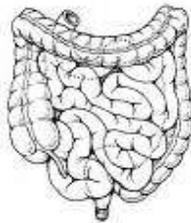


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## **SOME FACTS ABOUT BIOLOGIC THERAPY FOR IBD**

### **Biologic Therapies**

Biologic therapies represent a new class of drugs. These genetically engineered medications are made from living organisms and their products, such as proteins, genes, and antibodies. Biologics interfere with the body's inflammatory response in inflammatory bowel disease (IBD) by targeting specific molecular players in the process such as *cytokines*—specialized proteins that play a role in increasing or decreasing inflammation. Promising targets include tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukins, adhesion molecules, colony-stimulating factors, and others. Learning how these factors work has enabled researchers to design special treatment approaches that interrupt inflammation at various stages.

Biologic therapies offer a distinct advantage in treating IBD. Their mechanism of action is targeted. Unlike corticosteroids, which tend to suppress the entire immune system and thereby produce major side effects, biologic agents act *selectively*. Therapies are targeted to particular enzymes and proteins that have already been proven defective, deficient, or excessive in people with IBD and in animal models of colitis.

### **Intravenous (IV) Medications**

***Infliximab*** (Remicade®) is the first FDA-approved biologic therapy for Crohn's disease, and was recently approved for ulcerative colitis. It is given as a slow intravenous infusion. The infusions take about two hours to complete and usually are given as a series of three infusions and then every four to eight weeks.

This medication is a chimeric monoclonal antibody - In other words, it's a hybrid antibody made by joining human and mouse antibody genes together. It is about  $\frac{3}{4}$  human and  $\frac{1}{4}$  mouse in origin. ***Infliximab*** suppresses part of the immune system. It works by binding to and preventing the activity of TNF- $\alpha$ , a specialized protein (cytokine) that promotes inflammation in the intestine and other organs and tissues. People with active Crohn's disease have an increased production of TNF- $\alpha$  in their intestinal lining and increased excretion of this cytokine in their stool.

***Infliximab*** has been approved for the treatment and maintenance of remission of moderately to severely active Crohn's disease and ulcerative colitis that is unresponsive to conventional therapy. It also has been approved for the treatment and maintenance of fistulizing Crohn's disease. (Fistulas

are abnormal channels between two loops of intestine, or between the intestine and another structure, such as the skin.) Treatment with *infliximab* is often an effective method for tapering patients off steroids. A single infusion or a short series of three infusions have been shown to bring inflammation into remission and to allow closure of fistulas. The benefit may last approximately two months. However, recent studies have shown that repeated infusions of *infliximab* over a one-year period are generally well tolerated and can maintain remission. Two other antibodies to TNF, *adalimumab* (Humira®) and *certolizumab* (Cimzia®) are also FDA-approved for treatment of Crohn's disease. *Adalimumab* is also approved by the FDA for use in patients with rheumatoid arthritis and psoriatic arthritis. It is given as an injection, usually every two weeks. *Certolizumab* is an injection given every four weeks. Neither of these biologic agents is chimeric, that is, they are 100% human antibodies, and therefore may be associated with less allergic reactions compared to *infliximab*.

### **In the Pipeline**

Thalidomide and IL-11 are also being studied as biologic treatments. Drugs targeting a number of other cytokines and the inflammatory response, such as alpha 4 integrin, interleukin-6, interleukin-12, interferon gamma, and GM-CSF, are being evaluated in clinical trials. Another experimental therapy for Crohn's disease is a mixture of colon-extracted proteins derived from the individual patient. Self-derived proteins represent an individualized approach to treatment.

### **Side Effects**

Because *infliximab* is given intravenously, it may produce infusion reactions including headache, fever, chills, difficulty breathing, chest pain or pressure, low blood pressure, itching and hives. Additionally, patients may experience stomach pain, rash, nausea, and upper respiratory infection (cough and sore throat). When *infliximab* is given regularly rather than 'as needed' these reactions are very uncommon. Drug Interactions People taking several different medicines, whether prescription or over-the-counter, should always be on the lookout for interactions between drugs. Drug interactions may decrease a medication's effectiveness, intensify the action of a drug, or cause unexpected side effects. Before taking any medication, read the label carefully. Be sure to tell your doctor about all the drugs you're taking - even complementary therapies or over-the-counter medications - and any other medical conditions you may have.

### **Special Considerations**

There have been some reports of serious infections associated with biologic therapies such as *infliximab*, including tuberculosis (TB) and sepsis, a life-threatening blood infection. You should always have a TB skin test before you use *infliximab* as the drug can increase the risk of active TB for those who have been exposed. It's not that you will "catch" TB when taking *infliximab*, but if you have latent (inactive) TB, the drug can reactivate the infection. In this case, your doctor should begin TB treatment before you start *infliximab*.

*Infliximab* may reduce the body's ability to fight other infections as well. If you are prone to infections or develop any signs of infection, such as fever, fatigue, cough, or the flu, while taking *infliximab* you need to inform your doctor immediately. Live virus vaccines, measles, mumps, rubella and zoster should be avoided but inactivated vaccines including yearly flu shots (not via nasal spray) are recommended.

Be sure to tell dentists, surgeons and other healthcare providers that you are taking *infliximab*.

It may be inadvisable for people with heart failure to take *infliximab*, so tell your doctor if you have any heart condition before starting this medication. Inform your doctor at once if you develop new or worsening symptoms of heart failure—namely shortness of breath or swelling of the ankles or feet.

On rare occasions, blood disorders have been noted with *infliximab*. Inform your doctor if you develop possible signs such as persistent fever, bruising, bleeding, or paleness while taking *infliximab*. Nervous system disorders also have been reported occasionally. Let your doctor know 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 *infliximab*.

Although reports of cancer including skin, gastrointestinal, breast, lung and lymphoma (a cancer of the lymphatic system) in patients taking *infliximab* and other TNF-blockers are rare, they do occur approximately three times more often than in the general population.

Talk with your physician before taking *infliximab* if you are pregnant, planning to become pregnant or are breast-feeding.

Your physician will monitor you closely while you are on biologic therapy. It is not advisable to stop and then try to restart *infliximab*. To achieve and maintain remission, it is advisable to stay on the medication.

**Call Your Physician Immediately If You Have:**

Signs of a life-threatening reaction. These include wheezing, chest tightness, fever, itching, bad cough, swelling of face, lips, tongue or throat.

Signs or symptoms of infection. These include a fever of 100.5 degrees or higher, chills, severe sore throat, ear or sinus pain, cough, increased sputum or change in color, painful urination, mouth sores, wound that will not heal, or anal itching or pain.

Signs of arthritis, fever, weight loss, chest pain or pressure, or shortness of breath. Dark urine or yellow skin or eyes. Any rash.