RX.PA.016.CCH INFLIXIMAB PRODUCTS (REMICADE, INFLECTRA, RENFLEXIS, AVSOLA, AND ZYMFENTRA)

PURPOSE

The purpose of this policy is to define the prior authorization process for Remicade® (infliximab), Inflectra® (infliximab-dyyb), Renflexis® (infliximab-abda), and Avsola™ (infliximab-axxq), and Zymfentra (infliximab-dyyb, subcutaneous).

Remicade® (infliximab), Inflectra® (infliximab-dyyb), Renflexis® (infliximab-abda), and Avsola™ (infliximab-axxq) are indicated for the following:

- Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. Infliximab is indicated only in combination with methotrexate.
- Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.
- Reducing signs and symptoms in patients with active ankylosing spondylitis
- Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. Infliximab should only be administered to patients who are closely monitored and have regular follow-up visits with a physician.
- Reducing signs and symptoms and inducing and maintaining a clinical remission in adult and pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy AND for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.
- Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy AND for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older (Remicade only) with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

Zymfentra™ (infliximab-dyyb, subcutaneous) is indicated for the following:

- Maintenance treatment of moderately to severely active ulcerative colitis in adults following treatment with an infliximab product administered intravenously

- Maintenance treatment of moderately to severely active Crohn's disease in adults following treatment with an infliximab product administered intravenously

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity and approval by the Medical Policy Committee.

The drugs, Remicade® (infliximab), Inflectra® (infliximab-dyyb), Renflexis® (infliximab-abda), Avsola™ (infliximab-axxq), and Zymfentra (infliximab-dyyb, subcutaneous) are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

I. PLAN DESIGN SUMMARY

Requests for Avsola™ are subject to the preferred medical drug list program. This program applies to non-preferred autoimmune products used in the treatment of plaque psoriasis, inflammatory joint related conditions, or inflammatory bowel disease (FDA-approved indications *only*). Coverage for non-preferred products may be provided based on clinical circumstances that would exclude the use of the preferred product(s) for the indication.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products
Preferred	• Inflectra® (infliximab-dyyb) • Remicade® (infliximab) • Renflexis® (infliximab-abda) • Zymfentra™ (infliximab-dyyb)
Non-preferred	• Avsola™ (infliximab-axxq)

Requests for a non-preferred drug on the Medical Benefit must meet one of the following exception criteria in addition to clinical criteria:

II. ***EXCEPTION CRITERIA (Use for Non-Preferred Requests Only)***

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product(s) (as applicable).

Coverage for a non-preferred product is provided when ANY of the following criteria are met:

- Member has a documented intolerable adverse event with the preferred products and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.

III. CLINICAL CRITERIA (*Use for ALL Drug Requests on the Medical Benefit)*

Must meet all of the criteria listed under the respective diagnosis:

For All Diagnoses:

- Requests for non-preferred products must have documented trial and failure or intolerance or contraindication to ALL preferred products
- Must have a negative tuberculosis skin test [such as Tuberculin PPD (purified protein derivative) test] or Interferon-Gamma Release Assay (IGRA) whole-blood test [such as QuantiFERON®-TB Gold In-Tube test (QFT-GIT) or T-SPOT®.*TB* test (T-Spot)]
- Must currently not be using a tumor necrosis factor (TNF)-blocking agent or other biologic agents in combination with the Infliximab product
- Must have no evidence of infection
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc) listed in the FDA approved labeling

1. Rheumatoid Arthritis (*Avsola/Inflectra/infliximab/Remicade/Renflexis only*)**:**

- Must be prescribed by a rheumatologist
- Must be age 18 years or older
- Must have a diagnosis of moderate to severely active rheumatoid arthritis
- Must have documentation of testing of the following:
  - Rheumatoid factor (RF)
  - Anti-cyclic citrullinated peptide (anti-CCP)
  - C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR) – *not required if RF & anti-CCP are positive*
- Must be prescribed the requested medication in combination with methotrexate or leflunomide or has a clinical reason not to use methotrexate or leflunomide (see Appendix 1)
- Must have documentation showing ONE of the following:
  - Member has had an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week)

- Member has an intolerance or contraindication to methotrexate (see Appendix 1)

2. Psoriatic Arthritis (*Avsola/Inflectra/infliximab/Remicade/Renflexis only*)**:**

- Must be prescribed by a rheumatologist or dermatologist
- Must be age 18 years or older
- Must have a diagnosis of active psoriatic arthritis, with the severity of disease documented
- For mild-to-moderate disease *only*, must have ONE of the following:
  - Must have had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) or have a contraindication or intolerance to all drugs (see Appendix 1)
  - Must have enthesitis or predominantly axial disease

3. Ankylosing Spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) (*Avsola/Inflectra/infliximab/Remicade/Renflexis only*)**:**

- Must be prescribed by a rheumatologist
- Must be age 18 years or older
- Must have a diagnosis of ankylosing spondylitis
- Must have an adequate trial (of at least 4 weeks) with at least **TWO** NSAIDs at anti-inflammatory dose, with an inadequate response, significant side effects/toxicity, or have a contraindication to these therapies

