Infliximab (Remicade®) **Infliximab-abda (Renflexis®)** **Infliximab-axxq (Avsola®)** **Infliximab-dyyb (Inflectra®)**	**Place of Service** **Office Administration** **Home Infusion Administration** **Infusion Center Administration** **Outpatient Facility Infusion Administration*** [***Prior authorization required – see section (1)]** **HCPCS:** Remicade: **J1745** per 10 mg Inflectra: **Q5103** per 10 mg Renflexis: **Q5104** per 10 mg Avsola: **Q5121** per 10 mg

Conditions listed in policy (*see 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

AHFS therapeutic class: disease-modifying antirheumatic agent (DMARD)

Mechanism of action: a monoclonal antibody with affinity for human tumor necrosis factor (TNF)

(1) Special Instructions and Pertinent Information

Covered under the medical benefit, please submit clinical information for prior authorization review.

Members with the following plans: **PPO, Direct Contract HMO, and when applicable, ASO/Shared Advantage/HMO (non-direct contract)** may be required to have their medication administered at a preferred site of service, including the home, a physician's office, or an independent infusion center not associated with a hospital.

For members that cannot receive infusions in the preferred home or ambulatory setting AND meet one of the following criteria points, drug administration may be performed at a hospital outpatient facility infusion center.

CRITERIA FOR HOSPITAL OUTPATIENT FACILITY ADMINISTRATION

MCG™ Care Guidelines, 19th edition, 2015

ADMINISTRATION OF INFLIXIMAB IN THE HOSPITAL OUTPATIENT FACILITY SITE OF CARE REQUIRES ONE OF THE FOLLOWING: (*Supporting Documentation must be submitted)*

1. **Patient is receiving their first infusion of infliximab or is being re-initiated on infliximab after at least 6 months off therapy.** *Subsequent doses will require medical necessity for continued use in the hospital outpatient facility site of care.*

   Or

Additional clinical monitoring is required during administration as evidenced by one of the following:

2. **Patient has experienced a previous severe adverse event on infliximab based on documentation submitted.**

3. **Patient continues to experience moderate to severe adverse events on infliximab based on documentation submitted, despite receiving premedication such as acetaminophen, steroids, diphenhydramine, fluids, etc.**

4. **Patient is clinically unstable based on documentation submitted.**

5. **Patient is physically or cognitively unstable based on documentation submitted.**

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for infliximab must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Ankylosing spondylitis

1. Prescribed by or in consultation with a rheumatologist, **AND**
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, or
   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), or
   c. Patient unable to use NSAIDs due to history of GI bleed or ulcer

   AND
3. Not being used in combination with other targeted immunomodulators, **AND**
4. If request is for Remicade or Renflexis: 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

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-M45.9

Crohn's disease

1. Patient is ≥ 6 years of age, **AND**
2. Not being used in combination with other targeted immunomodulators, **AND**
3. If request is for Remicade or Renflexis: 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
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

Dose escalation-Adults:
Dose or frequency increases may be covered under the following conditions:

1. Only for adults, **and**
2. Only after the first 3 induction doses (at wks 0, 2 & 6) and at least one maintenance dose of 5 mg/kg every 8 weeks (week 14) **and**
3. The member has not responded to therapy or is experiencing flares **and**
4. The total dose should not exceed 10 mg/kg over an eight-week period

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

1. Fistulizing disease, **AND**
2. Not being used in combination with other targeted immunomodulators, **AND**
3. If request is for Remicade or Renflexis: 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
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.

