

Prior Authorization DRUG Guidelines

HUMIRA (Adalimumab)

Effective Date: 7/28/05

Date Developed: 7/11/05 by C. Wilhelmy MD

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Humira is an Antirheumatic, Disease Modifying Monoclonal Antibody Tumor Necrosis Factor (TNF) Blocking Agent. It is a recombinant monoclonal antibody that binds to human tumor necrosis factor alpha (TNF-alpha) receptor sites, thereby interfering with endogenous TNF-alpha activity. Elevated TNF levels in the synovial fluid are involved in the pathologic pain and joint destruction in rheumatoid arthritis. Adalimumab decreases signs and symptoms of rheumatoid arthritis and inhibits progression of structural damage.

VCHCP requires that Humira be prescribed by a Rheumatologist, Gastroenterologist or Dermatologist. Family Practitioner or Internal Medicine can prescribe if with previous consultation with the Rheumatologist or Gastroenterologist.

Pre-Authorization Criteria:

Coverage of adalimumab (**Humira**) is recommended in those who meet one of the following criteria:

FDA-Approved Indications

Adults with Rheumatoid Arthritis: Approve for 12 months if the patient has tried one DMARD (brand or generic; oral or injectable) for at least 2 months, [this includes patients who have tried other biologic DMARDs for at least 2 months] OR is concurrently receiving MTX.

Adalimumab is FDA-approved for moderate or severe active RA in adults and can be used alone or in combination with MTX or other DMARDs.

Juvenile Idiopathic Arthritis (JIA) or Juvenile rheumatoid arthritis (JRA): Approve if the patient meets one of the following conditions, a or b:

- a) the patient has tried MTX, sulfasalazine, or leflunomide or a biologic DMARD (e.g., etanercept, abatacept, infliximab, anakinra, tocilizumab), or will be starting on adalimumab concurrently with MTX, sulfasalazine, or leflunomide. Approve for 3 months without trying another DMARD if the patient has an absolute contraindication to MTX (e.g., pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias), sulfasalazine, or leflunomide, OR

- b) the patient has active sacroiliac arthritis.

Psoriatic Arthritis: Approve for 12 months. Adalimumab is FDA-approved for PsA and can be used alone or in combination with DMARDs. In clinical trials, adalimumab was effective in patients with active PsA despite therapy with a NSAID.

Ankylosing Spondylitis: Approve for 12 months. FDA-approved indication. According to ASAS/European League Against Rheumatism (EULAR) recommendations for ankylosing spondylitis, all patients should have an adequate trial of at least 2 NSAIDs for pain and stiffness. Recommendations for other therapies before receiving adalimumab (or other TNF blocker therapy) vary according to the manifestations of the disease, level of current symptoms, clinical findings, etc. According to these recommendations, patients with pure axial manifestations do not have to try traditional DMARDs before anti-TNF agents such as adalimumab; patients with symptomatic peripheral arthritis should have an insufficient response to at least one local corticosteroid injection, if appropriate; patients with persistent peripheral arthritis must have a trial of sulfasalazine; and patients with enthesitis should try appropriate local therapy (corticosteroid injection in selected cases).

Plaque Psoriasis: Authorization can be given for patients who meet *both* of the following criteria a and b:

- a. Patient has minimum body surface area (BSA) involvement with plaque psoriasis of $\geq 5\%$.⁵³⁻⁵⁴ Exceptions can be made to the requirement for $\geq 5\%$ BSA involvement in the following instances (i or ii):
 - i. Patients with plaque psoriasis of the palms, soles, head and neck, nails, intertriginous areas or genitalia are not required to have a minimum BSA involvement OR
 - ii. The patient who meets all three of the following conditions is not required to have a minimum BSA involvement:
 - Patient has had an inadequate response to 3-month trial of either topical therapy OR localized phototherapy with ultraviolet B (UVB) or oral methoxsalen plus UVA light [PUVA] for psoriasis and
 - Patient has had an inadequate response to a 3-month trial of systemic therapy (See b. below for list) or has a contraindication to all of these and
 - Patient has significant disability or impairment in physical or mental functioning, according to the treating physician.

Note: Patients who meet the criteria 5a ii are not required to meet 5b below.
and

- b. Patient has tried a systemic therapy or phototherapy for 3 months with one of the following agents: MTX, cyclosporine, acitretin (Soriatane[®]), etanercept, alefacept (Amevive[®]), infliximab (Remicade[®]), or ustekinumab (Stelara[™]) or has tried phototherapy with UVB or PUVA for psoriasis. Rarely, a patient may have contraindications to nearly all of these other therapies and patients will be evaluated by a pharmacist and/or a physician on a case-by-case basis to determine a coverage recommendation for the client. (In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.) Due to its toxicity, adalimumab therapy should be reserved for patients who have not responded well or are intolerant to other standard systemic therapy. In addition, the National Psoriasis Foundation Clinical Consensus, states that there currently are no prognostic factors that ascertain which therapies will be most efficacious and least toxic.⁵⁴

Crohn's Disease, Adults active (to induce or maintain remission) in adults.

