Etanercept

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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
Etanercept (e-tan-er-SEPT) is the generic name of the drug Enbrel® and is marketed by the pharmaceutical company Amgen for the treatment of several forms of inflammatory arthritis. At present, there is little published information available regarding the use of etanercept in the treatment of eye inflammations.

Chemistry
Etanercept is a human protein which has been engineered in the laboratory, rather than being isolated from the blood or tissues of another person, ensuring that the drug preparation is not contaminated by microorganisms such as hepatitis virus or human immunodeficiency virus (HIV).

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-α.

Etanercept consists of two identical TNF-α "receptors" linked together. Each of Etanercept’s “receptors” is able to recognize and bind to one TNF-α molecule, thereby preventing the interaction between the TNF-α molecule, as well as another molecule that is closely related to TNF-α, and the naturally occurring receptor. In this way etanercept inhibits the effects of TNF-α. Consequently, this drug has the potential to reduce inflammation.
History of Usage

Non-Eye Disease
In early large clinical studies, it was established that etanercept was beneficial for at least 2 forms of inflammatory joint disease: rheumatoid arthritis in adults and juvenile idiopathic arthritis (also known as juvenile rheumatoid arthritis) in children. More recently, new studies suggest it is likely that this drug will be useful in the treatment of other inflammatory diseases, such as psoriatic arthritis and ankylosing spondylitis.

Eye Disease
Several small studies have tested the use of etanercept in patients with different forms of uveitis. In one study involving 10 children with uveitis—most with juvenile idiopathic arthritis—the authors reported that etanercept was an effective treatment for some of the children. In a second study involving four academic institutions in the United States, patients with either uveitis or scleritis were included. Researchers found that only 2 of the 8 patients with uveitis and 2 of the 6 patients with scleritis appeared to benefit from etanercept therapy.

How it is Given
Etanercept is given by an injection under the skin using a very fine needle (subcutaneous injection, similar to the way that insulin shots are given). The drug is supplied from the pharmacist as a powder, with a package containing everything necessary to prepare it as a liquid ready for injection. The final volume is very small, generally 1 ml or less (less than 1/5 of a teaspoon). Injections are usually performed twice a week. Generally, patients or someone in their family are able to administer the injections without difficulty.

Possible Side Effects and Drug Interactions
The most common side effect of etanercept, which may occur in over one-third of persons taking the drug, is the development of some redness, itching, pain, or swelling at the injection site. Generally this reaction is not severe enough to require stopping the drug. Etanercept increases a person's susceptibility to infection. It can increase the risk of both common infections and unusual infections such as tuberculosis and fungal infections. Etanercept may lead to the development of proteins in the blood that can be associated with the development of an autoimmune lupus-like disease. There is theoretical concern that blocking the action of TNF-α could promote the development of cancer. However, in clinical trials to date, there is no evidence that patients treated with etanercept have a higher rate of cancer. This issue continues to receive careful monitoring. Some data suggest that etanercept may worsen multiple sclerosis, which is also considered to be an autoimmune disease. There have been cases of eye inflammation occurring in patients treated with etanercept or another TNF-α blocker called infliximab. In other words, this drug might be detrimental rather than beneficial for some patients with uveitis. There is no information regarding the safety of etanercept for very young children (less that 4 years old), although the drug appears to be well-tolerated by older children. It should be used only if clearly necessary in pregnant women, as safety for the unborn child is not established. 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 etanercept. It is also usual for a physician to order routine blood tests periodically for patients managed with etanercept. While undergoing treatment with etanercept, it is important that patients immediately report any symptoms of an infection, such as a fever or productive cough, to the treating physician. A form of uveitis called pars planitis is sometimes associated with multiple sclerosis. If a person is diagnosed with pars planitis, it may be advisable to undergo an MRI imaging study of the brain, checking for evidence of multiple sclerosis, before beginning etanercept therapy.

Conclusions
Studies are presently being conducted at United States centers on the use of etanercept in some forms of uveitis. Consequently, over the next few years, we should learn whether or not the etanercept is useful for the treatment of these conditions.

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