Dose escalation-Adults:
Dose or frequency increases may be covered under the following conditions:

1. Only for adults, **and**
2. Only after the first 3 induction doses (at wks 0, 2 & 6) and at least one maintenance dose of 5 mg/kg every 8 weeks (week 14) **and**
3. The member has not responded to therapy or is experiencing flares **and**
4. The total dose should not exceed 10 mg/kg over an eight-week period

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.X13 (X=0,1,3,8,9)

Graft versus host disease

1. Inadequate response to at least one prior drug for GVHD (i.e., systemic corticosteroids, immunosuppressants), **AND**
2. Not being used in combination with other targeted immunomodulators, **AND**
3. If request is for Remicade or Renflexis: 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
Up to 10 mg/kg IV once weekly

Coverage Period
Indefinite

ICD-10:
D89.810, D89.12, D89.813, T86.09

Hidradenitis suppurativa

1. Prescribed by or in consultation with a dermatologist, **AND**
2. Moderate to severe disease as evidenced by Hurley stage II or III disease *(see section 5 table 2),* **AND**
3. Not used in combination with a targeted immunomodulator, **AND**
4. Inadequate response, intolerable side effect, or contraindication to Hadlima or Humira, **AND**
5. If request is for Remicade or Renflexis: 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
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. Efficacy with greater than 5 mg/kg or increased frequency of administration has not been demonstrated.

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

1. Treatment for at least 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

    AND
2. If request is for Remicade or Renflexis: 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
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

1. Disease is moderate to severe, **AND**
2. Age ≥ 18 years of age, **AND**
3. Prescribed by or in consultation by a dermatologist or rheumatologist, **AND**
4. One of the following:
    a. Baseline PASI score is 10 or more prior to starting biological therapy, OR
    b. Baseline BSA (body surface area) affected is 3% or more prior to starting biological therapy, OR
    c. Sensitive area is involved (i.e., groin, face, etc.), OR
    d. Disease is otherwise debilitating

    AND
5. Inadequate response, intolerable side effect, or contraindication to one of the following:
    a. Methotrexate, cyclosporine (Neoral), acitretin (Soriatane), OR

b. PUVA or UVB treatment

AND

6. Not being used in combination with another targeted biologic, **AND**
7. If request is for Remicade or Renflexis: 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
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 if meets the following:

a. Not being used in combination with other targeted biologics, AND
b. One of the following:
    a. Improvement in PASI score from baseline, OR
    b. Improvement in BSA from baseline, OR
    c. Decrease in sensitive area disease severity, OR
    d. Decrease in debilitating disease severity

ICD-10:
L40.0-L40.9

Psoriatic arthritis

1. Prescribed by or in consultation with a rheumatologist, **AND**
2. Inadequate response to one or more disease modifying anti-rheumatic drug (DMARD - *see section 5*), or patient has a medical reason why methotrexate, sulfasalazine, and leflunomide cannot be used, **AND**
3. Not being used in combination with other targeted immunomodulators, **AND**
4. If request is for Remicade or Renflexis: 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-L40.59

Rheumatoid arthritis

1. Prescribed by or in consultation with a rheumatologist, **AND**
2. Inadequate response, intolerable side effect, or contraindication to methotrexate**, AND**
3. Not used in combination with another targeted immunomodulators, **AND**
4. If request is for Remicade or Renflexis: 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
Initial:
3 mg/kg I.V. followed with additional similar doses at 2 and 6 weeks after the initial infusion, then every 8 weeks thereafter.
Infliximab may be given in combination with methotrexate.

Dose escalation:
Dose or frequency increases may be covered under the following conditions:

- Only after the first 3 induction doses (at wks 0, 2 & 6) and at least one maintenance dose of 3 mg/kg every 8 weeks (week 14), **and**
- The patient is not responding or experiencing flares **and**
- The total dose should not exceed 10 mg/kg over an eight-week period

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

1. Patient is ≥ 6 years old, **AND**
2. Not being used in combination with other targeted immunomodulators, **AND**
3. If request is for Remicade or Renflexis: 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
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

Dose escalation-Adults:
Dose or frequency increases may be covered under the following conditions:

- Only for adults, **and**
- Only after the first 3 induction doses (at wks 0, 2 & 6) and at least one maintenance dose of 5 mg/kg q 8 weeks (week 14) **and**
- The member has not responded to therapy or is experiencing flares **and**
- The total dose should not exceed 10 mg/kg over an eight-week period

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-K51.919

(3) The following condition(s) DO NOT require Prior Authorization/Preservice
All requests for infliximab must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically necessary for the following condition(s)
Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- Multiple Sclerosis
- Hairy cell leukemia
- Infertility
- Adult Still's Disease
- Juvenile Idiopathic Arthritis

