



Centocor Files for First-Line Use of REMICADE(R) Regimen in Patients With Early Rheumatoid Arthritis

Filing Based on Early RA Study, Which Showed REMICADE Plus Methotrexate Superior to Current Standard of Care

MALVERN, Pa., Apr 6, 2004 /PRNewswire-FirstCall via COMTEX/ -- Centocor, Inc., announced today that the U.S. Food and Drug Administration (FDA) has accepted its filing of a supplemental Biologics License Application (sBLA) for REMICADE(R) (infliximab) as first-line therapy, in combination with methotrexate, for the treatment of early rheumatoid arthritis (RA) patients with moderately-to- severely active disease. REMICADE, in combination with methotrexate, is currently indicated in the U.S. for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately-to-severely active RA who have had an inadequate response to methotrexate alone.

REMICADE is the global market leader among anti-tumor necrosis factor alpha (TNF-alpha) therapies, the only agent approved for the treatment of both RA and Crohn's disease in North America, the European Union and Japan, and was the first biologic approved for ankylosing spondylitis (AS) in the European Union.

The submission is based on the results of the ASPIRE (Active Controlled Study of Patients Receiving Infliximab for Treatment of Rheumatoid Arthritis of Early Onset) trial. In this trial, REMICADE plus methotrexate was superior to the gold standard of methotrexate alone in the treatment of early RA patients who were methotrexate-naive. REMICADE plus methotrexate was superior to methotrexate alone in inhibiting the progression of structural damage, preventing bone erosions, improving physical function and improving clinical symptoms. To date, no anti-TNF monotherapy or combination strategy has been proven superior to methotrexate alone in a clinical study comprised exclusively of early RA patients.

"Increasingly, clinical evidence supports that earlier therapy for RA may enhance patient benefit. This submission for REMICADE represents Centocor's continued leadership and commitment to advancing research that we believe may ultimately provide meaningful benefit to patients with early RA," said Jerome A. Boscia, M.D., senior vice president, Clinical R&D, Centocor, Inc.

About Early Rheumatoid Arthritis

RA is a chronic, progressive disease and research demonstrates that a critical therapeutic window exists within the first two years of disease onset when the rate of radiographic progression of the disease can be "reset"(1,2,3). Radiographic changes occur within two years of disease onset in 50-70 percent of RA patients(4). The American College of Rheumatology (ACR) suggests control of disease progression should start early to limit joint damage in RA(3). RA is associated with substantial disability and economic losses, and one study showed that one-third of patients in the UK who were employed became work-disabled within two years of disease onset(5). Rheumatologic disorders also account for 25 percent of Social Security disability payments(6).

About ASPIRE

ASPIRE was a 54-week, randomized, double blind, active control study involving 1,049 patients with early RA (less than or equal to 3 years duration) enrolled in 125 centers in North America and Europe evaluating the efficacy and safety of REMICADE in combination with methotrexate compared to methotrexate alone. Patients in the ASPIRE study had an average of only seven months of disease duration and more than 80 percent already had evidence of erosive joint destruction. At randomization, all patients received methotrexate and either placebo, 3mg/kg of REMICADE or 6mg/kg of REMICADE at weeks 0, 2 and 6 and then every eight weeks thereafter. The ASPIRE trial had three co-primary endpoints at week 54: improvement of signs and symptoms, progression of structural damage and improvement in physical function. All three primary endpoints were met, with the REMICADE regimen being superior to methotrexate alone on all primary and major secondary endpoints.

The most commonly reported adverse events were upper respiratory infection, nausea and headache. Serious adverse events reported were similar to those observed in controlled clinical trials and clinical experience with REMICADE as described in the prescribing information. (See "Important Information" below.)

Important Information

Many people with heart failure should not take REMICADE; so, prior to treatment, patients should discuss any heart condition with their doctor. Patients should tell their doctor right away if they develop new or worsening symptoms of heart failure (such

as shortness of breath or swelling of their feet).

There are reports of serious infections, including tuberculosis (TB) and sepsis. Some of these infections have been fatal. Patients should tell their doctor if they have had recent or past exposure to people with TB. Their doctor will evaluate them for TB and perform a skin test. If a patient has latent (inactive) TB, his or her doctor should begin TB treatment before starting REMICADE. If a patient is prone to or has a history of infections, currently has one, or develops one while taking REMICADE, he or she should tell his or her doctor right away. Patients should also tell their doctor if they have lived in a region where histoplasmosis or coccidioidomycosis is common, or if they have or have had a disease that affects the nervous system, or if they experience any numbness, tingling or visual disturbances.

There are also reports of serious infusion reactions with hives, difficulty breathing and low blood pressure. In clinical studies, some people experienced the following common side effects: upper respiratory infections, headache, nausea, cough, sinusitis or mild reactions to the infusion, such as rash or itchy skin. Please read important information about REMICADE, including full prescribing information, at www.remicade.com.

About REMICADE

REMICADE is a monoclonal antibody that specifically targets and irreversibly binds to tumor necrosis factor-alpha (TNF-alpha) on the cell membrane and in the blood. Overproduction of TNF-alpha is believed to play a role in RA, ankylosing spondylitis and Crohn's disease (CD), a serious gastrointestinal disorder, in addition to a wide range of Immune-Mediated Inflammatory Disorders (I.M.I.D.) in which REMICADE is currently being studied.

REMICADE is the only anti-TNF biologic therapy that has received marketing authorizations for the treatment of both RA and CD and, in the European Union, ankylosing spondylitis. In most countries, REMICADE, in combination with methotrexate, is indicated for the treatment of patients with moderately-to- severely active rheumatoid arthritis who have had an inadequate response to methotrexate alone. REMICADE is the only biologic indicated for the treatment of patients with moderately-to- severely active Crohn's disease who have had an inadequate response to conventional therapy. REMICADE is also indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in patients with fistulizing Crohn's disease.

REMICADE is unique among available anti-TNF biologic therapies. Unlike self-administered therapies that require patients to inject themselves frequently, REMICADE is the only anti-TNF biologic administered directly by caregivers in the clinic or office setting. In RA and CD patients, REMICADE is administered every eight weeks, following a standard induction regimen that requires treatment at weeks 0, 2 and 6. As a result, REMICADE patients may require as few as six treatments each year. The safety and efficacy of REMICADE have been well established in clinical trials conducted over the past 10 years and through commercial experience with more than 400,000 patients treated worldwide(7).

Centocor discovered REMICADE and has exclusive marketing rights to the product in the United States. Schering-Plough Corporation has rights to market REMICADE in all countries outside of the United States, except in Japan and parts of the Far East where Tanabe Seiyaku, Ltd. markets the product.

Centocor is a leading biopharmaceutical company that creates, acquires and markets cost-effective therapies that yield long-term benefits for patients and the healthcare community. The company is dedicated to the research and development of treatments for a wide range of diseases including cancer, infectious diseases, cardiovascular and metabolic diseases and Immune-Mediated Inflammatory Disorders (I.M.I.D.), such as arthritis and inflammatory skin diseases. Centocor's products, developed primarily through monoclonal antibody technology, help physicians deliver innovative treatments to improve human health and restore patients' quality of life. Centocor is a wholly owned subsidiary of Johnson & Johnson (NYSE: JNJ), the worldwide manufacturer of healthcare products.

References:

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(6) Social Security Disability Insurance Program.

(7) Data on file at Centocor

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