Infliximab (Remicade) **Policy Number: M-0002**
Revision: 2 **Last Update: 6/4/2014**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

Coverage Guidelines:

FDA:

1. Ankylosing spondylitis
2. Psoriatic arthritis
3. Ulcerative colitis
4. Crohn's disease
5. Rheumatoid arthritis
6. Plaque psoriasis

Off Label:

1. Reactive arthritis
2. Inflammatory bowel disease arthritis
3. Autoimmune enteropathy

Coding Information:

HCPCS Code(s)

J1745	INJECTION INFLIXIMAB, 10 MG

ICD-9 Code(s)

555.0-555.2	REGIONAL ENTERITIS OF SMALL INTESTINE - REGIONAL ENTERITIS OF SMALL INTESTINE WITH LARGE INTESTINE
555.9	REGIONAL ENTERITIS OF UNSPECIFIED SITE
556.0-556.9	ULCERATIVE (CHRONIC) ENTEROCOLITIS - ULCERATIVE COLITIS UNSPECIFIED
565.1	ANAL FISTULA
569.81	FISTULA OF INTESTINE EXCLUDING RECTUM AND ANUS

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569.9	UNSPECIFIED DISORDER OF INTESTINE
619.1	DIGESTIVE-GENITAL TRACT FISTULA FEMALE
696.0	PSORIATIC ARTHROPATHY
696.1	OTHER PSORIASIS AND SIMILAR DISORDERS
711.10-711.49	ARTHROPATHY SITE UNSPECIFIED ASSOCIATED WITH REITER'S DISEASE AND NONSPECIFIC URETHRITIS - ARTHROPATHY INVOLVING MULTIPLE SITES ASSOCIATED WITH OTHER BACTERIAL DISEASES
713.1	ARTHROPATHY ASSOCIATED WITH GASTROINTESTINAL CONDITIONS OTHER THAN INFECTIONS
714.0	RHEUMATOID ARTHRITIS
714.1	FELTY'S SYNDROME
714.2	OTHER RHEUMATOID ARTHRITIS WITH VISCERAL OR SYSTEMIC INVOLVEMENT
714.30-714.33	CHRONIC OR UNSPECIFIED POLYARTICULAR JUVENILE RHEUMATOID ARTHRITIS - MONOARTICULAR JUVENILE RHEUMATOID ARTHRITIS
714.4	CHRONIC POSTRHEUMATIC ARTHROPATHY
714.81	RHEUMATOID LUNG
720.0	ANKYLOSING SPONDYLITIS
720.81	INFLAMMATORY SPONDYLOPATHIES IN DISEASES CLASSIFIED ELSEWHERE

Background:

Infliximab is a chimeric IgG1κ monoclonal antibody (composed of human constant and murine variable regions) specific for human tumor necrosis factor-alpha (TNFα). Infliximab neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors. Infliximab does not neutralize TNFβ (lymphotoxin-α), a related cytokine that utilizes the same receptors as TNFα. Biological activities attributed to TNFα include: induction of proinflammatory cytokines such as interleukins (IL) 1 and 6, enhancement of leukocyte migration by increasing endothelial layer permeability and expression of adhesion molecules by endothelial cells and leukocytes, activation of neutrophil and eosinophil functional activity, induction of acute phase reactants and other liver proteins, as well as tissue degrading enzymes produced by synoviocytes and/or chondrocytes. Cells expressing transmembrane TNFα bound by infliximab can be lysed *in vitro* or *in vivo*. Infliximab inhibits the functional activity of TNFα in a wide variety of *in vitro* bioassays utilizing human fibroblasts, endothelial cells, neutrophils, B and Tlymphocytes and epithelial cells. The relationship of these biological response markers to the mechanism(s) by which Remicade exerts its clinical effects is unknown.

Elevated concentrations of TNF-alpha have been found in the joints of rheumatoid arthritis (RA) patients and the stools of Crohn's disease patients, and correlate with elevated disease activity. In Crohn's

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disease, treatment with infliximab reduced infiltration of inflammatory cells and TNF alpha production in inflamed areas of the intestine, and reduced the proportion of mononuclear cells from the lamina propia able to express TNF alpha and interferon gamma. In RA, treatment with infliximab reduced infiltration of inflammatory cells into inflamed areas of the joint as well as expression of molecules mediating cellular adhesion, chemoattraction, and tissue degradation.

Definitions:

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

TNF—Tumor necrosis factor

FDA Black Box Warning:

WARNING: SERIOUS INFECTIONS and MALIGNANCY

SERIOUS INFECTIONS

Patients treated with REMICADE® are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. REMICADE should be discontinued if a patient develops a serious infection or sepsis.

Reported infections include:

• Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before REMICADE use and during therapy. Treatment for latent infection should be initiated prior to REMICADE use.

• Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.

• Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.

The risks and benefits of treatment with REMICADE should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with REMICADE, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including REMICADE.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including REMICADE. These cases have had a very aggressive disease course and have been fatal. All reported REMICADE cases have occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. All of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with REMICADE at or prior to diagnosis.

References:

1. Remicade [package insert]. Horsham, PA: Jannsen Biotech, Inc. October 2011. Available at: http://www.remicade.com/remicade/assets/hcp_ppi.pdf. Accessed May 21, 2012.
2. Local Coverage Determination (LCD) for Drugs and Biologicals: Infliximab (REMICADE®) (L30030) (Revision 6). Available at: http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=30030&ContrId=213&ver=23&ContrVer=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=Alabama&CptHcpcsCode=J1745&clickon=search&bc=gAAAABAAAAAA&. Accessed June 4, 2014.

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For the Archived Policy, please go to http://www.vivaprovider.com/Resources/CoveragePolicies.aspx and click on the Archived Policies Link.

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