OVERVIEW

Humira is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody specific for human tumor necrosis factor alpha (TNFα). It neutralizes the biological activity of TNFα and inhibits binding of TNFα with its receptors. TNF, a naturally occurring cytokine, mediates inflammation and modulates cellular immune responses. Increased levels of TNF are found in the synovial fluid of patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). TNF has an important role in both the pathologic inflammation and the joint destruction that are characteristic of these diseases. Increased levels of TNF are found in psoriasis plaques but the mechanism of action in plaque psoriasis and Crohn's disease are not known. The exact mechanism of action for hidradenitis suppurativa is unknown but may be due to decreased cytokines and other inflammatory cells.

Boxed Warnings

Humira has boxed warnings concerning risks of serious infection and the risk of malignancy. Prior to initiating therapy with Humira, patients should be evaluated for active tuberculosis (TB) infection; periodically during therapy, patients should be assessed for latent TB infection. Patients should also be monitored for signs and symptoms of infection during and after treatment with Humira, and if a serious infection or sepsis develops, Humira should be discontinued. It is also recommended that patients treated with any TNF antagonist should be monitored for malignancies.

POLICY STATEMENT

This policy involves the use of Humira. Prior authorization is recommended for medical benefit coverage of Humira. Approval is recommended for those who meet the conditions of coverage in the Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics for the diagnosis provided. Waste Management applies for all covered conditions that are administered by a healthcare professional. Conditions Not Recommended for Approval are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Humira as well as the monitoring required for AEs and long-term efficacy, initial approval requires Humira be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. Humira is subject to the Inflammatory Conditions Care Value Step Therapy.
RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Humira is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. Rheumatoid Arthritis (RA) an Adult

   a) **Initial Therapy.** Approve for 3 months if the patient meets BOTH of the following criteria (i and ii):
      i. The patient meets ONE of the following conditions (1, 2, 3, or 4):
         1. The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months (e.g., methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine). (NOTE: An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic disease-modifying antirheumatic drug (DMARD) [e.g., Cimzia, Enbrel, Remicade, Simponi {Aria or SC}, Actemra {IV or SC}, Kineret, Orenda {IV or SC}, and Rituxan]. These patients who have already tried a biologic for RA are not required to “step back” and try a conventional synthetic DMARD); OR
         2. Patient is concurrently receiving MTX; OR
         3. Patient has a contraindication or intolerance to MTX and leflunomide, as determined by the prescribing physician (This criterion is recommended based on the professional opinion of specialized physicians.); OR
         4. Patient has early RA (defined as disease duration of < 6 months) with at least one of the following features of poor prognosis: functional limitation (e.g., based on Health Assessment Questionnaire Disability Index [HAQ-DI] score); extraarticular disease such as rheumatoid nodules, RA vasculitis, or Felty’s syndrome; positive rheumatoid factor or anti-cyclic citrullinated protein (anti-CCP) antibodies; or bony erosions by radiograph; AND
      ii. Humira is prescribed by or in consultation with a rheumatologist.

   b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Dosing in RA. Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week. Dosing frequency may be increased to 40 mg every week)

2. Ankylosing Spondylitis (AS)

   a) **Initial Therapy.** Approve for 3 months if prescribed by or in consultation with a rheumatologist.

   b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., decreased pain or stiffness, improved function or activities of daily living), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.
Dosing in AS. Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week).

3. Crohn’s Disease in a Patient ≥ 6 Years of Age

   a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):

      i. Patient meets ONE of the following conditions (1, 2, 3, or 4):

         1. Patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
         2. Patient has tried one other agent for Crohn’s disease (e.g., azathioprine, 6-mercaptopurine, MTX, Cimzia, Remicade, or Entyvio); OR
         3. The patient has had ileocolonic resection (to reduce the chance of Crohn’s disease recurrence); OR
         4. The patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; AND

      ii. Humira is prescribed by or in consultation with a gastroenterologist.

   b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Dosing in Crohn’s Disease. Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., Pediatric 17-<40 kg: 80 mg on day one [given as two 40 mg injections in one day], then 40 mg two weeks later [day 15], followed two week later [day 29] with a maintenance dose of 20 mg every or week, ≥ 40 kg: 160 mg on day one [given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [given as two 40 mg injections in one day] [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week, Adult: 160 mg on day one [given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week).

