

**infliximab (Remicade<sup>®</sup>)  
 To Initiate a Coverage Review, call 1 800 753-2851**

**Covered Medication**

- Infliximab injection (Remicade<sup>®</sup>)

**What it does and how it is used**

- Remicade<sup>®</sup> is a biological agent that is used to treat plaque psoriasis, rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), and Ulcerative Colitis (UC).
- Remicade<sup>®</sup> is one of the biologics that inhibits tumor necrosis factor (TNF) activity, as does Enbrel<sup>®</sup> and Humira<sup>®</sup>. Infliximab is a monoclonal antibody that works by blocking the actions TNF-alpha at its receptors.
- **Plaque psoriasis** is a chronic skin disorder characterized by red, scaly, raised lesions that tend to form on the scalp, limbs, back, and genitalia. Symptoms of moderate to severe psoriasis include scaling, itching, redness, and tightness of the skin with burning sensations. Exposed skin, especially cracked or bleeding areas, can act as potential sites of infection.
- Psoriasis is equally common in men and women, and has a bimodal peak of onset. The largest peak occurs between 20 and 30 years of age, and a smaller peak is noticed between 50 and 60 years of age.
- Psoriasis is recognized as an immune system mediated disease. Plaques consist primarily of T cells, which are responsible for starting the changes seen in psoriasis and the maintenance of skin plaques. Plaques also contain a high level of tumor necrosis factor (TNF). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses.
- Initial treatment for stable plaque psoriasis is topical, including corticosteroids, emollients, anthralin, tar, retinoids, calcipotriene (Vitamin D analogue), and salicylic acid. Though corticosteroids are the mainstay of topical therapy, continuous use of these agents can cause tachyphylaxis (wearing off effect) and several side effects. Other treatments for plaque psoriasis include phototherapy, immunosuppressants, and systemic retinoids.
- Infliximab may be used for severe plaque psoriasis (affecting 10% or more of the patient's body surface area) initially or when other systemic therapies are not an option.
- **Rheumatoid arthritis** is a progressive chronic inflammatory disease that primarily affects large and small joints. The disease is characterized by joint deformities of the hands, wrists, neck, jaw, elbows, feet, and ankles. Patients with RA are found to have elevated levels of TNF- $\alpha$  in the joints. Chronic joint inflammation eventually leads to tissue destruction, cellular damage to the bone along with edema (swelling), warmth, redness, joint stiffness and pain.
- Patients with RA may also experience fatigue, weakness, low-grade fever, and loss of appetite. Other conditions associated with RA include cardiac abnormalities, pulmonary fibrosis, and corneal defects.
- Infliximab, in combination with methotrexate, is indicated for reducing the 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.
- Patients with rapidly, advancing progressive RA may need to start treatment with infliximab as part of the initial treatment.
- **Psoriatic arthritis** (PsA) is a chronic inflammatory joint disease that is associated with psoriasis. In approximately 70% of patients, psoriasis alone precedes the onset of PsA by an average of ten years. However, the onset of the skin condition and arthropathy can occur simultaneously in 11% to 15% of patients.
- Infliximab is also indicated for reducing signs and symptoms in patients with active **ankylosing spondylitis** (AS): a chronic, slowly progressive disease characterized by mild or moderate inflammation of the sacroiliac, intervertebral, and costovertebral joints within the spine alternating with periods of almost no symptoms. *Ankylos* in Greek means bent or crooked and *spondylos* means vertebrae. AS primarily affects the spine or back causing pain and stiffness and in severe cases can result in fusing of the spine leading to a forward-stooped position. AS can damage other joints in the hips, shoulders, ribs, and heels along with other parts in the body such as the heart, lungs, and eyes.
- Though some NSAIDs have the labeled indication for AS, they only provide modest anti-inflammatory analgesic effects for symptoms. Infliximab has been studied in patients with active disease. The Bath Ankylosing Spondylitis Disease Index (BASDAI) and a Visual Analog Scale (VAS) used to assess spinal pain, are used to measure the effect of drugs on this disease. Infliximab has demonstrated the ability to improve several disease parameters such as pain, inflammation, disease activity, function, and patient global assessment of well-being as measured by the Ankylosing Spondylitis Assessment criteria (ASAS). Patients that receive Infliximab can achieve 20%, 50%, or 70% improvement in their AS symptoms. NSAIDs were not previously reviewed using the ASAS criteria. Traditional DMARDs used for RA are ineffective for this condition.
- In situations where patients have not responded to traditional therapies such as NSAIDs, glucocorticoids, salicylates, analgesics, or methotrexate, infliximab may be used alone or in combination with these therapies for the treatment of ankylosing spondylitis.
- Infliximab is also indicated for the induction and maintenance of remission in patients with moderate to severe

