

Corporate Medical Policy: Infliximab (Remicade®) and Infliximab Biosimilars

Restricted Product(s):

- infliximab (Remicade®) intravenous infusion for administration by a healthcare professional
- Infliximab intravenous infusion for administration by a healthcare professional
- infliximab-abda (Renflexis®) intravenous infusion for administration by a healthcare professional
- *infliximab-axxq (Avsola™) intravenous infusion for administration by a healthcare professional
- *infliximab-dyyb (Inflectra®) intravenous infusion for administration by a healthcare professional

***preferred agent**

FDA Approved Use:

- For reducing signs and symptoms of Crohn's disease and inducing and maintaining clinical remission in patients 6 years and older with moderately to severely active disease who have had an inadequate response to conventional therapy
- For reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adults with fistulizing Crohn's disease
- For reducing signs and symptoms of ulcerative colitis, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients 6 years and older with moderately to severely active disease who have had an inadequate response to conventional therapy
- For reducing signs and symptoms of rheumatoid arthritis, inhibiting the progression of structural damage, and improving physical function in adults with moderately to severely active disease; in combination with methotrexate
- For reducing signs and symptoms of ankylosing spondylitis in adults with active disease
- For reducing signs and symptoms of active psoriatic arthritis, inhibiting the progression of structural damage, and improving physical function in adults
- For treatment of adults with chronic severe plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient has a diagnosis of moderately to severely active **rheumatoid arthritis (RA)**; **AND**
 - a. The patient is 18 years of age or older; **AND**

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- b. The patient has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3-months **[medical record documentation required]; OR**
 - c. The patient has tried and had an inadequate response to another conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA for at least 3-months **[medical record documentation required]; OR**
 - d. The patient has an intolerance or hypersensitivity to ONE of the following conventional agents (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **[medical record documentation required]; OR**
 - e. The patient has an FDA labeled contraindication to ALL of the following conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **[medical record documentation required]; AND**
 - f. The patient will be taking the requested agent in combination with methotrexate; **OR**
 - g. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to methotrexate **[medical record documentation required]; OR**
2. The patient has a diagnosis of chronic severe **plaque psoriasis (PS); AND**
- a. The patient is 18 years of age or older; **AND**
 - b. The patient has tried and had an inadequate response to ONE conventional agent (i.e., acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS for at least 3-months **[medical record documentation required]; OR**
 - c. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of PS **[medical record documentation required]; OR**
 - d. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of PS **[medical record documentation required]; OR**
 - e. The patient has severe chronic PS (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) **[medical record documentation required]; OR**
 - f. The patient has concomitant severe psoriatic arthritis (PsA) (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive) **[medical record documentation required]; OR**
3. The patient has a diagnosis of active **psoriatic arthritis (PsA); AND**
- a. The patient is 18 years of age or older; **AND**
 - b. The patient has tried and had an inadequate response to ONE conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3-months **[medical record documentation required]; OR**

- c. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of PsA [**medical record documentation required**]; **OR**
 - d. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of PsA [**medical record documentation required**]; **OR**
 - e. The patient has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive) [**medical record documentation required**]; **OR**
 - f. The patient has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) [**medical record documentation required**]; **OR**
4. The patient has a diagnosis of active **ankylosing spondylitis (AS)**; **AND**
- a. The patient is 18 years of age or older; **AND**
 - b. The patient has tried and had an inadequate response to two different NSAIDs used in the treatment of AS for at least a 4-week total trial [**medical record documentation required**]; **OR**
 - c. The patient has an intolerance or hypersensitivity to two different NSAIDs used in the treatment of AS [**medical record documentation required**]; **OR**
 - d. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of AS [**medical record documentation required**]; **OR**
5. The patient has a diagnosis of moderately to severely active **Crohn's disease (CD)**; **AND**
- a. The patient is 6 years of age or older; **AND**
 - b. The patient has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD for at least 3-months [**medical record documentation required**]; **OR**
 - c. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of CD [**medical record documentation required**]; **OR**
 - d. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of CD [**medical record documentation required**]; **OR**
6. The patient has a diagnosis of moderately to severely active **ulcerative colitis (UC)**; **AND**
- a. The patient is 6 years of age or older; **AND**