4. Juvenile Idiopathic Arthritis (JIA) [or juvenile rheumatoid arthritis {JRA}] [regardless of type of onset]  
   [Note: This includes patients with juvenile spondyloarthropathy/active sacroiliac arthritis]

   a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):

      i. The patient meets ONE of the following conditions (1, 2, 3, or 4):

         1. Patient has tried one other agent for this condition (e.g., MTX, sulfasalazine, or leflunomide, a nonsteroidal anti-inflammatory drug [NSAID], or a biologic DMARD [e.g., Enbrel, Orecia IV, Remicade, Kineret, Actemra IV]); OR
         2. Patient will be starting on Humira concurrently with MTX, sulfasalazine, or leflunomide; OR
         3. Patient has an absolute contraindication to MTX (e.g., pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias), sulfasalazine, or leflunomide; OR
         4. Patient has aggressive disease, as determined by the prescribing physician; AND

      ii. Humira is prescribed by or in consultation with a rheumatologist.
b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., has improvement in limitation of motion; less joint pain or tenderness; decreased duration of morning stiffness or fatigue; improved function or activities of daily living; reduced dosage of corticosteroids), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

**Dosing in Juvenile Idiopathic Arthritis (JIA) [or juvenile rheumatoid arthritis (JRA)].** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 10-<15 kg: 10 mg every other week, 15-<30 kg: 20 mg every other week; ≥30 kg: 40 mg every other week).

5. **Plaque Psoriasis**

   a) **Initial Therapy.** Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
   
   i. Patient is 18 years of age or older; AND
   
   ii. The patient meets ONE of the following conditions (1, 2, or 3):
   
   1. The patient has tried at least one of the following agents for at least 3 months for plaque psoriasis: an oral therapy for psoriasis (e.g., MTX, cyclosporine, Soriatane® [acitretin tablets]); oral methoxsalen plus ultraviolet A light (PUVA); or a biologic agent (e.g., Enbrel, Remicade, or Stelara); OR
   
   2. The patient experienced an intolerance to a trial of at least one oral or biologic therapy for plaque psoriasis (e.g., MTX, cyclosporine, Soriatane, Enbrel, Remicade, Stelara, Cosentyx, or Taltz); OR
   
   3. The patient has a contraindication to one oral agent for psoriasis such as MTX, as determined by the prescribing physician; AND
   
   iii. Humira is prescribed by or in consultation with a dermatologist.

   b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

**Dosing in Plaque Psoriasis.** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., initial dose of 80 mg, followed by 40 mg given every other week starting one week after the initial dose).

6. **Psoriatic Arthritis (PsA)**

   a) **Initial Therapy.** Approve for 3 months if Humira is prescribed by or in consultation with a rheumatologist or a dermatologist.

   b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants [for example, C-reactive protein (CRP)]), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

**Dosing in PsA.** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week).
7. Ulcerative Colitis (UC)

a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):
   i. The patient meets ONE of the following conditions (1 or 2):
      1. Patient has had a 2-month trial of one systemic agent (e.g., 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, Remicade, or a corticosteroid such as prednisone or methylprednisolone) or was intolerant to one of these agents for ulcerative colitis; OR
      2. The patient has pouchitis AND has tried therapy with an antibiotic (e.g., metronidazole, ciprofloxacin), probiotic, corticosteroid enema, or Rowasa® (mesalamine) enema; AND
   ii. Humira is prescribed by or in consultation with a gastroenterologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response (e.g., decreased stool frequency or rectal bleeding), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Dosing in Ulcerative Colitis. Dosage and administration consistent with U.S. Food and Drug Administration approved label† (i.e., 160 mg on day one [given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week).

†NOTE: Adalimumab should only be continued when evidence of clinical remission is shown within eight weeks of therapy.

8. Hidradenitis Suppurativa.

a) Approve for 3 months if the patient meets both of the following criteria (i and ii):
   i. The patient has tried ONE other therapy (e.g., intralesional or oral corticosteroids [such as triamcinolone, prednisone], systemic antibiotics [for example, clindamycin, dicloxacillin, erythromycin], isotretinoin); AND
   ii. Humira is prescribed by or in consultation with a dermatologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Dosing in hidradenitis suppurativa. Dosage and administration consistent with U.S. Food and Drug Administration approved label: 160 mg (given as four 40 mg injections on day 1 or given as two 40 mg injections per day over 2 consecutive days), then 80 mg 2 weeks later (day 15) and maintenance of 40 mg every other week.