Crohn's Disease, active (to induce remission). Approve adalimumab for 12 weeks of therapy in adults if the patient has tried corticosteroids or if corticosteroids are contraindicated or if the patient is currently on corticosteroids (to avoid increasing the dose of the corticosteroid). After 12 weeks (this is following 160 mg at week 0, 80 mg at week 2, and a maintenance dose of 40 mg every other week (EOW) beginning at week 4), patients are evaluated for response and further authorization for maintenance of remission. In patients who do not respond by Week 12, additional therapy does not result in significantly more responses.^{1,37} In clinical trials, the first 2 doses of adalimumab were given to induce remission and if patients responded at Week 4, then maintenance with EOW adalimumab was started.

Crohn's Disease (to maintain remission).

- If the patient (adult) has received 2 doses of adalimumab to induce remission or has had 12 weeks of therapy with adalimumab (i.e., 160 mg at week 0, 80 mg at Week 2, and a maintenance dose of 40 mg EOW) and has had a response to therapy, then authorization is recommended for 12 months. Further authorization is not recommended if there is no response by Week 12. In patients who do not respond by Week 12, additional therapy does not result in significantly more responses.^{1,44}
OR
- If the patient (adult) has not received adalimumab for induction of remission, then authorize adalimumab for maintenance (i.e., for 12 months) if the patient has tried azathioprine, 6-mercaptopurine, or MTX OR if the patient has tried infliximab (Remicade) or certolizumab pegol (Cimzia®). Patient is already in remission and adalimumab is being used to maintain remission.

MONITORING PARAMETERS — Improvement of symptoms; signs of infection; place and read PPD before initiation.

Exclusions

Coverage of adalimumab is not recommended in the following circumstances:

1. **Adalimumab should not be given in combination with abatacept (Orencia®), alefacept (Amevive®), anakinra (Kineret®), certolizumab pegol (Cimzia®), etanercept (Enbrel®), golimumab (Simponi™), rituximab (Rituxan®), tocilizumab (Actemra®), or ustekinumab (Stelara™).**
2. **Children with Crohn's disease who are less than 15 years of age.**
3. **Osteoarthritis**
4. **Ulcerative colitis**
6. **Intra-articular injection.**
7. **Recurrent spontaneous pregnancy loss (RSPL)**
8. **In vitro fertilization (IVF)**
9. **Other indications.**

DOSING: ADULTS — Rheumatoid arthritis: SubQ: 40 mg every other week; may be administered with other DMARDs; patients not taking methotrexate may increase dose to 40 mg/weekly

ADMINISTRATION — For SubQ injection; rotate injection sites. Do not use if solution is discolored. Do not administer to skin which is red, tender, bruised, or hard.

CONTRAINDICATIONS — Hypersensitivity to adalimumab or any component of the formulation

WARNINGS / PRECAUTIONS — Tuberculosis (disseminated or extrapulmonary) has been reactivated while on adalimumab. Most cases have been reported within the first 8 months of treatment. Patients should be evaluated for latent tuberculosis infection with a tuberculin skin test prior to therapy. Treatment of latent tuberculosis should be initiated before adalimumab is used. Use caution with chronic infection, history of recurrent infection, or predisposition to infection. Do not give to patients with a clinically-important, active infection. Adalimumab may affect defenses against infections and malignancies; serious infections (including sepsis and fatal infections) have been reported in patients receiving TNF-blocking agents, including adalimumab. Many of the serious infections have occurred in patients on concomitant immunosuppressive therapy. Other opportunistic infections (Histoplasma, Aspergillus, and Nocardia) have occurred during therapy. Use caution in patients who have resided in regions where histoplasmosis is endemic. Patients who develop a new infection while undergoing treatment with adalimumab should be monitored closely. If a patient develops a serious infection or sepsis, adalimumab should be discontinued. Impact on the development and course of malignancies is not fully defined. Rare cases of lymphoma have also been reported in association with adalimumab.

May exacerbate pre-existing or recent-onset demyelinating CNS disorders. Use caution in patients with CHF. Patients should be brought up to date with all immunizations before initiating therapy. No data are available concerning the effects of adalimumab on vaccination. Live vaccines should not be given concurrently. No data are available concerning secondary transmission of live vaccines in patients receiving adalimumab. Rare cases of pancytopenia (including aplastic anemia) have been reported with TNF-blocking agents; with significant hematologic abnormalities, consider discontinuing therapy. Safety and efficacy have not been established in pediatric patients.

DRUG INTERACTIONS

Anakinra: Concomitant use may increase risk of infections; not recommended.

Vaccines, live: Concomitant use has not been studied; currently recommended not to administer live vaccines during adalimumab therapy.

PREGNANCY RISK FACTOR — B

PREGNANCY IMPLICATIONS — Teratogenic effects were not observed in animal studies, however, there are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if clearly needed. A pregnancy registry has been established to monitor outcomes of women exposed to adalimumab during pregnancy (877-311-8972).

LACTATION — Excretion in breast milk unknown/not recommended

PATIENT EDUCATION — This medication may be administered by SubQ injection only. May cause headache, nausea, or stomach pain. Notify prescriber of any signs of infection.

REFERENCES

1. Humira injection [package insert]. North Chicago, IL: Abbott Laboratories; March 2011

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