SPECIALTY GUIDELINE MANAGEMENT

HUMIRA (adalimumab)

POLICY

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 rheumatoid arthritis (RA)
   2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
   3. Active psoriatic arthritis (PsA)
   4. Active ankylosing spondylitis (AS)
   5. Moderately to severely active Crohn’s disease (CD)
   6. Moderate to severely active ulcerative colitis (UC)
   7. Moderate to severe chronic plaque psoriasis (PsO)
   8. Moderate to severe Hidradenitis Suppurativa
   9. Non-infectious intermediate, posterior and panuveitis

B. Compendial Uses
   Axial spondyloarthritis

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

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:
A. Untreated latent TB infection (treatment must be initiated prior to starting Humira)
B. Active tuberculosis infection (treatment must be completed prior to starting Humira)

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira, 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 Humira.

   2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 25 mg/week).
      b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Active polyarticular juvenile idiopathic arthritis (pJIA)
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira or any other biologic DMARD indicated for active polyarticular juvenile idiopathic arthritis in
a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.

2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate.
   b. Member has intolerance or contraindication to methotrexate (see Appendix A).

C. Active psoriatic arthritis (PsA)
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira or any other biologic DMARD indicated for active psoriatic arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.
   2. Authorization of 24 months may be granted for treatment of active PsA when any of the following criteria is met:
      a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate, sulfasalazine, or leflunomide.
      b. Member has intolerance or contraindication to methotrexate, sulfasalazine, or leflunomide (see Appendix A and Appendix B).
      c. Member has active enthesitis and/or dactylitis (i.e., sausage digit).
      d. Member has predominant axial disease (i.e., extensive spinal involvement).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira 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 Humira.
   2. Authorizations 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 C).

E. Moderately to severely active Crohn’s disease (CD)
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira or any other biologic DMARD 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 Humira.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when the following criteria is met:
      a. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix D).

F. Moderately to severely active ulcerative colitis (UC)
   1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira or any other biologic DMARD 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 Humira.
      a. Members who are currently receiving or have received a biologic DMARD other than Humira must have lost response to a previous TNF inhibitor therapy due to antibody formation.
   2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when all of the following criteria are met:
      a. Member is naïve to TNF inhibitor therapy or has lost response to previous TNF inhibitor therapy due to antibody formation.
b. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix E)

G. Moderate to severe chronic plaque psoriasis (PsO)
1. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Humira or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Humira.

2. Authorization of 24 months may be granted for treatment of moderate to severe chronic 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 insufficient response to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin despite adequate dosing and duration (see Appendix F).
      ii. Member has had an intolerance or adverse event to a trial of phototherapy or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      iii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix G).
      iv. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

H. Moderate to severe hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of moderate to severe hidradenitis suppurativa.

I. Uveitis (non-infectious intermediate, posterior and panuveitis)
Authorization of 24 months may be granted for treatment of non-infectious intermediate, posterior and panuveitis.

IV. CONTINUATION OF THERAPY

A. For ulcerative colitis:
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve clinical remission by treatment day 56 (week 8) and maintain positive clinical response with Humira thereafter as evidenced by low disease activity or improvement in signs and symptoms of ulcerative colitis.

B. For all other indications:
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 Humira as evidenced by low disease activity or improvement in signs and symptoms of the condition.

V. DOSAGE AND ADMINISTRATION

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

A. Rheumatoid arthritis
   1. 40 mg per 2 weeks
   2. Without methotrexate due to intolerance or contraindication: 40 mg per week

B. Psoriatic arthritis and ankylosing spondylitis
   1. 40 mg per 2 weeks

C. Polyarticular juvenile idiopathic arthritis
1. The dosing limit is determined based on the member’s weight.
   a. Less than 15 kg (33 lbs): 10 mg per 2 weeks
   b. 15 kg (33 lbs) to 30 kg (66 lbs): 20 mg per 2 weeks
   c. 30 kg (66 lbs) or greater: 40 mg per 2 weeks

D. Pediatric Crohn’s disease
   1. The dosing limit is determined based on the member’s weight.
      a. Less than 40 kg (88 lbs)
         • Initial loading dose for the initial 15 days: 120 mg total
         • Maintenance dose: 20 mg per 2 weeks
      b. 40 kg (88 lbs) or greater
         • Initial loading dose for the initial 15 days: 240 mg total
         • Maintenance dose: 40 mg per 2 weeks

E. Adult Crohn’s disease
   1. Initial loading dose for the initial 15 days: 240 mg total
   2. Maintenance dose: 40 mg per 2 weeks

F. Ulcerative colitis
   1. Initial loading dose for the initial 15 days: 240 mg total
   2. Maintenance dose: 40 mg per 2 weeks

G. Plaque psoriasis
   1. Initial loading dose for the initial 7 days: 80 mg once on day 1 only
   2. Maintenance dose: 40 mg per 2 weeks

H. Hidradenitis suppurativa
   1. Initial loading dose for the initial 15 days: 240 mg total
   2. Maintenance dose: 40 mg per week

VI. 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 at least a 28-day supply of Humira, 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 exempted from requirements related to TB screening and treatment in this Policy.

VII. APPENDICES

Appendix A: 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 B: Examples of Contraindications to Sulfasalazine and/or Leflunomide
   1. History of intolerance or adverse event
2. Hypersensitivity
3. Intestinal obstruction
4. Porphyria
5. Pregnancy
6. Significant drug interaction
7. Urinary obstruction

Appendix C: 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 D: 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 E: 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 F: Time to Clinical Efficacy and Dose for Treatment of Plaque Psoriasis with Phototherapy, Methotrexate, Cyclosporine and Acitretin.
1. Phototherapy: at least 4 weeks or 10 sessions
2. Methotrexate: at least 1 month following a titration to the maximum tolerated dose. The maximum titrated dose must be 10 mg/week or higher.
3. Cyclosporine: 2.5 mg/kg/day or higher for at least 2 months
4. Acitretin: 25 mg/day or higher for at least 3 months

Appendix G: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.
1. Alcohol intake / alcoholic 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)

VIII. REFERENCES