

**Title:** *adalimumab (Humira)*

**Origination:** 12/16/05

**Revised:** 11/11/11

**Annual Review:** 12/15/11

**Purpose:**

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

**Background Information:**

***Medication Summary***

- Humira (adalimumab) is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF). Adalimumab binds specifically to TNF-alpha and blocks its interaction with the cell surface TNF receptors.
- Humira is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA) and in children (4 years of age or older) with Polyarticular Juvenile Rheumatoid Arthritis (JRA) who have an inadequate response to one or more disease modifying anti-Rheumatic drugs (DMARDs).
- Humira is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis (PsA).
- Humira is indicated for reducing signs and symptoms in patients with ankylosing spondylitis (AS).
- Humira is indicated for the treatment of adult Members (18 years or older) with chronic, moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
- Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy or have lost response to or are intolerant to Remicade (infliximab).
- Humira may be used alone or in combination with Methotrexate (MTX) or other DMARDs.

***Reference Statement***

- Guidelines will be compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

***Eligibility Criteria***

- Member must be eligible and have applicable benefits.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

***Title: adalimumab (Humira)***

**Background Information, continued:**

***Exclusions***

- Member less than four (4) years of age;
- Concurrent use of multiple biological response modifiers including, but not limited to: Kineret (anakinra), Humira (adalimumab), Cimzia (certolizumab), Amevive (alefacept), and Remicade (infliximab). Only one (1) agent at a time will be covered for the treatment of Rheumatoid Arthritis, Polyarticular Juvenile Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, or Plaque Psoriasis;
- Guttate, erythrodermic, or pustular psoriasis;
- Member experiencing acute infection or significant chronic infection including, but not limited to, sepsis, tuberculosis, aplastic anemia, opportunistic infections.

**Procedure:**

- 1.0 Request for *initial therapy* for **Rheumatoid Arthritis (RA)** with adalimumab (Humira) requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following:
- 1.1 Provider must be a rheumatologist; **AND**
- 1.2 Member is at least 18 years of age; **AND**
- 1.3 Diagnosis of moderate to severely active RA of at least six (6) months duration as evidenced by **at least one (1)** of the following:
- 1.3.1 Erythrocyte sedimentation rate (ESR)  $\geq$  28mm/hr;
  - 1.3.2 C-reactive protein (CRP)  $\geq$  2.0 mg/dL;
  - 1.3.3 Morning stiffness;
  - 1.3.4 Swollen and/or tender joints;
  - 1.3.5 Synovitis;
- AND**
- 1.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of Methotrexate; **OR**
- 1.4 Member has contraindication to Methotrexate as evidenced by **at least one (1)** of the following:
- 1.4.1 Chronic liver disease;
  - 1.4.1 Leukopenia;
  - 1.4.1 Thrombocytopenia;
  - 1.4.1 Creatinine clearance less than 40mL/minute;
  - 1.4.1 Immunodeficiency;

**AND**

***Title: adalimumab (Humira)***

**Procedure, continued:**

- 1.0 Request for *initial therapy* for **rheumatoid arthritis (RA)** with adalimumab (Humira) requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **ALL** of the following, continued:
    - 1.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of **OR** is not a candidate for any of the following DMARDs:
      - 1.5.1 Leflunomide (Arava);
      - 1.5.2 Hydroxychloroquine (Plaquenil);
      - 1.5.3 Sulfasalazine (Azulfidine);
    - 1.6 If all criteria are met, Humira 40mg SQ every other week may be approved for up to three (3) months, or Humira 40mg SQ weekly may be approved for up to three (3) months if not on concurrent Methotrexate therapy.
  - 2.0 Request for *continuation of therapy* beyond initial authorization period for **rheumatoid arthritis (RA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
    - 2.1 Reduction in Member's signs and symptoms (i.e., 20% improvement in painful joint count, ESR, CRP, or morning stiffness);
    - 2.2 If all criteria are met, Humira 40mg SQ every other week may be approved for up to one (1) year of therapy, or Humira 40mg SQ weekly may be approved for up to one (1) year if not on concurrent Methotrexate therapy.
- 
- 3.0 Request for *initial therapy* with adalimumab (Humira) for **juvenile rheumatoid arthritis (JRA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
    - 3.1 Provider is a rheumatologist; **AND**
    - 3.2 Member is at least four (4) years of age; **AND**
    - 3.3 Diagnosis of active JRA as evidenced by:
      - 3.3.1 Swollen joints, typically large weight-bearing joints, such as the knees or ankles;
      - 3.3.2 Limitation of motion as well as pain and/or tenderness;

