



# News Release

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## FDA APPROVES REMICADE<sup>®</sup> FOR NINTH INDICATION: PSORIATIC ARTHRITIS

*Latest Approval Demonstrates Significant Reduction in Arthritis and Psoriasis Symptoms as Early as Week Two*

**MALVERN, PA, May 17, 2005** – Centocor, Inc. announced today that the U.S. Food and Drug Administration (FDA) has approved REMICADE<sup>®</sup> (infliximab) to reduce the signs and symptoms of active arthritis in patients with psoriatic arthritis. An immune-mediated inflammatory disease, psoriatic arthritis affects approximately one million men and women in the U.S.<sup>1</sup> and is often characterized by the complex symptoms of joint inflammation (arthritis) and skin lesions (psoriasis)<sup>2</sup>. This marks the ninth time the FDA has approved a new indication for REMICADE, which has now achieved approvals in the treatment of such inflammatory diseases as Crohn's disease, rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. First approved in 1998 for Crohn's disease, REMICADE has been used to treat over a half a million patients worldwide.

"The approval of REMICADE is a promising development in the treatment of psoriatic arthritis," said Arthur Kavanaugh, MD, Professor of Medicine at University of California at San Diego. "Study results show that patients treated with REMICADE rapidly achieved profound improvement in arthritis symptoms and dramatically improved clearance in skin disease."

Data from the Induction and Maintenance of Psoriatic Arthritis Clinical Trial 2 (IMPACT 2) served as the primary basis for the approval. Significant improvements in both ACR 20 and PASI 75 were observed in REMICADE-treated patients as early as week 2, with further improvements through 24 weeks. At week 14, 58 percent of REMICADE-treated patients experienced at least 20 percent improvement in arthritis symptoms, according to the American College of Rheumatology scoring criteria (ACR 20) vs. 11 percent of placebo-treated patients ( $P < 0.001$ ). At week 24, 27 percent of REMICADE-treated patients experienced at least 70 percent improvement (ACR 70) vs. 2 percent of placebo-treated patients ( $P < 0.001$ ). Additionally, at week 24, 60 percent of REMICADE-treated patients experienced at least 75 percent improvement from baseline in psoriasis, as assessed by Psoriasis Area Severity Index (PASI 75) vs. 1 percent of placebo-treated patients. At week 24, more than one-third (39 percent) of patients receiving REMICADE achieved PASI 90, a dramatic improvement in psoriasis symptoms. No patients receiving placebo achieved a PASI 90 response at week 24.

Importantly, patients in the REMICADE group also experienced decreased symptoms of dactylitis and enthesopathy, two common disease manifestations causing pain and swelling. Dactylitis, swelling of digits in the hands or feet, and enthesopathy, inflammation of a tendon, or ligament insertion to the bone, are estimated to affect more than one-third of people with psoriatic arthritis. In the study, 40 percent of REMICADE patients and 41 percent of patients in the placebo group had dactylitis in at least one digit at baseline. After 24 weeks of treatment, only 15 percent of

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REMICADE patients continued to experience symptoms, compared to 33 percent of patients receiving placebo ( $P < 0.05$ ). At baseline, enthesopathy was observed in 42 percent of patients in the REMICADE group and 35 percent of patients receiving placebo. At week 24, only 22 percent of REMICADE patients still experienced enthesopathy, compared to 36 percent in the placebo group ( $P = 0.004$ )<sup>3</sup>.

According to 2004 National Psoriasis Foundation surveys of more than 1000 people with psoriasis and psoriatic arthritis, approximately 85 percent of psoriatic arthritis patients reported their condition to be a problem in their everyday lives<sup>4,5</sup>. Additionally, less than 20 percent of patients with psoriatic arthritis reported high satisfaction with their treatments<sup>5b, 6b</sup>.

"Our surveys show that patients have consistently noted the negative physical and emotional impact that psoriatic arthritis can have on their quality of life," said Gail Zimmerman, President and CEO, National Psoriasis Foundation. "The approval of REMICADE is important because of the renewed hope that this therapy may offer for many people with psoriatic arthritis."

In September 2004, REMICADE was approved in the European Union (EU), in combination with methotrexate, for the treatment of active and progressive psoriatic arthritis in patients who have responded inadequately to disease-modifying anti-rheumatic drugs (DMARDs).

### **Study Results**

IMPACT 2 was a Phase III randomized, double-blind, placebo-controlled study of 200 patients with active psoriatic arthritis (defined as affecting at least five joints). The study evaluated the safety and efficacy of REMICADE in patients who had an inadequate response to DMARDs or nonsteroidal anti-inflammatory drugs (NSAIDs). Patients received REMICADE (5mg/kg) or placebo at weeks 0, 2, 6 and every 8 weeks until week 22. In patients with  $\geq 3$  percent body surface area (BSA) psoriasis involvement at baseline, psoriasis activity was assessed using PASI at baseline and weeks 2, 6, 14 and 24. Responses were achieved regardless of methotrexate use or level of joint involvement at baseline.

Patients treated with REMICADE also experienced significant improvement in the physical component summary (PCS) and mental component summary (MCS) scores of the short form 36 (SF-36). The SF-36 is a 36-item questionnaire that assesses impact in eight areas, including physical functioning, pain, vitality, social functioning, psychological functioning, general health perceptions and role limitations due to physical and emotional problems. SF-36 scores range from 0 to 100, and lower scores indicate poorer functioning and well-being. At week 14, REMICADE patients experienced an average increase in PCS score of 9.1 units, compared to an average 1.1-unit increase in patients receiving placebo ( $P < 0.001$ ). Additionally, patients in the REMICADE group experienced an average 3.8-unit increase in MCS score, while patients receiving placebo averaged a decrease of 1.2 units ( $P = 0.001$ ).

