

Prior Authorization DRUG Guidelines

REMICADE® (infliximab)

Effective Date: 10/27/05

Date Developed: 9/1/05 by C. Wilhelmy MD

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Infliximab is an Antirheumatic, Disease Modifying Gastrointestinal Agent and Miscellaneous Monoclonal Antibody Tumor Necrosis Factor (TNF) Blocking Agent. It is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNF alpha), thereby interfering with endogenous TNF alpha activity. Biological activities of TNF alpha include the induction of proinflammatory cytokines (interleukins), enhancement of leukocyte migration, activation of neutrophils and eosinophils, and the induction of acute phase reactants and tissue degrading enzymes. Animal models have shown TNF alpha expression causes polyarthritis, and infliximab can prevent disease as well as allow diseased joints to heal.

Pre-Authorization Criteria:

FDA Approved Indications:

- **Rheumatoid Arthritis:** in combination with methotrexate for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis .
- **Crohn's disease:** for reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Remicade is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.
- **Ulcerative Colitis:** for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

- **Ankylosing Spondylitis:** for reducing signs and symptoms in patients with active ankylosing spondylitis.
- **Psoriatic Arthritis:** for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in patients with psoriatic arthritis.
- **Plaque Psoriasis:** for the treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. Remicade should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

VCHCP requires that infliximab be prescribed by a gastroenterologist or rheumatologist.

WARNINGS / PRECAUTIONS — Serious infections (including sepsis, pneumonia, and fatal infections) have been reported in patients receiving TNF-blocking agents. Many of the serious infections in patients treated with infliximab have occurred in patients on concomitant immunosuppressive therapy. Caution should be exercised when considering the use of infliximab in patients with a chronic infection or history of recurrent infection. Infliximab should not be given to patients with a clinically important, active infection. Patients who develop a new infection while undergoing treatment with infliximab should be monitored closely. If a patient develops a serious infection or sepsis, infliximab should be discontinued. Reactivation of hepatitis B has occurred in chronic virus carriers; evaluate prior to initiation and during treatment. Patients should be evaluated for latent tuberculosis infection with a tuberculin skin test prior to infliximab therapy. Treatment of latent tuberculosis should be initiated before infliximab is used. Tuberculosis (may be disseminated or extrapulmonary) has been reactivated in patients previously exposed to TB while on infliximab. Most cases have been reported within the first 3-6 months of treatment. Other opportunistic infections (eg, invasive fungal infections, listeriosis, Pneumocystis) have occurred during therapy. The risk/benefit ratio should be weighed in patients who have resided in regions where histoplasmosis is endemic.

Impact on the development and course of malignancies is not fully defined. As compared to the general population, an increased risk of lymphoma has been noted in clinical trials; however, rheumatoid arthritis has been previously associated with an increased rate of lymphoma.

Severe hepatic reactions have been reported during treatment. Use caution with CHF; if a decision is made to use with CHF, monitor closely and discontinue if exacerbated or new symptoms occur. Use caution with history of hematologic abnormalities; hematologic toxicities (eg, leukopenia, neutropenia, thrombocytopenia, pancytopenia) have been reported; discontinue if significant abnormalities occur. Autoimmune antibodies and a lupus-like syndrome have been reported. If antibodies to double-stranded DNA are confirmed in a patient with lupus-like symptoms, infliximab should be discontinued. Rare cases of demyelinating disease have been reported, use with caution in patients with pre-

existing or recent onset CNS demyelinating disorders, or seizures; discontinue if significant CNS adverse reactions develop.

Medications for the treatment of hypersensitivity reactions should be available for immediate use. Safety and efficacy for use in juvenile rheumatoid arthritis and in pediatric patients with Crohn's disease have not been established.

CONTRAINDICATIONS — Hypersensitivity to murine proteins or any component of the formulation; doses >5 mg/kg in patients with moderate or severe congestive heart failure (NYHA Class III/IV).

PREGNANCY RISK FACTOR — B

MONITORING PARAMETERS — Improvement of symptoms; signs of infection; LFTs (discontinue if >5 times ULN); place and read PPD before initiation.

REFERENCES

1. Centers for Disease, Control. Testing and Treatment of Latent Tuberculosis Infection. MMWR Recomm Rep 2000; 49(RR-6).
2. Chung, ES, Packer, M, Lo, KH, et al. Randomized, Double-Blind, Placebo-Controlled, Pilot Trial of Infliximab, a Chimeric Monoclonal Antibody to Tumor Necrosis Factor-Alpha, in Patients With Moderate-to-Severe Heart Failure: Results of the Anti-TNF Therapy Against Congestive Heart Failure (ATTACH) trial. Circulation 2003; 107:3133.
3. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Official Statement of the American Thoracic Society and the Centers for Disease Control and Prevention. Am J Respir Crit Care Med 2000; 161:1376.
4. Remicade [Prescribing Information]. Malvern, PA: Centocor, Inc.; April 2010.

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