**Crohn's disease:** a chronic, episodic inflammatory condition of the gastrointestinal (GI) tract, which mostly occurs in persons between the age of 15 and 35, and often presents with cramp-like pain in the lower right abdomen, diarrhea, rectal bleeding and weight loss.

- Untreated, Crohn's disease can lead to small bowel stricture or obstruction requiring surgery. Fistulas may also occur as a consequence of CD in the areas of worst inflammation.
- Infliximab is also approved for reducing the number of draining enterocutaneous fistulas in patients with fistulizing CD. Fistulizing CD can connect one segment of the GI tract to skin, bladder, or another area of the GI tract and often necessitates surgical treatment.
- Currently there is no cure Crohn's disease, however, symptomatic treatment often includes aminosalicylates (5-ASAs), corticosteroids (prednisone and methylprednisolone), immunomodulators (azathioprine or 6-mercaptopurine), biologic agents (Humira<sup>®</sup>, Remicade<sup>®</sup>, and Tysabri<sup>®</sup>), and antibiotics to help control inflammation and heal fistulas.
- Patients with CD are found to have elevated levels of tumor necrosis factor alpha (TNF- $\alpha$ ) the substance that promotes damage to the GI tract. Consequently, patients may develop extensive intestinal wall injury leading to ulcers, bleeding, anemia, skin lesions, liver disease, and weight loss and growth failure due to nutritional deficiencies. Infliximab reduces inflammation of the intestine in CD.
- **Ulcerative colitis** is a chronic inflammation of the large intestine which produces open sores along the lining of the colon.
- Symptoms of ulcerative colitis include bloody diarrhea, abdominal pain and cramping and frequent/urgent bowel movements. The patient will experience symptoms in cycles of exacerbations and remissions.
- The cause of ulcerative colitis is unknown but it is thought to be related to environmental factors or due to a disorder of the immune system.
- Infliximab can reduce the signs and symptoms of ulcerative colitis, induce/maintain remission, and promote intestinal healing. Infliximab may also help to reduce or completely eliminate the need for steroid use in these patients.

#### Rationale for coverage authorization

To reduce exposure to cost associated with uncovered uses of Remicade<sup>®</sup> such as for the treatment of mild rheumatoid arthritis, mild Crohn's disease, mild psoriatic arthritis, or mild plaque psoriasis and for situations where the use of other therapies may be an option.

#### Benefit design

- Coverage for Remicade<sup>®</sup> is determined through prior authorization for every claim.

#### Coverage authorization criteria

This prescription benefit provides coverage in accord with the following criteria:

Coverage is provided for the treatment of the following:

1. Moderate to severely active rheumatoid arthritis or psoriatic arthritis
2. Rapidly advancing, progressive rheumatoid arthritis
3. Induction and maintenance treatment for moderate to severe Crohn's disease
4. Fistulizing Crohn's disease
5. Ankylosing spondylitis in situations where the patient has experienced inadequate symptom relief from other treatments such as NSAIDs or COX-2 inhibitors, or methotrexate unless the patient is unable to receive treatment with these drugs.
6. Severe plaque psoriasis affecting (affecting  $\geq$  10% of the patient's body surface area)
7. Mild ulcerative colitis in situations where the patient has had an inadequate response to conventional treatments (i.e. sulfasalazine, olsalazine, mesalamine, etc.)
8. Moderate to severe ulcerative colitis
9. Coverage is provided in situations where the patient has been evaluated and screened for the presence of latent TB infection prior to initiating treatment with Remicade<sup>®</sup>

Coverage duration: 5 years. Coverage may be renewed.

#### References

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- Spondylitis Association of America. Guidelines for the use of anti-TNF therapy in patients with ankylosing spondylitis: breakdown of criteria. November 2003. Available at <http://www.spondylitis.org/MedicalResearch/spartanguideline.aspx> Accessed October 12, 2006.