

## **ABBOTT'S HUMIRA<sup>®</sup> (ADALIMUMAB) RECEIVES FDA APPROVAL FOR TREATMENT OF ANKYLOSING SPONDYLITIS**

- *HUMIRA Now Approved to Treat Three Forms of Inflammatory Arthritis; Being Studied for Three Other Autoimmune Diseases* –

ABBOTT PARK, Ill., July 31, 2006 – Abbott announced today that the U.S. Food and Drug Administration (FDA) approved HUMIRA<sup>®</sup> (adalimumab) for reducing signs and symptoms in patients with active ankylosing spondylitis (AS). AS is an autoimmune disease affecting the spine and large peripheral joints that causes inflammatory back pain and stiffness and also can be associated with other inflammatory diseases of the skin, eyes and intestines. In its severe form, AS over time can result in complete spinal fusion, causing extreme physical limitation and reduction in health-related quality of life.

AS is the third of six autoimmune diseases targeted for HUMIRA therapy that has received FDA approval. HUMIRA also is approved by the FDA to treat rheumatoid arthritis (RA) and psoriatic arthritis (PsA) and clinical trials are currently under way evaluating the potential of HUMIRA in other autoimmune diseases. HUMIRA received European approval to treat patients with severe, active AS on June 1, 2006.

"Medications like HUMIRA represent another option in the way we treat ankylosing spondylitis, a painful and potentially disabling disease that tends to strike mostly young adults," said Jane Bruckel, BSN, RN, Spondylitis Association of America co-founder and executive director.

AS affects young adults and commonly develops during the second and third decades of life. Because the pain and stiffness of AS are hard to distinguish from other

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common causes of back pain, patients may go undiagnosed for many years from the onset of their symptoms. AS is one of the most overlooked causes of persistent back pain in young adults.

The recommended dose of HUMIRA for AS is 40 mg every other week, by subcutaneous injection (a shot beneath the skin), the usual dose recommended for HUMIRA in the treatment of moderate to severe RA and PsA. HUMIRA is available to patients with AS in the United States in a pre-filled syringe. Beginning in August, patients will be able to take advantage of the HUMIRA Pen, a new delivery device for the self-administration of HUMIRA. Approved by the FDA on June 23, 2006, the HUMIRA Pen offers improved ease of use and a less painful experience compared to the HUMIRA pre-filled syringe.

**Clinical Trial Results**

The approval of HUMIRA for the treatment of patients with active AS is based on data from the ATLAS (Adalimumab Trial Evaluating Long-Term Efficacy and Safety in AS) trial.

ATLAS was a randomized, placebo-controlled, double-blind, Phase III study conducted in Europe and the United States. Results showed that HUMIRA was successful in reducing pain and inflammation in patients with AS after 12 weeks of treatment, the study's primary endpoint. Other findings demonstrated significant improvement in measures of disease activity for many patients treated with HUMIRA that were first observed at week two and maintained through 24 weeks.

ATLAS also explored the impact of HUMIRA on enthesitis, a condition in AS characterized by inflammation of the ligaments that attach to the bone. At week 24, the

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mean change in the enthesitis symptom score as measured by Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) in patients treated with HUMIRA showed significant reduction. MASES is an index that assesses enthesitis in certain locations, such as the rib cage, lower back, and Achilles tendons.

"The approval of HUMIRA in the treatment of ankylosing spondylitis marks an important milestone for Abbott," said Rebecca Hoffman, M.D., divisional vice president, Immunology Development, Abbott. "HUMIRA is now approved to treat three forms of autoimmune rheumatic diseases – all of them chronic, progressive, debilitating diseases where patients have limited treatment options. With its proven efficacy and established safety profile and the convenience of every other week self-administered dosing, HUMIRA offers an outstanding treatment option for the diverse patient populations who suffer from these conditions."

In the ATLAS trial, a similar rate of treatment-emergent adverse events leading to discontinuation of study drug was observed among placebo-treated (1.9 percent) and HUMIRA-treated (1.4 percent) patients. The overall incidence of adverse events reported by patients treated with HUMIRA was higher than the placebo-treated patients. The most common adverse events included nasopharyngitis, injection site reactions and headache.

