited to case series where TNF blockers are often used third line, after treatment with corticosteroids and other immunosuppressants (e.g., azathioprine, MTX, MMF, cyclophosphamide).[40-44] Infliximab has been effective in a very limited number of patients with vasculitis (e.g., RA, cryoglobulinemia, polyangiitis, polymyalgia rheumatica, Takayasu's arteritis) who were refractory to standard therapy.[40-41,45-49] However, in a randomized study in 51 patients with newly diagnosed polymyalgia rheumatica, adding Infliximab 3 mg/kg to prednisone was of no benefit and may have been harmful.[50-51]

4. 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 Reviewed
Annual revision	Clarify criteria for Crohn's disease, ulcerative colitis, Behcet's disease, JIA, and uveitis. For these conditions, the criterion that directs patients to previous therapy prior to approval of infliximab was reworded to clarify its intent such that patients are now directed to conventional agents with a note that prior use of a biologic would count towards this requirement. Previously, criteria were worded more generally and both conventional and biologic therapies were listed.	07/12/2017
Selected revision	Add Renflexis to the policy with the same criteria as Inflectra and Remicade.	07/26/2017
Selected revision	For initial therapy of plaque psoriasis, add criteria to require that the patient be to be at least 18 years of age.	10/18/2017
Annual revision	**Immunotherapy-Related Toxicity Related to Checkpoint Inhibitor Therapy:** New indication added to align with ASCO/NCCN guidelines for patients who develop GI, joint, or ophthalmic toxicity while on a checkpoint inhibitor. Approval is for 3 months, if the patient has tried a corticosteroid, and if prescribed by or in consultation with a gastroenterologist, ophthamalogist, rheumatologist, or oncologist. Reauthorization is for 1 year, if the patient responded and needs continued treatment, according to the prescriber. **Patients Established on Infliximab:** Remove this criterion for patients currently established on infliximab for ≥ 90 days. Patients currently taking infliximab are now addressed in the criteria section for each specific indication. • To align with the infliximab PA Policy, remove requirement that the patient be receiving infliximab for ≥ 90 days for the following indications: RA, AS, CD, PsO, PsA, UC, and JIA.	08/01/2018

	• Add a requirement that the patient must have responded to initial therapy for the following indications: Behcet's disease, GVHD, HS, indeterminate colitis, pyoderma gangrenosum, sarcoidosis, slceritis or sterile corneal ulcerations, Still's disease, SpA, and uveitis. **Preferred Drug:** Remove this section from the policy (previously applied to RA, AS, CD, PsO, PsA, JIA, and SpA). **Previous Therapies:** For these indications, add the following agents to the list of therapies the patient may have tried prior to infliximab: • CD: Stelara IV/SC • PsO: Cimzia, Illumya, Siliq, Tremfya • UC: Entyvio • JIA: Actemra SC **Behcet's disease:** Modify criteria to change previous therapy from biologic to more specifically say TNFi. **Other:** Throughout the policy, references to Humira and Enbrel were reworded as adalimumab and etanercept products, respectively, with the innovator names listed as examples of these products.	
Selected revision	**Ulcerative colitis:** For the requirement that another agent be tried prior to Entyvio, remove the requirement that the trial is a duration of at least 2 months (not supported in updated guidelines).	03/27/2019
Selected revision	**Spondyloarthritis (SpA), Other Subtypes:** This off-label approval condition was reworded (previously listed as Spondyloarthritis, Subtypes Other than Ankylosing Spondylitis or Psoriatic Arthritis). There is a note which directs to criteria for FDA-approved subtypes of SpA (AS, PsA). For patients with primarily axial disease, a criterion was added to require objective signs of inflammation, defined as C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory or sacroiliitis reported on magnetic resonance imaging. For patients currently receiving therapy, examples of a response to therapy were added; the requirement that patients be on an infliximab product for ≥ 90 days was removed.	04/24/2019
Annual revision	**Dosing:** Throughout the policy, dosing was updated to clarify the dose which may be approved up to the maximum dose and shortest treatment interval listed in the dosing criteria for each indication. All wording that referred to patients who had an inadequate response was removed from the dosing section (not needed – already included in the criteria section of the policy). **Crohn's Disease:** Move requirement that the patient be 6 years of age or older into the criteria section for initial therapy. Previously, age was listed as part of the diagnosis (i.e., previously listed as Crohn's disease in a patient ≥ 6 years of age) and applied to initial and continuation of therapy. **Plaque Psoriasis:** For the exception applying to patients with a contraindication to methotrexate, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). Skyrizi was added to the list of biologics that the patient may have tried prior to infliximab. **Rheumatoid Arthritis:** Truxima was added to as an example of a rituximab product that the patient may have tried prior to infliximab. **Ulcerative Colitis:** Move requirement that the patient be 6 years of age or older into the criteria section for initial therapy. Previously, age was listed as part of the diagnosis (i.e., previously listed as Ulcerative Colitis in a patient ≥ 6 years of age) and applied to initial and continuation of therapy. **Behcet's Disease:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Graft versus Host Disease:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Hidradentitis Suppurativa:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed.therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy:** When a response to therapy is required for patients continuing infliximab, wording was changed to be according to the prescriber (previously worded as prescribing physician). **Indeterminate Colitis:** Move requirement that the patient be 6 years of age or older into the criteria section for initial therapy. Previously, age was listed as part of the diagnosis	08/28/2019

	(i.e., previously listed as Indeterminate Colitis in a patient ≥ 6 years of age) and applied to initial and continuation of therapy. For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Juvenile Idiopathic Arthritis:** For the exception applying to patients with aggressive disease, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). **Pyoderma Gangrenosum:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Sarcoidosis:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. When a response to therapy is required for patients continuing infliximab, wording was changed to be according to the prescriber (previously worded as prescribing physician). **Scleritis/Sterile Corneal Ulceration:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. When a response to therapy is required for patients continuing infliximab, wording was changed to be according to the prescriber (previously worded as prescribing physician). **Still's Disease:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. **Uveitis:** For patients currently receiving therapy, the requirement that patients be on an infliximab product for ≥ 90 days was removed. When a response to therapy is required for patients continuing infliximab, wording was changed to be according to the prescriber (previously worded as prescribing physician).	
Revision	**Overview:** Update to include new approval indications for biosimilars. No changes to the criteria.	11/25/2019
Selected 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.	06/03/2020

APPENDIX

Brand (generic name)	Mechanism of Action
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6
Kevzara® (sarilumab SC injection)	Inhibition of IL-6
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator
Rituximab IV Products (Rituxan®, biosimiars)	CD20-directed cytolytic antibody
Kineret® (anakinra SC injection)	Inhibition of IL-1
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist
Otezla® (apremilast tablets)	Inhibition of PDE4
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.