infliximab

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: IMMUNOLOGICAL AGENTS
Mechanism of Action: a monoclonal antibody with affinity for human tumor necrosis factor (TNF)
HCPCS:
J1745:Injection, infliximab, excludes biosimilar, 10 mg
Q5103:Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104:Injection, infliximab-abda, biosimilar, (renflexis), 10 mg
Q5121:Injection, infliximab-axxq, biosimilar, (avsola), 10 mg
How Supplied:

- 100 mg (single use vial)

Condition(s) listed in policy (see coverage criteria for details)

- Ankylosing Spondylitis
- Crohn's Disease
- Fistulizing Crohn's Disease
- Graft Versus Host Disease
- Hidradenitis Suppurativa
- Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
- Plaque Psoriasis
- Psoriatic Arthritis
- Rheumatoid Arthritis
- Ulcerative Colitis

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

For members enrolled in our Blue Shield Select (PPO) and Blue Shield Medicare (PPO) plans:
Renflexis, Remicade, and infliximab requires step therapy. Step therapy requires you to try other drug(s) first before a drug can be covered. The BSC preferred step drugs are Avsola and Inflectra. Both of these drugs will need to be tried for members newly initiating Renflexis, Remicade, or infliximab therapy.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Ankylosing Spondylitis

Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a rheumatologist
2. ONE of the following:
   a. For patient with no bleeding or ulcer risk factors: Either inadequate response or non-GI related intolerable side effect with TWO prescription-strength oral NSAIDs, OR intolerable GI side effect with ONE prescription-strength oral NSAID monotherapy not relieved with addition of concomitant proton pump inhibitor (PPI) therapy
   b. For patient with high-risk potential for development of GI bleed or ulcer: Inadequate response or intolerable side effect to ONE prescription-strength oral NSAID in combination with a proton pump inhibitor (PPI)
   c. Patient unable to use NSAIDs due to history of GI bleed or ulcer
3. Not being used in combination with other targeted immunomodulators
4. **For PPO request for Remicade, Renflexis, or infliximab:** Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV weeks 0, 2, and 6. Maintenance every 6 weeks thereafter.

Requests for doses greater than 5 mg/kg for induction or maintenance are not covered. Efficacy with greater than 5mg/kg or increased frequency of administration has not been demonstrated.

Coverage Period:
Initial approval: 3 induction doses then maintenance for a total of 1 year
Subsequent authorizations: Yearly

ICD-10:
M45.0, M45.1, M45.2, M45.3, M45.4, M45.5, M45.6, M45.7, M45.8, M45.9

Crohn's Disease

Meets medical necessity if all the following are met:

1. Age is consistent with the FDA approved indication
2. Not being used in combination with other targeted immunomodulators

3. For PPO request for Remicade, Renflexis, or infliximab: Intolerable side effect with preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV infusion for induction therapy at 0, 2, 6, followed by 5 mg/kg for maintenance therapy every 8 weeks

Coverage Period:
Initial approval: 3 induction doses and maintenance for a total of 1 year
Reauthorization for maintenance of adults and children: Yearly

ICD-10:
K50.00-K50.119, K50.80-K50.919

Fistulizing Crohn's Disease
Meets medical necessity if all the following are met:
1. Fistulizing disease
2. Not being used in combination with other targeted immunomodulators
3. For PPO request for Remicade, Renflexis, or infliximab: Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV infusion for induction therapy at 0, 2, 6, followed by 5 mg/kg for maintenance therapy every 8 weeks.

Coverage Period:
Initial approval: 3 induction doses then maintenance for total of 1 year
Reauthorization for maintenance of adults and children: Yearly

ICD-10:
K50.013, K50.113, K50.813, K50.913

Graft Versus Host Disease
Meets medical necessity if all the following are met:
1. Inadequate response to at least one prior drug for GVHD (i.e., systemic corticosteroids, immunosuppressants)
2. Not being used in combination with other targeted immunomodulators
3. For PPO request for Remicade, Renflexis, or infliximab: Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 10 mg/kg IV once weekly

Coverage Period:
yearly

ICD-10:
D89.810, D89.812, D89.813, T86.09

Hidradenitis Suppurativa
Meets medical necessity if all the following are met:
1. Prescribed by or in consultation with a dermatologist
2. Moderate to severe disease as evidenced by Hurley stage II or III disease
3. Not used in combination with a targeted immunomodulator
4. Inadequate response, intolerable side effect, or contraindication to adalimumab
5. **For PPO request for Remicade, Renflexis, or infliximab:** Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV weeks 0, 2, and 6. Maintenance every 8 weeks thereafter.

Requests for dose greater than 5 mg/kg for induction or maintenance are not covered.

Coverage Period:
Initial approval: 3 induction doses and 1 maintenance dose.
Reauthorization for maintenance: Yearly

ICD-10:
L73.2

Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
Meets medical necessity if all the following are met:
1. Treatment for ONE of the following immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy:
   a. Moderate or severe diarrhea or colitis refractory to corticosteroids
   b. Severe pneumonitis refractory to methylprednisolone
   c. Severe acute renal failure/elevated serum creatinine refractory to corticosteroids
   d. Severe uveitis refractory to high-dose corticosteroids
   e. Severe myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities refractory to pulse-dose methylprednisolone
   f. Severe inflammatory arthritis refractory to high-dose corticosteroids
   g. Moderate or severe myalgias or myositis refractory to corticosteroids

2. **For PPO request for Remicade, Renflexis, or infliximab:** Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV weeks 0, 2, and 6

Coverage Period:
Cover up to 3 doses

ICD-10:
K52.1, J70.2, J70.4, N17.8, N17.9, I30.8, I30.9, I40.8, I40.9, I44.0, I44.1-I44.3, I44.30, I44.39, I47.0, I45.0, I45.10, I45.19, I45.2-I45.6, I45.81, I45.89, I45.9, I49.9, R19.7, M06.4, M60.80, M60.811, M60.812, M60.819, M60.821, M60.822, M60.829, M60.831, M60.832, M60.839, M60.841, M60.842, M60.849, M60.851, M60.852, M60.859, M60.861, M60.862, M60.869, M60.871, M60.872, M60.879, M60.88, M60.89, M60.9, M79.1

Plaque Psoriasis
Meets medical necessity if all the following are met:
Initial

1. Disease is moderate to severe
2. Age is consistent with the FDA approved indication
3. Prescribed by or in consultation by a dermatologist or rheumatologist
4. ONE of the following:
   a. Baseline PASI score is 10 or more prior to starting biological therapy
   b. Baseline BSA (body surface area) affected is 3% or more prior to starting biological therapy
   c. Sensitive area is involved (i.e., groin, face, etc.)
   d. Disease is otherwise debilitating
5. Inadequate response, intolerable side effect, or contraindication to ONE of the following:
   a. Methotrexate, cyclosporine (Neoral), acitretin (Soriatane)
   b. PUVA or UVB treatment
6. Not being used in combination with another targeted biologic
7. **For PPO request for Remicade, Renflexis, or infliximab:** Intolerable side effect with infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Reauthorization:

1. Not being used in combination with other targeted biologics
2. ONE of the following:
   a. Improvement in PASI score from baseline
   b. Improvement in BSA from baseline
   c. Decrease in sensitive area disease severity

d. Decrease in debilitating disease severity

Covered Doses:
Induction: Up to 5 mg/kg IV weeks 0, 2, and 6
Maintenance: As frequently as every 8 weeks after induction dosing

Requests for dose greater than 5 mg/kg for induction or maintenance are not covered. Efficacy with greater than 5 mg/kg or increased frequency of administration has not been demonstrated.

Coverage Period:
Initial: 24 weeks
Reauthorization: Yearly

ICD-10:
L40.0, L40.1, L40.2, L40.3, L40.4, L40.8, L40.9

Psoriatic Arthritis
Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a rheumatologist
2. Inadequate response to one or more disease modifying anti-rheumatic drug or patient has a medical reason why methotrexate, sulfasalazine, and leflunomide cannot be used
3. Not being used in combination with other targeted immunomodulators
4. **For PPO request for Remicade, Renflexis, or infliximab:** Intolerable side effect with infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
5 mg/kg IV weeks 0, 2, and 6. Maintenance every 8 weeks thereafter.
Requests for dose greater than 5 mg/kg for the induction or maintenance of psoriatic arthritis are not covered. Efficacy with greater than 5mg/kg or increased frequency of administration has not been demonstrated.

Coverage Period:
Initial approval: 3 induction doses then maintenance for total of 1 year
Subsequent authorizations: Yearly

ICD-10:
L40.50, L40.51, L40.52, L40.53, L40.54, L40.59

Rheumatoid Arthritis
Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a rheumatologist
2. Inadequate response, intolerable side effect, or contraindication to methotrexate
3. Not used in combination with another targeted immunomodulators

4. For PPO request for Remicade, Renflexis, or infliximab: Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
3 mg/kg I.V. followed with additional similar doses at 2 and 6 weeks after the initial infusion, then every 8 weeks thereafter.

Coverage Period:
Initial approval: 3 induction doses then maintenance for total of 1 year
Subsequent authorizations: Yearly

ICD-10: (X=0-9)
M05.XXX, M06.0XX, M06.2XX, M06.3XX, M06.8XX, M06.9

Ulcerative Colitis
Meets medical necessity if all the following are met:

1. Age is consistent with the FDA approved indication
2. Not being used in combination with other targeted immunomodulators
3. For PPO request for Remicade, Renflexis, or infliximab: Intolerable side effect with the preferred infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra

Covered Doses:
Up to 5 mg/kg IV infusion for induction therapy at 0, 2, 6, followed by 5 mg/kg for maintenance therapy every 8 weeks

Coverage Period:
Initial approval: 3 induction doses and maintenance for a total of 1 year
Subsequent authorizations: Yearly

ICD-10:
K51.0-K51.319, K51.5-K51.519, K51.80-K51.91

Additional Information

Summary of Evidence
The contents of this policy were created after examining the following resources:

1. The prescribing information for Avsola, Inflectra, Remicade, and Renflexis
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text

c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A"
e. Clinical Pharmacology - supportive narrative text

