

**adalimumab (Humira<sup>®</sup>)**

To initiate a coverage review, call 1 800 753-2851

Covered Medication
➤ Adalimumab injection (Humira <sup>®</sup> )

What it does and how it is used
<ul style="list-style-type: none"> <li>➤ Humira<sup>®</sup> is a biological agent that is used to treat plaque psoriasis, rheumatoid arthritis (RA), juvenile idiopathic arthritis (JRA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and Crohn's disease (CD).</li> <li>➤ Humira<sup>®</sup> is one of the biologics that inhibits tumor necrosis factor (TNF) activity, as does Enbrel<sup>®</sup> and Remicade<sup>®</sup>. Humira<sup>®</sup> is a monoclonal antibody that works by blocking the actions TNF-alpha at receptors located in body tissues.</li> <li>➤ <b>Plaque psoriasis</b> is a chronic skin disorder characterized by red, scaly, raised lesions that tend to form on the scalp, limbs, back, and genitalia. Symptoms of moderate to severe psoriasis include scaling, itching, redness, and tightness of the skin with burning sensations. Exposed skin, especially cracked or bleeding areas, can act as potential sites of infection.</li> <li>➤ Psoriasis is equally common in men and women, and has a bimodal peak of onset. The largest peak occurs between 20 and 30 years of age, and a smaller peak is noticed between 50 and 60 years of age.</li> <li>➤ Psoriasis is recognized as an immune system mediated disease. Plaques consist primarily of T cells, which are responsible for starting the changes seen in psoriasis and the maintenance of skin plaques. Plaques also contain a high level of tumor necrosis factor (TNF). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses.</li> <li>➤ Initial treatment for stable plaque psoriasis is topical, including corticosteroids, emollients, anthralin, tar, retinoids, calcipotriene (Vitamin D analogue), and salicylic acid. Though corticosteroids are the mainstay of topical therapy, continuous use of these agents can cause tachyphylaxis (wearing off effect) and several side effects. Other treatments for plaque psoriasis include phototherapy, immunosuppressants, and systemic retinoids.</li> <li>➤ Biological treatments such as Amevive<sup>®</sup>, Raptiva<sup>®</sup>, Enbrel<sup>®</sup>, Humira<sup>®</sup>, and Remicade<sup>®</sup> are usually used after conventional treatments fail to provide benefit or when a patient is not able to receive conventional therapy (drug and phototherapy).</li> <li>➤ <b>Rheumatoid arthritis (RA)</b> is a progressive chronic inflammatory disease that primarily affects large and small joints. The disease is characterized by joint deformities of the hands, wrists, neck, jaw, elbows, feet, and ankles. In addition to pain, patients can experience neuropathy (numbness or loss of feeling in hands or feet). Other conditions associated with RA include cardiac abnormalities, pulmonary fibrosis, and corneal defects. RA is associated with a significant amount of morbidity, which can lead to a higher risk of mortality.</li> <li>➤ When arthritis occurs in children, it is referred to as <b>juvenile idiopathic arthritis (JIA)</b>, or <b>juvenile rheumatoid arthritis (JRA)</b>. Some children will "outgrow" their condition, while others may continue to have arthritis symptoms into adulthood.</li> <li>➤ In addition to the joint pain and inflammation that adults with RA experience, JIA is associated with medical conditions such as inflammation of the inner parts of the eye (known as uveitis) that may persist independent of arthritis symptoms. If untreated, uveitis can lead to glaucoma, cataracts, and permanent vision damage so patients must see ophthalmologists regularly.</li> <li>➤ RA treatment is aggressive soon after diagnosis with the goal of treatment being to eliminate synovitis (joint swelling) and joint destruction. Joint erosion is due to the presence of inflammatory mediators which cause joint and cartilage destruction. These damaging substances include; prostaglandins, cytokines, and tumor necrosis factor.</li> <li>➤ Initial treatment in the mild stages can include NSAIDs and then usually a conventional disease modifying antirheumatic drug (DMARD). DMARDs decrease pain, slow disease progression, and retard development of joint erosions.</li> <li>➤ Methotrexate is the most commonly used DMARD. It may be used alone or with a biologic agent (e.g., Enbrel<sup>®</sup>, Remicade<sup>®</sup>, Kineret<sup>®</sup> or Humira<sup>®</sup>). Humira<sup>®</sup> is indicated for reducing signs and symptoms and inhibiting the progression of structural damage in adult patients with <i>moderately to severely active</i> RA.</li> <li>➤ Initial treatment with Humira<sup>®</sup> plus methotrexate has been shown to be more effective in treating RA than either agent alone.</li> <li>➤ <b>Psoriatic arthritis (PsA)</b> is a chronic inflammatory joint disease that is associated with psoriasis. In approximately 70% of patients, psoriasis alone precedes the onset of PsA by an average of ten years. However, the onset of the skin condition and arthropathy can occur simultaneously in 11% to 15% of patients.</li> <li>➤ Humira<sup>®</sup> is also indicated for reducing signs and symptoms in patients with active <b>ankylosing spondylitis (AS)</b>: a chronic, slowly progressive disease characterized by mild or moderate inflammation of the sacroiliac, intervertebral, and costovertebral joints within the spine alternating with periods of almost no symptoms. <i>Ankylos</i> in Greek means bent or crooked and <i>spondylos</i> means vertebrae. AS primarily affects the spine or back causing pain and stiffness and in severe cases can result in fusing of the spine leading to a forward-stooped position. AS can damage other</li> </ul>