- b. The patient has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC for at least 3-months **[medical record documentation required]; OR**
 - c. The patient has severely active ulcerative colitis **[medical record documentation required]; OR**
 - d. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of UC **[medical record documentation required]; OR**
 - e. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of UC **[medical record documentation required]; OR**
7. The patient has a diagnosis of **refractory sarcoidosis; AND**
- a. The patient has tried and had an inadequate response to glucocorticoids AND methotrexate **[medical record documentation required]; OR**
 - b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all glucocorticoids AND methotrexate; **[medical record documentation required]; AND**
 - i. The provider has submitted medical records in support of use of infliximab for the requested indication **[medical record documentation required]; OR**
8. The patient has a diagnosis of **immune checkpoint inhibitor-related gastrointestinal toxicity; AND**
- a. The patient is being treated for moderate to severe diarrhea or colitis that developed as a result of immune checkpoint inhibitor (i.e., PD-1, PD-L1) therapy; **AND**
 - b. A stool evaluation has ruled out an infectious etiology; **AND**
 - c. The patient has gastrointestinal symptoms that are not responsive to up to 3 days of corticosteroid therapy **[medical record documentation required]; OR**
9. The patient has a diagnosis of moderate to severe refractory **hidradenitis suppurativa (HS); AND**
- a. The patient has tried and had an inadequate response to adalimumab (e.g., Humira[®], Amjevita[™]) OR secukinumab (Cosentyx[®]) for the treatment of HS **[medical record documentation required]; OR**
 - b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to adalimumab (e.g., Humira[®], Amjevita[™]) AND secukinumab (Cosentyx[®]) **[medical record documentation required]; AND**
10. If the request is for Remicade[®] (infliximab), Infliximab, infliximab-abda (Renflexis[®]) or a non-preferred infliximab biosimilar product, ONE of the following:

- a. The patient has tried and had an inadequate response to BOTH of the following preferred products: Avsola™ (infliximab-axxq) AND Inflectra® (infliximab-dyyb) **[medical record documentation required]; OR**
 - b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred products (i.e., Avsola™ [infliximab-axxq], Inflectra® [infliximab-dyyb]) that is NOT expected to occur with the requested agent **[medical record documentation required]; AND**
11. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., dermatologist for PS; rheumatologist for AS, PsA, RA; gastroenterologist for CD, UC) or has consulted with a specialist in the area of the patient’s diagnosis; **AND**
 12. The patient will NOT be using infliximab (Remicade®) or infliximab biosimilars in combination with another biologic immunomodulator agent, Otezla® or Zeposia®; **AND**
 13. The patient does NOT have any FDA labeled contraindications to infliximab (Remicade®) or infliximab biosimilars; **AND**
 14. The patient has been tested for latent tuberculosis (TB) when required by the prescribing information for the requested agent AND if positive the patient has begun therapy for latent TB; **AND**
 15. The requested quantity (dose) does NOT exceed the maximum FDA labeled dosing, OR the dose supported in DrugDex with 1 or 2A level of evidence, AHFS, or NCCN compendium recommended use 1 or 2A for the requested indication previously mentioned above (see table below) **[medical record documentation required]; AND**
 16. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting**, Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

FDA Label Reference

Medication	Indication	Dosing	HCPCS
infliximab (Remicade®) or Infliximab intravenous (IV) infusion	RA in patients ≥ 18 years old	IV: 3 mg/kg at 0, 2, and 6 weeks, then every 8 weeks (with methotrexate); may increase up to 10 mg/kg every 8 weeks or treatment as often as every 4 weeks	J1745

infliximab-abda (Renflexis®) intravenous (IV) infusion	PS in patients ≥ 18 years old	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks	Q5104
infliximab-axxq (Avsola™) intravenous (IV) infusion	PsA in patients ≥ 18 years old	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks	Q5121
infliximab-dyyb (Inflectra®) intravenous (IV) infusion	AS in patients ≥ 18 years old	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 6 weeks	Q5103
CD in patients ≥ 6 years old	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks; Adults only, may increase up to 10 mg/kg every 8 weeks if loss of response after initially responding		
UC in patients ≥ 6 years old	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks		
<u>Off-label:</u> Sarcoidosis	IV: 3-5 mg/kg at 0, 2, and then every 4-6 weeks		
Immune Ckpt Inh GI Toxicity (ICI GI Tox)	IV: 5 mg/kg as single dose, may repeat with 2 nd dose 14 days later if no improvement		

	HS	IV: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks; may increase up to 10 mg/kg every 4 to 8 weeks	
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Quantity Limit Exception Criteria:

1. The quantity (dose) requested is for documented titration purposes at the initiation of therapy (authorization for a 90 day titration period); **AND**
2. The prescribed dose cannot be achieved using a lesser quantity of a higher strength; **AND**
3. The quantity (dose) requested does not exceed the maximum FDA labeled dose, when specified, or to the safest studied dose per the manufacturer's product insert; **OR**
4. If the quantity (dose) requested exceeds the maximum FDA labeled dose, when specified, or to the safest studied dose per the manufacturer's product insert, then the prescriber must submit documentation in support of therapy with a higher dose for the intended diagnosis (submitted documentation may include medical records OR fax form which reflects medical record documentation that shows the length of time the requested dose has been used, and what other medications and doses have been tried and failed).

