

POLICY Document for REMICADE

The overall objective of this policy is to support the appropriate and cost effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall clinically appropriate use. This document provides specific information to each section of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

GUIDELINES FOR HOSPITAL OUTPATIENT SPECIALTY MEDICATION INFUSION

I. INTRODUCTION

There is a wide variation in the site-of-service utilization patterns for specific medications and therapy classes. This is driven by several factors. Some of these specialty medications are derived from pooled blood plasma, and therefore have the potential for an increased risk of infusion-related complications. These differences can affect patient tolerance and a physician's decision to utilize a more acute site of care such as the outpatient hospital. However, many patients that have been established on this treatment with one to several infusions safely administered may be candidates for infusions in a less acute lower-cost site of care.

Outpatient hospital infusion costs may be 2-3 times more compared to other sites of care suggesting an immediate opportunity exists for lowering spend on select specialty medications that require infusion.

Services for patients requiring infused specialty medications may be provided through a physician's in office infusion program or free standing ambulatory infusion center. These options provide access to quality care at a lower cost that may be more convenient for the patient. In addition, many patients who receive home or in office infusion therapy have been shown to experience better outcomes, fewer complications and, improved quality of life and preference, including more personalized attention which helps avoid stress.

This document describes the medical necessity criteria required for hospital outpatient infusion of the medications included in this policy.

II. GENERAL REQUIREMENTS: OUTPATIENT MEDICAL NECESSITY

Infusion in a hospital outpatient setting may be considered medically necessary for medications included in this policy when the criteria below OR individual medication policy criteria are met as outlined section III.

A. Clinical documentation that supports one or more of the following:

1. History of repeated moderate adverse reactions not responding to conventional interventions OR,
2. Laboratory confirmation of autoantibody development (autoantibodies to IgA, anti-infliximab, etc)
3. The patient is medically unstable which may include respiratory, cardiovascular, or renal conditions that may predispose the member to a severe adverse event that cannot be managed in an alternate setting without appropriate medical personnel and equipment.
4. The patient has previously experienced a severe adverse event during or immediately after an infusion including but not limited to: anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures.
5. Significant venous access issues requiring phlebotomy

B. Patient specific criteria that meets the following:

1. All alternate non-hospital outpatient settings are not within a reasonable distance from the member's home (10-30miles) AND,
2. The patient's home has been determined to be inappropriate for home infusion by a social worker, case manager or previous home nurse assessment or home infusion services are not available due to limited network access

III. MEDICATION SPECIFIC CRITERIA FOR HOSPITAL OUTPATIENT MEDICAL NECESSITY

In addition to the general criteria in Section II, the following guidelines will be applied:

A. INFLIXIMAB One or more of the following criteria must be met:

1. To determine tolerance of the therapy, the first three infusions may be permitted in the hospital outpatient setting.
2. Patients that are re-initiating therapy after a gap in treatment exceeding 2 infusions are at a higher risk for antibody development. The first three infusions may be permitted in the hospital outpatient setting to determine tolerance
3. Pediatric patients who are less than 21 years of age. The use of non-hospital based alternate site infusion services are at the discretion of the prescribing physician.
4. Patients with laboratory confirmed anti-infliximab antibodies
5. Patients who have experienced moderate infusion reactions including hypertension, hypotension, tachycardia, syncope, etc that have not responded to standard interventions including infusion rate adjustment and premedication.

IV. GENERAL CONSIDERATIONS: HOME INFUSION

Home Infusion therapy has the potential to deliver cost-effective, quality care.

Efforts to support patients who can receive infused medications care in a lower-cost setting versus an inpatient or clinic-based setting seems appealing, particular if that lower-cost setting is the patient's home.

The home infusion provider will complete an assessment to determine the appropriateness of a patient, caregiver if applicable, and their home prior to initiating care. This assessment may include an evaluation of the following:

- A. Accessibility to 911 services and urgent care. Volunteer services may be acceptable if urgent care is readily available.
- B. Adequate refrigeration is available if required.
- C. Home is not located in a high crime area as determined by local authorities
- D. Home environment does not meet general cleanliness standards determined by onsite home nursing assessment

V. BACKGROUND

Remicade (infliximab) was approved by the Food and Drug Administration (FDA) in 1998 (Remicade Prescribing Information: 2011). The current indications for Remicade approved by the FDA include Crohn's Disease, Pediatric Crohn's Disease, Ulcerative Colitis, Pediatric Ulcerative Colitis, Ankylosing Spondylitis, Psoriatic Arthritis, and Plaque Psoriasis. Remicade (infliximab) is administered by intravenous infusion a period of not less than two hours. Data from the manufacturer states approximately 20% of Remicade (infliximab)-treated patients in all clinical trials experienced an infusion reaction compared with 10% of placebo-treated patients. In phase 3 clinical studies, 18% of Remicade (infliximab)-treated patients experienced an infusion reaction compared to 5% of placebo-treated patients. Serious infusion reactions occurred in <1% of patients and included anaphylaxis, convulsions, erythematous rash and hypotension. Approximately 3% of patients discontinued Remicade (infliximab) because of infusion reactions, and all patients recovered with treatment and/or discontinuation of the infusion. The manufacturer recommends appropriate personnel and medication available to treat anaphylaxis if it occurs. In addition, Remicade (infliximab) has been associated with hypersensitivity reactions that vary in their time of onset and required hospitalization in some cases. Most hypersensitivity reactions, which include urticaria, dyspnea, and/or hypotension, have occurred during or within two hours of Remicade (infliximab) infusion.