4. Plaque Psoriasis (*Avsola/Inflectra/infliximab/Remicade/Renflexis only*)**:**

- Must be prescribed by a dermatologist
- Must be age 18 years or older
- Must have a diagnosis of moderate-to-severe chronic plaque psoriasis
- Must have documentation of ONE of the following:
  - Affected area(s) include hands, feet, face, neck, scalp, genitals/groin, intertriginous areas
  - Minimum body surface area (BSA) involvement of >10%
  - At least 3% of BSA affected AND the member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) **OR** pharmacologic treatment with methotrexate, cyclosporine, or acitretin (unless there is a clinical reason to not take pharmacologic treatment – see Appendix 1)

5. Crohn's Disease:

- Must be prescribed by a gastroenterologist
- Must be age:
  - 6 years or older (Avsola/Inflectra/infliximab/Remicade/Renflexis only)
  - 18 years or older (Zymfentra only)

- Must have a diagnosis of moderate to severely active Crohn's disease or fistulizing Crohn's disease, as described in the 2018 ACG guidelines (Table 1)

6. Ulcerative Colitis:

- Must be prescribed by a gastroenterologist
- Must be age:
  - 6 years or older (Avsola/Inflectra/infliximab/Remicade/Renflexis only)
  - 18 years or older (Zymfentra only)
- Must have a diagnosis of moderate to severely active Ulcerative Colitis, as evidenced by ONE of the following:
  - Dependency on or refractory to corticosteroids
  - Severe endoscopic disease activity (e.g., presence of ulcers)
  - High risk of colectomy
  - Mayo Clinic scores of 6-12, with an endoscopic subscore of 2 or 3
  - Hospitalized with ≥6 bloody bowel movements per day with at least 1 marker of systemic toxicity (e.g., heart rate >90 beats/min, temperature >37.8C, hemoglobin <10.5 g/dL, and/or erythrocyte sedimentation rate -30 mm/h)

7. Bechet's disease (*off-label supported indication)*

- Must have an inadequate response to at least one non-biologic medication for Behcet's disease (e.g., azathioprine, colchicine, cyclosporine, systemic corticosteroids)

8. Hidradenitis suppurativa (*off-label supported indication)*

- Must have a diagnosis of severe, refractory hidradenitis suppurativa
- Must have had an inadequate response to an oral antibiotic used for the treatment of hidradenitis suppurativa (e.g., clindamycin, metronidazole, moxifloxacin, rifampin, tetracyclines) for at least 90 days

9. Pyroderma gangrenosum (*off-label supported indication)*

- Must have had an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine, mycophenolate mofetil)

10. Sarcoidosis (*off-label supported indication)*

- Must have had an inadequate response to corticosteroids or immunosuppressive therapy

11. Takayasu's arteritis (*off-label supported indication)*

- Must have had an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, mycophenolate mofetil)

12. Uveitis (*off-label supported indication)*
- Must have had an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine, methotrexate, azathioprine, mycophenolate mofetil)

13. Reactive arteritis (*off-label supported indication)*
- Must have had an inadequate response to methotrexate or sulfasalazine

14. Immune checkpoint inhibitor-related toxicity (*off-label supported indication)*
- Must have had an inadequate response to corticosteroids or a conventional synthetic drug (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine)

15. Acute graft versus host disease (*off-label supported indication)*
- Must have had an inadequate response to systemic corticosteroids

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member has achieved or maintained a clinical response and/or remission, as evidenced by low disease activity or improvement in signs and symptoms of the condition.

EXCEPTION: Reauthorization requests for immune checkpoint inhibitor related toxicity and acute graft versus host disease must meet initial criteria.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 1 year
Reauthorization	Same as initial

If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.

Codes:

Code	Brand	Description
J1745	Remicade	INJ, INFLIXIMAB, EXCLUDES BIOSIMILAR, 10 MG
J1748	Zymfentra	INJECTION, INFLIXIMAB-DYYB (ZYMFENTRA), 10MG
Q5103	Inflectra	INJ INFLIXIMAB-DYYB BIOSIMILR 10 MG

Q5104	Renflexis	INJ INFLIXIMAB-ABDA BIOSIMILR 10 MG
Q5121	Avsola	INJ INFLIXIMAB-AXXQ BIOSIMILR 10 MG

Appendix 1 – Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine, Acitretin, or Leflunomide

- Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
- Drug interaction
- Risk of treatment-related toxicity
- Pregnancy or currently planning pregnancy
- Breastfeeding
- Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
- Hypersensitivity
- History of intolerance or adverse event

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Table 1 – 2018 ACG Clinical Guidelines Classification of Moderate-to-Severe Disease

Moderate-to-Severe disease	Severe-fulminant disease
One of the following: • CDAI 220-450 • Have failed treatment for mild to moderate disease • Prominent symptoms such as fever, weight loss, abdominal pain and tenderness, intermittent nausea or vomiting, or anemia • Moderate to severely active endoscopic mucosal disease	*One of the following:* • CDAI >450 • Persistent symptoms despite glucocorticoids or biologic agents • Individuals presenting with high fever, persistent vomiting, intestinal obstruction, peritoneal signs, cachexia, or evidence of an abscess

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RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Initial review	3/22
Added Zymfentra Updated criteria for RA, psoriasis, psoriatic arthritis, and ankylosing spondylitis Removed prerequisite trials for Crohn's and Ulcerative Colitis; Added diagnostic criteria for Crohn's and Ulcerative Colitis Added 9 indications: Bechet's disease, Hidradenitis suppurativa, Pyroderma gangrenosum, Sarcoidosis, Takayasu's arteritis, Uveitis, Reactive arteritis, Immune checkpoint inhibitor-related, Acute Graft Versus Host	07/2024