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information
How supplied: 100mg single use vial, powder for reconstitution

Examples of maximum doses totalling 10 mg/kg over an eight-week period given no more frequently than q 4 weeks:

5 mg/kg q 4 weeks
6.25 mg/kg q 5 weeks
7.5 mg/kg q 6 weeks
8.75 mg/kg q 7 weeks
10 mg/kg q 8 weeks

DMARD examples:

- Auranofin (Ridaura®)
- Azathioprine (Imuran®)
- Cyclosporine (Neoral®)
- Hydroxychloroquine (Plaquenil®)
- Methotrexate (Rheumatrex®)
- D-Penicillamine (Cuprimine®)
- Sulfasalazine (Azulfidine®)
- Leflunomide (Arava®)

Table 1: Therapeutic Approaches for Treatment of Hidradenitis Suppurativa

	Stage	Therapy examples
Medical	Limited	• antiseptic measures • topical antibiotics (clindamycin)
	Advanced	• oral antibiotic: clindamycin, clindamycin + rifampin, doxycycline, minocycline) • cyclosporine • oral prednisone • intralesional corticosteroids (triamcinolone) • antiandrogen therapy (OCPs) • TNF (etanercept, adalimumab, infliximab)
Surgical	Intractable	• Wide excision with healing by secondary intention (wound edges left open) Results may be disfiguring. • laser surgery

Table 2: Hurley Stage Definition for Hidradenitis Suppurativa Disease Severity

Hurley Stage I	Solitary or multiple, isolated abscess formation without scarring or sinus tracts
Hurley Stage II	Recurrent abscesses, single or multiple widely separated lesions, with sinus tract formation
Hurley Stage III	Diffuse or broad involvement, with multiple interconnected sinus tracts and abscesses.

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- American College of Gastroenterology Adult Ulcerative Colitis Practice Guidelines (March 2010): Kornbluth A. Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol 2010; 105:501-523.
- American Gastroenterological Association Institute Technical Review on Corticosteroids, Immunomodulators, and Infliximab in Inflammtory Bowel Disease. Gatroenterology 2006;130:940-987.
- Avsola® (infliximab-axxq) [Prescribing Information]. Thousand Oaks, CA: Amgen Inc. 9/2021.
- Ducharme J Pelletier, C and Zacharias R. The safety of infliximab infusions in the community setting. Can J Gastroenterol 2010; 24(5):307-11
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- Feuerstein JD, Isaacs KL, Schneider Y et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology 2020; 158:1450–1461. Available at https://gastro.org/
- Fraenkel, L., Bathon, J.M., et al., E.A. (2021), 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol, 73: 1108-1123. https://doi.org/10.1002/art.41752
- Inflectra® (infliximab-dyyb) [Prescribing Information]. New York, NY: Pfizer. 4/2023.
- Kimball AB, Okun MM, Williams DA et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa. N Engl J Med 2016; 375(5):422-34.
- Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481-517.
- MCG™ Care Guidelines, 19th edition, 2015, Home Infusion Therapy, CMT: CMT-0009(SR)
- 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.
- Remicade® (infliximab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 10/2021.

- Renflexis® (infliximab-abda)[Prescribing Information]. Whitehouse Station, NJ: Merck & Co. Inc. 1/2022.
- Ringold, S, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroilitis, and Enthesitis. Arthritis Care & Research 2019; 71: 717-734. Available at https://www.rheumatology.org
- Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019;114:384-413.
- 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.
- 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

(7) Policy Update

Date of last review: 4Q2023

Date of next review: 4Q2024

Changes from previous policy version:

- Section (2): Hidradenitis suppurativa - Effective 1/1/2024, Will add Hadlima as a preferred step therapy
  Rationale: Selection of preferred drugs is supported by similar safety and efficacy and are guideline supported agents
- Section (2): Spondyloarthritis – Updated nomenclature to Ankylosing spondylitis
  Rationale: FDA indications; 2019 ACR/SAA/SPARTAN treatment guidelines

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee