

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. 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 Humira 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 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 20 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 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)**

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

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 24 months may be granted for members who have received 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. 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 B).

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

1. Authorization of 24 months may be granted for members who have received Humira 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 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 C).

F. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have received Humira 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 Humira.
2. Authorization of 24 months may be granted for treatment of moderately to severely active UC if the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix D).

G. Moderate to severe chronic plaque psoriasis (PsO)

1. Authorization of 24 months may be granted for members who have received Humira, Otezla, 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 inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a 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.

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.

III. 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.

IV. 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 Humira 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.

V. 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 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 C: 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 D: 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 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)

VI. REFERENCES

1. Humira [package insert]. North Chicago, IL: AbbVie Inc.; June 2016.
2. van der Heijde D, Sieper J, Maksymowych WP, et al. 2010 Update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. *Ann Rheum Dis*. 2011;70:905-908.
3. Sieper J, van der Heijde D, Dougados M, et al. Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). *Ann Rheum Dis*. 2013;72(6):815-22.
4. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Rhem Dis*. 2014;73:492-509.
5. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1)1-26.
6. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum*. 2008;59(6):762-784.
7. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
8. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
9. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64(Suppl II):ii14–ii17.
10. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. *Clin Rheumatol*. 2014 May 8. [Epub ahead of print].
11. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
12. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
13. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2015: 10.1002/art.39298. [Epub ahead of print].
14. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.