9. Uveitis (including other posterior uveitides and panuveitis syndromes).

a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):
   i. The patient has tried ONE of the following therapies: periocular, intraocular, or systemic corticosteroids [for example, triamcinolone, betamethasone, methylprednisolone, prednisone]; immunosuppressives (e.g.,...
methotrexate [MTX], mycophenolate mofetil, cyclosporine, azathioprine, cyclophosphamide); Enbrel (etanercept SC injection), or Remicade (infliximab IV infusion) for this condition; AND

ii. Humira is prescribed by or in consultation with an ophthalmologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Other Uses with Supportive Evidence

10. Behcet’s Disease Approve for 1 year if the patient meets the following criteria (a and b):

   a) The patient meets ONE of the following conditions (i or ii):
      
      i. The patient has tried at least ONE conventional therapy (e.g., systemic corticosteroids, immunosuppressants [azathioprine, MTX, mycophenolate mofetil, tacrolimus, Leukeran® [chlorambucil], cyclophosphamide, or cyclosporine], interferon alfa) or Enbrel or Remicade; OR

      ii. The patient has ophthalmic manifestations of Behcet’s disease; AND

   b) Humira is prescribed by or in consultation with an ophthalmologist.

11. Spondyloarthritis (SpA), Subtypes Other than Ankylosing Spondylitis or Psoriatic Arthritis (e.g., undifferentiated arthritis, non-radiographic axial SpA, Reactive Arthritis [Reiter’s disease], arthritis associated with inflammatory bowel disease [IBD]) [NOTE: For AS or PsA, refer to the respective criteria under FDA-approved indications]. Approve for 1 year if BOTH of the following conditions are met (a and b):

   a) The patient meets one of the following conditions (i or ii):
      
      i. The patient has arthritis primarily in the knees, ankles, elbows, wrists, hands, and/or feet AND has tried at least ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) [e.g., methotrexate {MTX}, leflunomide, sulfasalazine] has been tried; OR

      ii. The patient has axial spondyloarthritis; AND

   b) Humira is prescribed by or in consultation with a rheumatologist.

12. Patient has been Established on Humira for ≥ 90 days

   For conditions that do not have criteria for Patients Currently Receiving Humira but are indications or conditions addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications and Other Uses with Supportive Evidence), approve Humira for 1 year, if the patient is currently taking Humira for ≥ 90 days.

Exclusion:
Coverage of Humira is recommended in circumstances that are listed in the Recommended Authorization Criteria (FDA-Approved Indications and Other Uses with Supportive Evidence). The following provides rationale for specific Exclusions. This is not an exhaustive list of Exclusions.
1. **Concurrent Use with a Biologic DMARD or Targeted Synthetic DMARD.** Humira should not be administered in combination with another biologic agent for an inflammatory condition (e.g., TNF antagonists [Cimzia, Enbrel, Remicade, Simponi SC, or Simponi Aria], Actemra, Kineret, Ocrenia, or Rituxan® [rituximab for IV infusion], or Stelara). Combination therapy with two biologic agents is not recommended due to a higher rate of AEs with combinations and/or lack of additive efficacy. Xeljanz should not be used in combination with biologic DMARDs such as Humira. Targeted synthetic DMARDs (e.g., Xeljanz, Otezla) do not have data supporting use in combination with biologic DMARDs. Do to similar safety concerns (i.e., increased risk of AEs) plus no evidence of additive efficacy, targeted synthetic DMARDs should not be used in combination with biologic DMARDs such as Humira. **Note:** This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Humira.

2. **Polymyalgia Rheumatica (PMR).** EULAR/ACR guidelines for the management of PMR (2015) strongly recommend against the use of TNFis for treatment of PMR. This recommendation is based on lack of evidence for benefit as well as considerable potential for potential harm.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**Approval Duration:** dependent on indication. See criteria above.

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**References**


Drug Policy