**About Ankylosing Spondylitis**

Ankylosing spondylitis, or arthritis of the spine, is an autoimmune disorder in which a human protein, tumor necrosis factor-alpha, has been suggested to play a role in the disease development. AS is a form of arthritis known as spondyloarthritis, which is a group of closely linked rheumatic diseases that can cause pain in the spine and joints

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as well as ligaments and tendons. A chronic disease, AS primarily affects the spine causing back stiffness and potential deformity over time.

AS is associated with a number of other conditions including peripheral arthritis and enthesitis (inflammation of the muscle-bone insertion). Other associated affected organ systems may include the eyes, intestines and skin.

**Important Safety Information**

Cases of tuberculosis (TB) have been observed in patients receiving HUMIRA. Serious infections and sepsis, including fatalities, have been reported with the use of TNF-blocking agents, including HUMIRA. Many of these infections occurred in patients also taking other immunosuppressive agents that in addition to their underlying disease could predispose them to infections. Treatment with HUMIRA should not be initiated in patients with active infections. TNF-blocking agents, including HUMIRA, have been associated with reactivation of hepatitis B (HBV) in patients who are chronic carriers of this virus. Some cases have been fatal. Patients at risk for HBV infections should be evaluated for prior evidence of HBV infections before initiating HUMIRA. The combination of HUMIRA and anakinra is not recommended.

TNF-blocking agents, including HUMIRA, have been associated in rare cases with demyelinating disease and severe allergic reactions. Infrequent reports of serious blood disorders have been reported with TNF-blocking agents. More cases of malignancies have been observed among patients receiving TNF blockers, including HUMIRA, compared to control patients in clinical trials. These malignancies, other than lymphoma and non-melanoma skin cancer, were similar in type and number to what would be expected in the general population. There was an approximately four-fold higher rate of lymphoma in combined controlled and uncontrolled open label

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portions of HUMIRA clinical trials. The potential role of TNF-blocking therapy in the development of malignancies is not known.

The most frequent adverse events seen in the placebo-controlled clinical trials in rheumatoid arthritis (HUMIRA vs. placebo) were injection site reactions (20 percent vs. 14 percent), upper respiratory infection (17 percent vs. 13 percent), injection site pain (12 percent vs. 12 percent), headache (12 percent vs. 8 percent), rash (12 percent vs. 6 percent) and sinusitis (11 percent vs. 9 percent). Discontinuations due to adverse events were 7 percent for HUMIRA and 4 percent for placebo. As with any treatment program, the benefits and risks of HUMIRA should be carefully considered before initiating therapy.

In HUMIRA clinical trials for ankylosing spondylitis and psoriatic arthritis, the safety profile for patients treated with HUMIRA was similar to the safety profile seen in patients with rheumatoid arthritis.

**About HUMIRA**

HUMIRA is the only fully human monoclonal antibody approved by the FDA for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. HUMIRA can be used alone or in combination with methotrexate or other disease-modifying anti-rheumatic drugs (DMARDs).

HUMIRA is indicated for reducing the signs and symptoms of active arthritis in patients with psoriatic arthritis. HUMIRA can be used alone or in combination with DMARDs.

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HUMIRA is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

**Abbott's Commitment to Immunology**

Abbott is focused on the discovery and development of innovative treatments for immunologic diseases. The Abbott Bioresearch Center, founded in 1989 in Worcester, Mass., United States, is a world-class discovery and basic research facility committed to finding new treatments for autoimmune diseases. More information about HUMIRA, including full prescribing information, is available on the Web site [www.rxabbott.com](http://www.rxabbott.com) or in the United States by calling Abbott Medical Information at 1-800-633-9110.

**About Abbott**

Abbott is a global, broad-based health care company devoted to the discovery, development, manufacture and marketing of pharmaceuticals and medical products, including nutritionals, devices and diagnostics. The company employs 65,000 people and markets its products in more than 130 countries.

Abbott's news releases and other information are available on the company's Web site at [www.abbott.com](http://www.abbott.com).