Section 2: Clinical Criteria

REMICADE (infliximab)

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Moderately to severely active Crohn's disease
2. Moderately to severely active ulcerative colitis
3. Moderately to severely active rheumatoid arthritis in combination with methotrexate
4. Active ankylosing spondylitis
5. Active psoriatic arthritis
6. Chronic severe plaque psoriasis

B. Compendial Uses

1. Axial spondyloarthritis
2. Behçet's syndrome
3. Granulomatosis with polyangiitis (Wegener's granulomatosis)
4. Hidradenitis suppurativa
5. Juvenile idiopathic arthritis
6. Pyoderma gangrenosum
7. Sarcoidosis
8. Takayasu's arteritis
9. Uveitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn's disease (CD)

1. Authorization of 24 months may be granted for members who have received Remicade, Inflectra, or any other biologic indicated for the treatment of Crohn's disease in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade or Inflectra.
2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when any of the following criteria is met:
 - a. Member has fistulizing disease.
 - b. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix A).

B. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have received Remicade, Inflectra, or any other biologic indicated for moderately to severely active ulcerative colitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade or Inflectra.
2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when the member has an inadequate response, intolerance or contraindication to at least ONE conventional therapy option (see Appendix B).

C. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted for members who have received Remicade, Inflectra, or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for the medication. Remicade or Inflectra must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.
2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
 - a. Member is prescribed Remicade or Inflectra in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
 - b. Member has any of the following:
 - i. Inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 25 mg/week)
 - ii. Intolerance or contraindication to methotrexate (see Appendix C)

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 24 months may be granted for members who have received Remicade, Inflectra, or any other biologic DMARD indicated for active ankylosing spondylitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade or Inflectra.
2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs) over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose.
 - b. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix D).

E. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

F. Chronic severe plaque psoriasis

1. Authorization of 24 months may be granted for members who have received Remicade, Inflectra, Otezla, or any other biologic DMARD indicated for the treatment

of severe psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade or Inflectra.

2. Authorization of 24 months may be granted for treatment of chronic severe plaque psoriasis when all of the following criteria are met:
 - a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
 - ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix E).
 - iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

G. Behçet's syndrome

Authorization of 24 months may be granted for treatment of Behçet's syndrome.

H. Granulomatosis with polyangiitis (Wegener's granulomatosis)

Authorization of 24 months may be granted for treatment of granulomatosis with polyangiitis.

I. Hidradenitis suppurativa

Authorization of 24 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

J. Juvenile Idiopathic arthritis (JIA)

1. Authorization of 24 months may be granted for members who have received Remicade or Inflectra in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade or Inflectra.
2. Authorization of 24 months may be granted for treatment of JIA when any of the following criteria is met:
 - a. Member has experienced an inadequate response to at least a 3-month trial of a self-injectable TNF inhibitor indicated for JIA (e.g., Enbrel or Humira).
 - b. Member has experienced an intolerable adverse event (e.g., hypersensitivity reaction) to a self-injectable TNF inhibitor indicated for JIA.
 - c. Member has developed antibodies against Enbrel or Humira.

K. Pyoderma gangrenosum

Authorization of 24 months may be granted for treatment of pyoderma gangrenosum.

L. Sarcoidosis

Authorization of 24 months may be granted for treatment of sarcoidosis.

M. Takayasu's arteritis

Authorization of 24 months may be granted for treatment of Takayasu's arteritis.

N. Uveitis

Authorization of 24 months may be granted for treatment of uveitis in members who have experienced an inadequate response or intolerance or have a contraindication to a trial of immunosuppressive therapy for uveitis (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Remicade or Inflectra as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

V. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Remicade, Inflectra, or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) in a paid claim through a pharmacy or medical benefit within the previous 120 days of the continuation request are exempt from requirements related to TB screening in this Policy.

VI. APPENDICES

Appendix A: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide, oral mesalamine
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission:

- a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission
 - a. Metronidazole ± ciprofloxacin
 6. Perianal and fistulizing disease – maintenance of remission
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

Appendix C: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix D: Examples of Contraindications to the Use of NSAIDs

1. Allergic-type reaction following aspirin or other NSAID administration
2. Asthma
3. Gastrointestinal bleeding
4. History of intolerance or adverse event

5. Significant drug interaction
6. Urticaria

Appendix E: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

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