3. Noridian Healthcare Solutions Medicare: Drugs, Biologics and Injections
4. NCCN Guideline: Hematopoietic Stem Cell Transplantation
5. NCCN Guideline: Management of Immunotherapy-Related Toxicities
6. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis
7. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis
8. 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

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Avsola, Inflectria, Remicade, and Renflexis are covered in addition to the following:

- Hidradenitis Suppurativa
- Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- Support for using biosimilars as step requirement is found in Noridian Health Care Solutions and supported by the FDA. Noridian will accept a biosimilar drug on the same criteria as the drug to which it is a biosimilar unless an article is published to the contrary. Per the FDA, a biosimilar is highly similar to and has no clinically meaningful difference from an existing FDA approved biologic reference drug.
- Support for using biosimilars in oncology can be found in The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) via the footnote on the reference product (an FDA-approved biosimilar is an appropriate substitute) and in the NCCN Drugs & Biologics Compendium® by the notation that a biosimilar agent may be an appropriate substitute for the reference product.
- **Ankylosing spondylitis**: American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (ACR/SAA/SPARTAN) support treatment with TNF inhibitors in active ankylosing spondylitis despite treatment with NSAIDs.
- **Graft-versus-host disease:** Support for using infliximab for graft-versus-host disease is found in the National Comprehensive Cancer Network's guideline for hematopoietic stem cell transplantation. The NCCN Guideline for hematopoietic stem cell transplantation supports the use of infliximab for acute graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options .
- **Hidradenitis suppurativa**

- Support for using infliximab for hidradenitis suppurativa (HS) is found in DrugDex compendium. DrugDex compendium supports use of infliximab for severe, refractory HS [Evidence favors efficacy, Class IIb recommendation]
- United States and Canadian Hidradenitis Suppurativa Foundations support use of select biologics] for treatment of hidradenitis suppurativa (HS), including infliximab [Strength of Recommendation: B] and adalimumab [FDA-approved for treatment of HS; Strength of Recommendation: A].

- **Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy:** Support for using infliximab for immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy is found in the National Comprehensive Cancer Network's guideline for management of immunotherapy-related toxicities. The NCCN Guideline for management of immunotherapy-related toxicities supports the use of infliximab for immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy for the management of the following immunotherapy-related toxicities: 1) myocarditis as additional immunosuppression if no improvement within 24-48 hours of starting high-dose methylprednisolone; 2) mild (G1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin; 3) moderate (G2) and strongly consider for severe (G3-4) diarrhea or colitis if no response or unable to transition to oral corticosteroids; 4) moderate or severe inflammatory arthritis if no improvement after holding immunotherapy and treating with oral corticosteroids or if unable to taper corticosteroids, or no response to conventional synthetic (cs)DMARDs; 5) G1 -4 uveitis that is refractory to high-dose systemic corticosteroids (treatment guided by ophthalmology); 6) moderate (G2) pneumonitis if no improvement after 48-72 hours of corticosteroids or severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone; and 7) stage 3 acute kidney injury/elevated serum creatinine if toxicity remains >stage 2 after 4-6 weeks of corticosteroids or if creatinine increases during steroid taper (or once off corticosteroids) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options .
- **Psoriatic arthritis**
  - American College of Rheumatology/National Psoriasis Foundation (ACR/NPF) supports use of TNF inhibitors in DMARD-naïve and DMARD-experienced patients.
  - FDA approval of infliximab for psoriatic arthritis is (PsA) based upon safety and efficacy assessed in a multicenter, double-blind, placebo-controlled study in 200 adult patients with active PsA despite DMARD or NSAID therapy
- **Rheumatoid arthritis**: American College of Rheumatology supports use of TNF inhibitors in patients with rheumatoid arthritis taking maximally tolerated doses of methotrexate who are not at target.

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS®. Available by subscription at http://www.lexi.com
5. 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;81(1):91-101.
6. Avsola® (infliximab-axxq) [Prescribing Information]. Thousand Oaks, CA: Amgen Inc. 9/2021.
7. DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
8. Inflectra® (infliximab-dyyb) [Prescribing Information]. New York, NY: Pfizer. 4/2023.
9. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol 2019;80:1029-72.
10. National Comprehensive Cancer Network. Hematopoietic Stem Cell Transplantation (Version 1.2024). Available at: www.nccn.org.
11. National Comprehensive Cancer Network Drugs and Biologics Compendium. Infliximab (2024). Available at: www.nccn.org.
12. National Comprehensive Cancer Network. Management of Immunotherapy-Related Toxicities (Version 1.2024). Available at: www.nccn.org.
13. Remicade® (infliximab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 10/2021.
14. Renflexis® (infliximab-abda)[Prescribing Information]. Whitehouse Station, NJ: Merck & Co. Inc. 1/2022.
15. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheum 2019;71:5-32.
16. Ward, MM, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis & Rheumatology 2019; 71: 1599-1613. Available at http://www.rheumatology.org

Review History

Date of Last Annual Review: 4Q2024
Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity
Reviewed by P&T Committee