- joints in the hips, shoulders, ribs, and heels along with other parts in the body such as the heart, lungs, and eyes.
- Though some NSAIDs have the labeled indication for AS, they only provide modest anti-inflammatory analgesic effects for symptoms. Humira® improves several disease parameters, such as pain, inflammation, disease activity, function, and global assessment. These criteria are known as ASAS Ankylosing Spondylitis Assessment criteria, and Humira® can provide from 20%, to 50% or even 70% improvement in patients beginning at week 12 and sustain improvement up to week 52. The FDA agreed upon this criteria for assessing efficacy of drugs for AS. NSAIDs were not previously reviewed using the ASAS criteria.
  - In situations where patients have not responded to traditional therapies such as NSAIDs, glucocorticoids, salicylates, analgesics, or methotrexate, Humira® may be used alone or in combination with these therapies for the treatment of ankylosing spondylitis. Traditional DMARDs used for RA are ineffective for this condition.
  - Humira® is also indicated for the induction and maintenance of remission in patients with moderate to severe **Crohn's disease**: a chronic, episodic inflammatory condition of the gastrointestinal (GI) tract, which mostly occurs in persons between the age of 15 and 35, and often presents with cramp-like pain in the lower right abdomen, diarrhea, rectal bleeding and weight loss.
  - Currently there is no cure Crohn's disease, however, symptomatic treatment often includes aminosaliclates (5-ASAs), corticosteroids (prednisone and methylprednisolone), immunomodulators (azathioprine or 6-mercaptopurine), biologic agents (Humira®), and antibiotics to help control inflammation and heal fistulas.

#### Rationale for coverage authorization

To reduce the cost associated with using Humira® in situations where the use of other DMARDs such as methotrexate is warranted and to provide coverage for usual doses of Humira® (40 mg every other week).

#### Benefit design:

- Coverage for Humira® is determined through prior authorization for every claim a coverage authorization process in accord with the criteria listed below.

#### Coverage authorization criteria

Coverage is provided for Humira® for 5 years for a quantity not to exceed two 40-mg doses per month for the treatment of psoriatic arthritis OR moderate to severe rheumatoid arthritis in the following situations:

- the patient requires Humira® treatment for rapidly advancing, progressive disease OR
- the patient is using Humira® in combination with methotrexate as first line treatment OR
- the patient has experienced a therapeutic failure with methotrexate or has had an inadequate response to methotrexate OR the patient is unable to receive methotrexate

Coverage is provided for up to four 40-mg doses per month in the following situations:

- the patient has experienced an inadequate response to twice monthly dosing of Humira®

Coverage is provided for Humira® for 5 years for a quantity not to exceed two 40-mg doses per month for the treatment of:

- Juvenile idiopathic arthritis (JIA)/ juvenile rheumatoid arthritis (JRA)

Coverage is provided for Humira® for 5 years for a quantity not to exceed two 40-mg doses per month to treat AS in the following situations:

- the patient has experienced inadequate symptom relief from at least two NSAIDs or COX-2 inhibitors, unless the patient is unable to receive treatment with these drugs.

Coverage is provided for Humira® for 5 years for a quantity sufficient for 280 mg for the first month and 80 mg per month thereafter [accommodates for a 160-mg loading dose on day 1 then 80 mg two weeks after followed by 40 mg every other week] to treat Crohn's disease in the following situations:

- For the induction and maintenance of remission in patients with moderate to severe Crohn's disease

Coverage is provided for Humira® for 5 years for a quantity sufficient for 160 mg for the first month and 80 mg per month thereafter [accommodates for an 80-mg loading dose on day 1 then 40 mg one week later followed by 40 mg every other week] to treat plaque psoriasis in the following situations:

- For the treatment of moderate to severe plaque psoriasis

Coverage is not provided unless the patient has been evaluated for the presence of latent TB infection.

Coverage is not provided for use of Humira® in combination with other biologics e.g., Kineret®, Enbrel®, Remicade®, Rituxan®.

#### References

- Braun, J., Pham, T., Sieper, J., et al. for the ASAS working group. International ASAS consensus statement for the use of anti-tumour necrosis factor agents in patients with ankylosing spondylitis, *Ann Rheum Dis*; May 2003. 62:817–824.
- Colombel J, Sandborn WS, Rutgeerts P, Enns R, Hanauer SB, Panaccione R et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: The CHARM Trial. *Gastroenterology*. 2007 Jan; 132:52-65
- Hanauer SB, Sandborn WJ, Rutgeerts P, Fedorak RN, Lukas M, Macintosh D, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I Trial. *Gastroenterology*. 2006 Feb; 130:323–333.

- Humira® (adalimumab). Prescribing information. North Chicago: Abbott Laboratories, January 2008.
- Nlm.nih.gov [Homepage on the Internet]. Bethesda, MD. A service of the U.S. National Library of Medicine and National Institutes of Health [Updated March 6, 2007; accessed August 13, 2007] Available from:  
<http://www.nlm.nih.gov/medlineplus/ency/article/000249.htm#Causes,%20incidence,%20and%20risk%20factors>
- Spondylitis Association of America. Guidelines for the use of anti-TNF therapy in patients with ankylosing spondylitis: breakdown of criteria. November 2003. Available at <http://www.spondylitis.org/MedicalResearch/spartanguideline.aspx>\_Accessed October 12, 2006.
- Weinblatt, M., Keystone, E., Furst, D., et al. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate. *Arthritis & Rheumatism*. Jan 2003; 48:35-45. Jan 2003.