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met **AND** the inpatient admission is **NOT** for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met **AND ONE** of the following must be met:
 - a. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
 - b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
 - c. New to therapy, defined as initial injection or infusion **OR** less than 3 months since initial injection or infusion; **OR**
 - d. Re-initiation of therapy, defined as **ONE** of the following:
 - i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**

- ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
 - e. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: a publication from the United States and Canadian Hidradenitis Suppurativa Foundations. Part II: Topical, intralesional, and systemic medical management. *J Am Acad Dermatol.* 2019 Jul;81(1):91-101.
2. Grant A, Gonzalez T, Montgomery MO, et al. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol.* 2010 Feb;62(2):205-17.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Management of Immunotherapy-Related Toxicities, version 2.2019. Revised April 8, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf.
4. Postow MA, Sidlow R, Hellmann MD. Immune-related adverse events associated with immune checkpoint blockade. *N Engl J Med.* 2018 Jan 11;378(2):158-168.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

November 2023: Criteria change: For HS: Added secukinumab (Cosentyx) as an option within trial and failure requirements due to newly approved indication for Cosentyx for HS.

September 2023: Criteria change: For PsA: Removed hydroxychloroquine from list of conventional agents. For CD: Removed aminosalicylates, mesalamine, and sulfasalazine from list of conventional agents. For UC: Updated policy to allow bypassing conventional agents for severely active ulcerative colitis; removed steroid suppositories from list of conventional agents. Separated out intolerance/hypersensitivity criteria from FDA labeled contraindication criteria for clarity. Added Zeposia as agent not to be used in combination with another biologic immunomodulator agent for clarity. Updated FDA label reference table for clarity according to FDA label.

January 2023: Criteria change: Changed requirement for trial and failure of preferred agents to include two agents: Avsola and Inflectra; adjusted non-preferred agents to include Remicade and Infliximab. **Policy notification given 10/17/2022 for effective date 1/1/2023.**

April 2022: Criteria change: Changed diagnosis of neurosarcoidosis to all refractory sarcoidosis; added step through glucocorticoids and methotrexate; updated dosing for sarcoidosis. **Policy notification given 2/15/2022 for effective date 4/21/22.**

March 2022: Criteria update: Correction made by removing “generic” in reference to Infliximab product.

January 2022: Criteria update: Added infliximab (generic product) to policy with same criteria requirements and product preference as infliximab (Remicade); removed alternative disease-modifying antirheumatic drugs (DMARDs) as combination therapy requirement option for rheumatoid arthritis; removed maximum units column from FDA dosing reference table.

August 2021: Criteria change: Changed requirement for trial and failure of preferred agents to include three agents: Remicade, Avsola, and Inflectra; removed criteria points regarding medication history indicating use of another biologic immunomodulator agent FDA labeled for the treatment of the same condition; removed criterion regarding maximum units, added criterion for quantity (dose) not to exceed maximum FDA labeled or compendia supported dosing for covered indications. **Policy notification given 6/1/2021 for effective date 8/1/2021.**

July 2021: Criteria change: Changed requirement for trial and failure of preferred agents to include Avsola or Inflectra.

June 2021: Criteria change: Medical record documentation required for all indications.

April 2021: Criteria change: Removal of Ixifi from policy due to market availability.

April 2021: Criteria change: Addition of criteria for history of use of another biologic immunomodulator agent (or Otezla) for the same indication; RA: added requirement for trial of methotrexate or another conventional agent; PS: added option for concomitant severe PsA; PsA: added requirement for trial of one conventional agent, added option for severe active PsA or concomitant severe psoriasis; CD: added requirement for trial of one conventional agent; added requirements to be prescribed by or in consultation with a specialist, and for TB testing; added maximum units; medical policy formatting change. **Policy notification given 2/26/2021 for effective date 4/28/2021.**

*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.