**AND**

    - 3.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of methotrexate; **OR**
    - 3.4 Member has a contraindication to methotrexate (as listed in section 1.4);

**AND**

**Title: adalimumab (Humira)**

**Procedure, continued:**

3.0 Request for *initial therapy* with adalimumab (Humira) for **juvenile rheumatoid arthritis (JRA)** requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying the following, continued:

3.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of adequate doses of **OR** is not a candidate for any DMARDs (as listed in section 1.5);

3.6 If all criteria are met, Humira may be approved for up to three (3) months using the following dosing:

Weight	Dose
30kg or more (66 lbs)	40mg every other week
15kg to 29kg (33-65lbs)	20mg every other week

4.0 Request for *continuation of therapy* beyond initial authorization period for **juvenile rheumatoid arthritis (JRA)** requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying there is reduction in Member’s signs and symptoms of JRA:

4.1 If all criteria are met, Humira may be approved for up to one (1) year using the following dosing:

Weight	Dose
30kg or more (66 lbs)	40mg every other week
15kg to 29kg (33-65lbs)	20mg every other week

5.0 Request for *initial therapy* with adalimumab (Humira) for **Psoriatic Arthritis (PsA)** requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying the following:

5.1 Provider must be a rheumatologist or dermatologist; **AND**

5.2 Member must be at least 18 years of age; **AND**

5.3 Diagnosis of moderate to severe psoriatic arthritis as evidenced by:

5.3.1 At least three (3) swollen and three (3) tender joints; **AND**

5.3.2 Erythrocyte sedimentation rate (ESR)  $\geq$  28mm/hr.; **AND**

***Title: adalimumab (Humira)***

**Procedure, continued:**

- 5.0 Request for *initial therapy* with adalimumab (Humira) for **Psoriatic Arthritis (PsA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:
- 5.4 Member shows inadequate response to a three (3) month trial of an adequate dose of, or is not a candidate for, at least one non-steroidal anti-inflammatory medication (NSAIDs) including, but not limited to, the following:
- 5.4.1 Diclofenac (with or without misoprostol);
  - 5.4.2 Ibuprofen (Motrin);
  - 5.4.3 Indomethacin (Indocin);
  - 5.4.4 Meloxicam (Mobic);
  - 5.4.5 Naproxen (Naprosyn);
  - 5.4.6 Celecoxib (Celebrex);
- AND**
- 5.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of or is not a candidate for at least one (1) of the following DMARDs (either alone or in combination):
- 5.5.1 Sulfasalazine (Azulfidine);
  - 5.5.1 Leflunomide (Arava);
  - 5.5.1 Methotrexate;
  - 5.5.1 Cyclosporine;
- 5.6 If all criteria are met, Humira 40mg SQ every other week may be approved for up to three (3) months.
- 6.0 Request for *continuation of therapy* beyond initial authorization period for **psoriatic arthritis (PsA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in Member's signs and symptoms of PsA (i.e., improvement in tender/swollen joint count or ESR level) and/or an improvement in Member's physical functioning:
- 6.1 If all criteria are met, Humira 40mg SQ every other week may be approved for up to one (1) year.
-

***Title: adalimumab (Humira)***

**Procedure, continued:**

7.0 Request for *initial therapy* with adalimumab (Humira) for **plaque psoriasis** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:

7.1 Provider is a dermatologist; **AND**

7.2 Member is at least 18 years of age; **AND**

7.3 Diagnosis of moderate to severe plaque psoriasis as evidenced by **at least one (1)** of the following:

7.3.1 Involvement of at least 10% of the body surface area (BSA); **OR**

7.3.1 Psoriasis Area and Severity Index (PASI) Score of 10 or greater; **OR**

7.3.1 Psoriasis leading to incapacitation due to plaque location (i.e., head and neck, palms, soles, or genitalia);

**AND**

7.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of **OR** is not a candidate for any one (1) of the following topical agents:

7.4.1 Anthralin;

7.4.2 Coal Tar Preparations;

7.4.3 Corticosteroids;

7.4.4 Emollients;

7.4.5 Immunosuppressives;

7.4.6 Keratolytics;

7.4.7 Retinoic Acid Derivatives;

7.4.8 Vitamin D Analogues;

**AND**

7.5 Member shows inadequate response to three (3) to six (6) month minimum trial of an adequate dose of **OR** is not a candidate for **at least one (1)** of the following systemic agents:

7.5.1 Immunosuppressives;

7.5.1 Retinoic Acid Derivatives;

7.5.1 Methotrexate;

**AND**

7.6 Member shows inadequate response to three (3) month to six (6) month minimum trial of **OR** is not a candidate for treatment with phototherapy (PUVA);

7.7 If all criteria are met, Humira Psoriasis Starter Package may be approved for one (1) month (4 syringes – 80mg given as 2 injections on day 1, then 40mg every other week starting at week 1), then 40mg SQ every other week for two (2) additional months (for a total of 3 months of therapy).

