

## Infliximab

A Patient Education Monograph prepared for the American Uveitis Society

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**NOTE:** The opinions expressed in this monograph are those of the author(s) and not necessarily those of the membership of the American Uveitis Society, its leadership, or the Editorial Board of UveitisSociety.org. All medical decisions should be made in consultation with one's personal physician.

### Introduction

Infliximab (in-FLICKS-eh-mab) is a drug that is manufactured by the United States-based pharmaceutical company, Centocor. Centocor markets this drug under the brand name Remicade®. Infliximab is approved by the US Food and Drug Administration for the treatment of certain inflammatory diseases that affect parts of the body other than the eye. To date, there have been no large clinical trials to tell us about the usefulness of this drug for treatment of inflammatory eye diseases.

### Chemistry

Infliximab is a protein that was originally produced in mice. When a protein from an animal (or from another person or the environment) enters a person's body, the body's immune system will generally recognize this protein as being foreign and an allergic reaction may result. To ensure that this drug would be less likely to cause an allergic reaction, many of the parts of the protein that are unique to a mouse were removed and replaced with human parts.

### How it Works

Many forms of uveitis are presumed to be autoimmune in origin, that is, caused by a patient's own white blood cells, which move into the eye to cause inflammation, in the absence of the usual triggers such as an infection. These cells cause inflammation in part by producing small molecules called cytokines. One such molecule is named *tumor necrosis factor alpha* or TNF- $\alpha$ .

Infliximab belongs to a group of proteins known as antibodies. Antibodies are molecules that recognize and stick to foreign particles, initiating a process of disposal by the immune system. Infliximab recognizes and sticks to TNF- $\alpha$ . When this occurs, infliximab inhibits the action of TNF- $\alpha$ . Therefore, infliximab has the potential to reduce inflammation.

## **History of Usage**

### ***Non-Eye Disease***

Large clinical trials of infliximab have proven that this drug is beneficial for the treatment of certain *non-eye* autoimmune diseases, including rheumatoid arthritis (inflammation of the joints) and Crohns disease (an inflammation of the bowel). Smaller studies suggest infliximab may also be beneficial for patients with other inflammatory diseases, including psoriasis and sarcoidosis.

### ***Eye Disease***

To date, little information has been published in the medical literature about the treatment of uveitis with infliximab. In one small study, five patients with Behcet's disease and severe uveitis were treated successfully with this drug. Other studies testing the use of infliximab for patients with uveitis are still underway or have been recently completed, but results have not yet been published except in a preliminary form called an abstract. There are no published studies about the use of infliximab for the treatment of scleritis.

## **How it is Given**

Infliximab is always given into the vein (intravenous). It may be given as a single dose for an acute flare of inflammation. For chronic inflammation, it is usually given for an extended period of time. The second dose is given 2 weeks after the first dose, and the third dose is given one month after the second dose. Then it is generally given every 8 weeks, although it is possible to use the drug more frequently if necessary. In general, if infliximab does not produce a beneficial effect after three doses, then it is unlikely that a patient will benefit from further treatment. It is common to take another immunosuppressive drug along with infliximab, most often methotrexate. This may reduce the risk of allergic reactions and it allows a smaller dose of infliximab to be used.

## **Possible Side Effects and Drug Interactions**

Approximately six in every 100 patients who take infliximab stop this treatment due to side effects, the most common of which are shortness of breath, rash, and headache. During the infusion, it is possible to experience some discomfort around the infusion site, fever or chills, itching or an allergic skin rash, chest pain, an increase or decrease in blood pressure. Because of its effects on the immune system, infliximab increases a person's susceptibility to infection. It can increase the risk of common infections, but also unusual infections such as tuberculosis and fungal infections. Infliximab may lead to the development of proteins in the blood that can be associated with an autoimmune disease. There is theoretical concern that blocking the action of TNF- $\alpha$  could promote the development of cancer. However, in clinical trials to date, there is no evidence that patients treated with infliximab have a higher rate of cancer. This issue continues to receive careful monitoring. Some data suggest that infliximab may worsen multiple sclerosis, which is also considered an autoimmune disease. Paradoxically, there have been cases of eye inflammation occurring in patients treated with infliximab or another drug that inhibits the action of TNF- $\alpha$  called etanercept. In other words, infliximab might be detrimental rather than beneficial for some patients with uveitis. Infliximab is not approved for administration to children below 18 years of age, and it must be used cautiously in elderly people, and only if clearly necessary in pregnant women. Specific drug interaction studies have not been undertaken for this drug.

### **Monitoring**

A skin test for tuberculosis exposure should be performed prior to the first treatment with infliximab. It is also usual for a physician to order routine blood tests periodically for patients treated with infliximab. While having treatment with infliximab, it is important that the patient immediately report any symptoms of an infection, such as a fever or productive cough, to the treating physician. One form of uveitis, named pars planitis, is sometimes associated with multiple sclerosis. If a person is diagnosed with pars planitis, it may be advisable for them to undergo an MRI imaging study of the brain, to check for evidence of multiple sclerosis, before beginning infliximab therapy.

### **Conclusions**

Over the next 3 years, we should learn much more about the usefulness of infliximab for the treatment of uveitis. At present, in view of the lack of published studies, potential for serious side effects—in particular, infection—and the high cost, infliximab is generally reserved for the management of uveitis resistant or unresponsive to other treatments.

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