Through 24 weeks, a similar number of patients experienced adverse events (AE) in each treatment group. No deaths, cases of tuberculosis or other opportunistic infections, or serious infusion reactions were reported and serious infections were uncommon. Also, with the exception of one case of basal cell carcinoma in the placebo group, no malignancies were reported. Significant laboratory abnormalities were unusual, with an elevation in liver function tests being the most common abnormality<sup>3e</sup>. There were more patients with serious AEs in the REMICADE group (8.7 percent) than in the placebo group (6.2 percent)<sup>3f</sup>. See "Important Safety Information" below.

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### **About Psoriatic Arthritis**

Psoriatic arthritis involves joint pain and swelling that can lead to debilitation coupled with inflamed, scaly, red patches of psoriasis. Symptoms may include stiffness and tenderness of the joints and surrounding tissue, reduced range of motion, nail changes and redness and pain of the eye, or uveitis. Joints of the hands, wrists, knees, ankles, feet, lower back and neck are commonly affected. Approximately one million Americans have psoriatic arthritis, and the disease affects both men and women equally, most commonly between the ages 30 and 50.

### **About REMICADE**

REMICADE is the global market leader among anti-tumor necrosis factor alpha (TNF-alpha) therapies and the only agent approved for the treatment of both RA and Crohn's disease in North America, the EU and Japan. In the EU and in the US, REMICADE is approved for the treatment of active ankylosing spondylitis and psoriatic arthritis.

In the U.S., REMICADE, in combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA). REMICADE is the only biologic indicated for the treatment of patients with moderately-to-severely active Crohn's disease (CD) 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 CD. In December 2004, REMICADE was approved for the treatment of active ankylosing spondylitis in the US.

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, CD, and PsA, REMICADE is a two-hour infusion 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. In AS, REMICADE is a two-hour infusion (5 mg/kg) administered every 6 weeks, following a standard induction regimen that requires treatment at weeks 0, 2, and 6. The safety and efficacy of REMICADE have been well established in clinical trials over the past 12 years and through commercial experience with over a half a million patients treated worldwide.

### **Important Information for Patients**

Many people with heart failure should not take REMICADE; so prior to treatment you should discuss any heart condition with your doctor. Tell your doctor right away if you develop new or worsening symptoms of heart failure (such as shortness of breath or swelling of your ankles or feet).

There are reports of serious infections, including tuberculosis (TB), sepsis and pneumonia. Some of these infections have been fatal. Tell your doctor if you have had recent or past exposure to people with TB. Your doctor will evaluate you for TB and perform a skin test. If you have latent (inactive) TB, your doctor should begin TB treatment before you start REMICADE. REMICADE can lower your ability to fight infections, so if you are prone to or have a history of infections, or develop any signs of an infection such as fever, fatigue, cough, or the flu while taking REMICADE, tell your doctor right away. Also tell your doctor if you have lived in a region where histoplasmosis or coccidioidomycosis is common.

There have been rare cases where people taking REMICADE have developed severe liver problems. Signs that you could be having a problem include: jaundice (skin and eyes turning yellow), dark brown-colored urine, right-sided abdominal pain, fever, and severe fatigue (tiredness). You should contact your doctor immediately if you develop any of these symptoms. Blood disorders

have been reported, some fatal. Tell your doctor if you develop possible signs of blood disorders such as persistent fever, bruising, bleeding, or paleness while taking REMICADE. Nervous system disorders have also been reported. Tell your doctor if you have or have had a disease that affects the nervous system, or if you experience any numbness, weakness, tingling, or visual disturbances while taking REMICADE.

Reports of lymphoma (a type of cancer) in patients on REMICADE and other TNF blockers are rare but occur more often than in the general population. Tell your doctor if you have or have had cancer.

Serious infusion reactions have been reported with REMICADE, including hives, difficulty breathing, and low blood pressure. Reactions have occurred during or after infusions. In clinical studies, some people experienced the following common side effects: respiratory infections (that may include sinus infections and sore throat), coughing, and stomach pain or mild reactions to infusion such as rash or itchy skin. Please read important information about REMICADE, including full prescribing information, at [www.remicade.com](http://www.remicade.com).

### **About Centocor**

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, the worldwide manufacturer of healthcare products.

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.

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<sup>1</sup> National Institute of Arthritis and Musculoskeletal and Skin Disorders. Questions and Answers About Psoriasis. U.S. Department of Health and Human Services, National Institutes of Health; 2003. NIH Publication No. 03-5040.

<sup>2</sup> Mease, PJ, Recent advances in the management of psoriatic arthritis. *Curr Opin Rheumatol*. 2004;31:366-370.

<sup>3</sup> Kavanaugh A, Mease P, Beutler A, Antoni C. Efficacy of infliximab in psoriatic arthritis related dactylitis and enthesopathy: Results from the IMPACT 2 Trial. Centocor, data on file.

<sup>4</sup> National Psoriasis Foundation. Survey Panel Highlights. Fall 2004.

<sup>5</sup> National Psoriasis Foundation. Survey Panel Highlights. Spring 2004.