Reference number
2182-A

SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendia uses are considered a covered benefit provided 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 REMICADE

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

1. Authorization of 12 months may be granted for members who have received Remicade, 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.

2. Authorization of 12 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 12 months may be granted for members who have received Remicade, 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.

2. Authorization of 12 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 12 months may be granted for members who have received Remicade, or any other biologic DMARD or targeted synthetic DMARD 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 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 12 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 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 20 mg/week)
      ii. Intolerance or contraindication to methotrexate (see Appendix C)

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have received Remicade, 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.

2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following are 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 12 months may be granted for members who have received at least one previous trial of a traditional DMARD or targeted synthetic DMARD for the treatment of active psoriatic arthritis (PsA).

F. Chronic severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have received Remicade, 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.

2. Authorization of 12 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 12 months may be granted for treatment of Behçet's syndrome.

H. Granulomatosis with polyangiitis (Wegener's granulomatosis)
Authorization of 12 months may be granted for treatment of granulomatosis with polyangiitis.

I. Hidradenitis suppurativa
Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

J. Juvenile Idiopathic arthritis (JIA)
1. Authorization of 12 months may be granted for members who have received Remicade in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Remicade.

2. Authorization of 12 months may be granted for treatment of JIA.

K. Pyoderma gangrenosum
Authorization of 12 months may be granted for treatment of pyoderma gangrenosum.

L. Sarcoidosis
Authorization of 12 months may be granted for treatment of sarcoidosis.

M. Takayasu's arteritis
Authorization of 12 months may be granted for treatment of Takayasu's arteritis.

N. Uveitis
Authorization of 12 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).

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III. CRITERIA FOR INITIAL APPROVAL INFLECTRA or RENFLEXIS

A. Moderately to severely active Crohn's disease (CD)
1. Authorization of 12 months may be granted for members who have received Inflectra, Renflexis, 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 Inflectra and have had a treatment failure or contraindication Remicade.

2. Authorization of 12 months may be granted for treatment of moderately to severely active CD when there is documentation of treatment failure or contraindication to Remicade, and any of the following criteria is met:

c. Member has fistulizing disease.
d. 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)

3. Authorization of 12 months may be granted for members who have received Inflectra, Renflexis 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 Inflectra and there is documentation of treatment failure or contraindication to Remicade

4. Authorization of 12 months may be granted for treatment of moderately to severely active UC when there is documentation of treatment failure or contraindication to Remicade, and 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)

3. Authorization of 12 months may be granted for members who have received Inflectra, Renflexis or any other biologic DMARD or targeted synthetic DMARD 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, and there is documentation of treatment failure or contraindication to Remicade. Inflectra must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.

4. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   c. There is documentation of treatment failure or contraindication to Remicade.
   d. Member is prescribed Inflectra in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
   e. Member has any of the following:
      iii. Inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week)
      iv. Intolerance or contraindication to methotrexate (see Appendix C)

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

3. Authorization of 12 months may be granted for members who have received Inflectra, Renflexis 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 Inflectra AND there is documentation of treatment failure or contraindication to Remicade

4. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when there is documentation of treatment failure or contraindication to Remicade and any of the following criteria is met:
   c. 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.
   d. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix D).

E. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA) when there is documentation of treatment failure or contraindication to Remicade.

F. Chronic severe plaque psoriasis

3. Authorization of 12 months may be granted for members who have received Inflectra, Renflexis 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 Inflectra and there is documentation of treatment failure or contraindication to Remicade.

4. Authorization of 12 months may be granted for treatment of chronic severe plaque psoriasis when all of the following criteria are met:
   a. There is documentation of treatment failure or contraindication to Remicade.
   b. 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.
   c. 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 12 months may be granted for treatment of Behçet's syndrome when documentation confirms treatment failure or contraindication to Remicade.

H. Granulomatosis with polyangiitis (Wegener's granulomatosis)

Authorization of 12 months may be granted for treatment of granulomatosis with polyangiitis when documentation confirms treatment failure or contraindication to Remicade.

I. Hidradenitis suppurativa

Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when documentation confirms treatment failure or contraindication to Remicade

J. Juvenile Idiopathic arthritis (JIA)

3. Authorization of 12 months may be granted for members who have received Inflectra or Renflexis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Inflectra and there is documentation or treatment failure or contraindication to Remicade

4. Authorization of 12 months may be granted for treatment of JIA.

K. Pyoderma gangrenosum

Authorization of 12 months may be granted for treatment of pyoderma gangrenosum when documentation confirms treatment failure or contraindication to Remicade.

L. Sarcoidosis

Authorization of 12 months may be granted for treatment of sarcoidosis when documentation confirms treatment failure or contraindication to Remicade.

M. Takayasu's arteritis

Authorization of 12 months may be granted for treatment of Takayasu's arteritis when documentation confirms treatment failure or contraindication to Remicade.

N. Uveitis

Authorization of 12 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) and documentation confirms treatment failure or contraindication to Remicade

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IV. CONTINUATION OF THERAPY

Authorization of 12 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, Renflexis or Inflectra as evidenced by low disease activity or improvement in signs and symptoms of the condition.

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 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)

VII. REFERENCES

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