***Title: adalimumab (Humira)***

**Procedure, continued:**

8.0 Request for *continuation of therapy* beyond initial authorization period for **plaque psoriasis** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in Member's signs and symptoms (i.e., improvement in body surface area affected, skin lesions and/or PASI score):

8.1 If all criteria are met, Humira 40mg SQ every other week may be approved for up to one (1) year.

-----

9.0 Request for *initial therapy* with adalimumab (Humira) for **Ankylosing Spondylitis (AS)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:

9.1 Provider must be a rheumatologist; **AND**

9.2 Member must be at least 18 years of age; **AND**

9.3 Diagnosis of active **Ankylosing Spondylitis (AS)** as evidenced by:

9.3.1 Inflammatory back pain (as defined as: stiffness and pain that worsens at rest, and improves with exercise); **AND**

9.3.2 Morning stiffness of 45 minutes or longer;

**AND**

9.4 Member shows inadequate response to at least two different trials of NSAID therapy. Treatment should be three (3) to six (6) months at maximum recommended doses **OR** member is not a candidate for NSAIDs due to contraindications (i.e. GI bleed, anticoagulation intake). These include, but are not limited to, the following:

9.4.1 diclofenac (with or without misoprostol);

9.4.2 ibuprofen;

9.4.3 indomethacin;

9.4.4 meloxicam;

9.4.5 naproxen;

9.4.6 celecoxib;

**AND**

***Title: adalimumab (Humira)***

**Procedure, continued:**

9.0 Request for *initial therapy* with adalimumab (Humira) for **Ankylosing Spondylitis (AS)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:

9.5 Member shows an inadequate response to a three (3) to six (6) month trial of an adequate dose of **sulfasalazine (Azulfidine)** if the Member has a component of *peripheral arthritis* defined as pain/inflammation in arms, legs, elbows, wrist, knees, and/or ankles; (*This step (5.5) is not required for axial arthritis*);

**OR**

9.5 Member has a contraindication to sulfasalazine as evidenced by at least one (1) of the following:

9.5.1 GI tract obstruction;

9.5.2 Porphyria;

9.5.3 Urinary Tract Obstruction;

9.5.4 Sulfasalazine hypersensitivity;

9.6 If all criteria are met, Humira 40mg SQ every other week may be approved for up to three (3) months.

10.0 Request for *continuation of therapy* beyond initial authorization period for **Ankylosing Spondylitis** requires clinical documentation that there is reduction in Member's signs and symptoms of AS (i.e., 20% improvement in morning stiffness and degree of nocturnal spinal pain):

10.1 If all criteria are met, Humira 40mg SQ every other week may be approved for up to one (1) year.

-----  
11.0 Request for *initial therapy* with adalimumab (Humira) for **Crohn's Disease (CD)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:

11.1 Provider must be a gastroenterologist; **AND**

11.2 Member must be at least 18 years of age; **AND**

***Title: adalimumab (Humira)***

**Procedure, continued:**

11.0 Request for *initial therapy* with adalimumab (Humira) for **Crohn's Disease (CD)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:

11.3 Diagnosis of moderate to severe active **Crohn's Disease (CD)** as evidenced by:

11.3.1 Radiological or endoscopic evidence; **AND**

11.3.2 **At least one (1)** of the following more prominent symptoms:

11.3.2.1 Fevers;

11.3.2.1 Significant weight loss;

11.3.2.1 Abdominal pain or tenderness;

11.3.2.1 Intermittent nausea or vomiting (without obstructive findings);

11.3.2.1 Significant anemia;

11.3.2.1 Diarrhea:

**OR**

11.3.2 Crohn's Disease Activity Index (CDAI) score of 220-450 points;

**AND**

11.4 Member shows an inadequate response to a three (3) to six (6) month trial of an adequate dose of **OR** is not a candidate for **at least two (2)** of the following medications:

11.4.1 Mesalamine (Asacol, Lialda, Pentasa, Rowasa, Canasa);

11.4.2 Sulfasalazine (Azulfidine);

11.4.3 Corticosteroids (prednisone, methylprednisolone, budesonide, Entocort);

11.4.4 Azathioprine (Imuran);

11.4.5 Mercaptopurine (6-MP);

11.4.6 Methotrexate;

11.5 If all criteria are met, Humira Crohn's Disease Starter Package may be approved for one (1) month (6 syringes - 160mg given as 4 injections on day 1, then 80mg at week 2), then 40mg SQ every other week for 2 additional months (for a total of 3 months of therapy).

