Fact Sheet

Medications: Biologic Therapy

Medical treatment for Crohn's disease and ulcerative colitis (also known as inflammatory bowel diseases, or "IBD") has two main goals: *1) induction* of remission (the absence of symptoms and inflammation in the affected part of the gastrointestinal tract) followed by 2) *maintenance* of remission (prevention of flare-ups). These goals should be achieved with as few side effects and as little risk as possible. To accomplish these goals, treatment is aimed at controlling the ongoing inflammation in the intestine—the cause of IBD symptoms.

During the last several years, new treatments called *biologics* have been available for the treatment of IBD and other inflammatory diseases. These include Adalimumab (Humira®), Certolizumab pegol (Cimzia®), Infliximab (Remicade®), and Natalizumab (Tysabri®). These treatments are called biologics because, unlike chemical medications, they are made out of materials found in life—usually proteins. These proteins are genetically modified, and then the gene for the protein is inserted into bacteria or yeast. Large quantities of the protein of interest are then collected from the bacteria or yeast culture and purified for human treatment. Many biologic treatments are proteins called *antibodies*, which normally are part of the body's immune defense. Antibodies bind and help eliminate infections. The antibodies used for biologic therapy have been developed to bind and interfere with certain components of the inflammatory reaction in disease states. Basic research into the inflammatory reaction in IBD has allowed scientists to develop biologics that will interfere with these components (usually other proteins) of the inflammatory response. Certolizumab pegol, infliximab, and adalimumab block a small inflammatory protein called *tumor necrosis factor alpha (TNF-alpha),* a *cytokine* (specialized protein) that promotes inflammation in the intestine and other organs and tissues. Natalizumab prevents inflammatory cells from moving into disease sites by blocking a protein on the surface of those cells. There are many other promising targets for biologic treatments and new therapies are being investigated.

Biologic therapies offer a distinct advantage in IBD treatment. Their mechanism of action is targeted. Unlike corticosteroids like prednisone, which have many effects on the whole body and, therefore, produce major side effects, biologic agents act *selectively*. Therapies are targeted to particular proteins that have already been proven defective, deficient, or excessive in people with IBD and in animal models of IBD.

Intravenous (IV) Medications

Infliximab (Remicade®) is the first FDA-approved (in the year 1998) biologic therapy for Crohn's disease, and was later approved for ulcerative colitis. Infliximab is approved for the treatment of adults and children over the age of six years old. The medication is a *chimeric monoclonal antibody*. In other words, it's a hybrid consisting of 75 percent human and 25 percent mouse protein sequence. It works by binding to and preventing the activity of TNF-alpha. It is given as a drip via intravenous infusion. Infusions take about two hours to complete and usually are given every eight weeks.

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.)

Natalizumab (Tysabri®) has been approved for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies, including inhibitors of TNF-alpha.

It is infused into a vein at a certified infusion center and usually given once every four weeks. It takes about one hour to receive the entire dose.

Subcutaneous Injections

Adalimumab (Humira®) is taken by injection every other week. The patient or family member, once instructed by a healthcare professional, can administer it at home.

Adalimumab has been approved for adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, and in those patients who did not benefit from treatment, or who were intolerant to previous treatment with infliximab.

Certolizumab pegol (Cimzia®) is a biologic approved by the FDA for the treatment of Crohn's disease in adults. Certolizumab pegol is used to reduce the signs and symptoms of moderately to severely active Crohn's disease in adult patients who have not been helped enough by usual treatments.

Certolizumab pegol is a partial antibody that is bound to a special chemical called *polyethelyene glycol (PEG)*, which delays its excretion from the body.

Patients treated with certolizumab pegol receive an injection every two weeks for the first three injections. Once benefit has been established, Cimzia® is usually given once every four weeks. Depending on the physician's orders, it is injected by either a health care professional (typically a nurse) or the patient.

In the Pipeline

Additional biologic therapies under investigation for IBD include antibodies to other targets involved in the inflammatory response. Other proteins that are not antibodies, but have their own anti-inflammatory effect, are also being investigated.

Side Effects

Because biologics are given either by intravenous infusions or subcutaneous injections, they may produce redness, itching, bruising, pain, or swelling on the injection site. Other side effects may include: headache, fever, chills, difficulty breathing, low blood pressure, and hives. Occasional severe allergic reactions may occur. Additionally, patients may experience stomach pain, back pain, rash, nausea, and upper respiratory infection (cough and sore throat).

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 over-the-counter medications or complementary therapies—and any medical conditions you may have. Your pharmacist can also look for possible interactions between treatments.

Special Considerations

- There have been some reports of serious infections associated with infliximab, adalimumab, and certolizumab use, including tuberculosis (TB) and sepsis, a life-threatening blood infection. The manufacturers indicate it is important to speak to your doctor to determine if you may need a TB test before you use infliximab, adalimumab, or certolizumab because the drugs can increase the risk of re-activating TB for those who have been exposed.

  Cases of new infection with TB have also been reported. If you have prior exposure to TB, your doctor may advise you on the need to begin TB treatment before you start infliximab, adalimumab, or certolizumab. The same precautions are needed before beginning treatment with corticosteroids.

- Biologics may reduce the body's ability to fight other infections as well. If you develop any signs of infection while taking these medications, such as fever, fatigue, cough, or the flu, inform your doctor immediately.

- Tell your doctor if you have any other health problems such as heart failure, hepatitis or multiple sclerosis before taking these treatments.

- On rare occasions, blood disorders have been noted with infliximab, adalimumab,, and certolizumab. Inform your doctor if you develop possible signs such as persistent fever, bruising, bleeding, or paleness while taking one of these medications. 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, adalimumab, and certolizumab.

- For children and adults taking TNF-blocker medicines, the chances of getting lymphoma or other cancers may increase.

- *Progressive multifocal leukoencephalopathy (PML)*, a rare brain infection, has been reported with natalizumab use. Natalizumab may also cause liver damage and allergic reactions.

- Your physician will monitor you closely while you are on biologic therapy. Follow recommendations closely. It is generally recommended to take these treatments continuously, not as needed.

- Be educated—learn as much as possible about these treatments from your doctor and pharmacist. Other information can be obtained from reliable Internet sources such as the CCFA web site (www.ccfa.org) and treatment manufacturer web sites.

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