**Title: adalimumab (Humira)**

**Procedure, continued:**

- 12.0 Request for *continuation of therapy* beyond the initial authorization period for **Crohn's disease** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in Member's signs and symptoms (i.e., decrease in pain, fever, weight loss, diarrhea, anemia):
- 12.1 If all criteria are met, Humira 40mg SQ every other week may be approved for up to one (1) year of therapy.

**References:**

1. Abbott Laboratories, Inc. Humira® (adalimumab) Solution for Injection. Package Insert. Revised March 2009.
2. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the Management of Rheumatoid Arthritis: 2002 Update. *Arthritis & Rheumatism*. 2002;46(2):328-46.
3. Bruan J. et al. International ASAS consensus statement for the use of anti-tumor necrosis factor agents in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2003;52:817-824.
4. Bruan J. et al. Therapy of ankylosing spondylitis and other spondylitis and other spondylarthritides: established medical treatment, anti-TNF-therapy and other novel approaches. *Arthritis Res*. 2002;4:307-321.
5. Buning, C. et al. Conventional therapy for Crohn's disease. *World J Gastroenterol*. 2006 Aug 14;12(30): 4794-806.
6. Carter, MJ. Et al. Guidelines for management of inflammatory bowel disease in adults. *Gut*. 2004;53:1-16.
7. Colombel, J. et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: The CHARM trial. *Gastroenterology*. 2007 Jan; 132(1):52-65. Epub 2006 Nov 29.
8. Gladman, D. et al. Adalimumab for long term treatment of psoriatic arthritis: forty-eight week data from the adalimumab effectiveness in psoriatic arthritis trial. *Arthritis Rheum*. 2007 Feb;56(2):476-88.
9. Hanauer, S. et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. *Gastroenterology*. 2006 Feb;130(2):323-33.
10. Hanauer, S. et al. Management of Crohn's Disease in Adults. *Am J Gastroenterol* 2001; 96:635-643.

**Title: *adalimumab (Humira)***

**References, continued:**

11. Keystone, E. et al. Radiographic, Clinical, and Functional Outcomes of Treatment With Adalimumab (a Human Anti-Tumor Necrosis Factor Monoclonal Antibody) in Patients With Active Rheumatoid Arthritis Receiving Concomitant Methotrexate Therapy: A Randomized, Placebo-Controlled, 52-Week Trial. *Arthritis & Rheumatism*. 2004;50(5):1400-1411.
12. Kyle, S. et al. Guideline for Anti-TNF-Therapy in Psoriatic Arthritis. *Rheumatology* 2005;44 : 390-397.
13. Mease PJ, Gladman DD, Ritchlin CT, et al. Adalimumab Effectiveness in Psoriatic Arthritis Trial Study Group. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis & Rheumatism*. 2005 Oct;52(10):3279-89.
14. Sandborn, WJ. Et al. Adalimumab Induction Therapy for Crohn disease previously Treated with Infliximab: the GAIN trial. *Annals of Internal Medicine*. 2007;146:829-838.
15. Van de Putte, L. B. A. et al. Efficacy and Safety of Adalimumab As Monotherapy In Patients With Rheumatoid Arthritis For Whom Previous Disease Modifying Anti-Rheumatic Treatment Has Failed. *Ann Rheum Dis*. 2004;63:508-516.
16. Gottlieb A, Korman NJ, Gordon KB, Feldman SR, Lebwohl M, Koo JY, Van Voorhees AS, Elmets CA, Leonardi CL, Beutner KR, Bhushan R, Menter A. Guidelines of care for the management of psoriasis and psoriatic arthritis. *J Am Acad Dermatol* 2008 May; 58 (5):851-64.
17. Saag, KG. et al. American College of Rheumatology 2008 Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis & Rheumatism (Arthritis Care & Research)*. 2008; 59, 762–784.

**Disclaimer Information:**

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.