



North Shore Eye Centre

Ophthalmologist: **Dr Michael Branley** Orthoptist: Hulya Keskin
North Shore Private Hospital · Westbourne Street and Reserve Road · St Leonards NSW 2065 · AUSTRALIA
Tel: +61-2-9439 9649 · Fax: +61-2-9437 3522 · Roving (local call): 0500 THE EYE (0500 843 393)
E-mail: info@northshoreeye.com.au Website: www.northshoreeye.com.au

UVEITIS AND TREATMENT WITH CYCLOSPORIN AND METHOTREXATE

UVEITIS

What is uveitis?

Uveitis is the inflammation of the middle layer of the eye, known as the **uvea**. The uvea includes the **choroid** (a blood-filled layer which provides oxygen and nutrients to the retina and lies between the retina and the sclera), the **ciliary body** (which produces the fluid for the eye), and the **iris** (the coloured part of the eye).

What causes uveitis?

Uveitis may be caused by a traumatic injury to the eye or by an infection inside the eye (e.g. herpes or shingles), but most commonly is caused by an autoimmune response. Some autoimmune diseases affect only the eye (e.g. pars planitis and birdshot chorioretinitis). Others can affect the eye as well as other parts of the body (e.g. juvenile rheumatoid arthritis, Behcet's disease, sarcoidosis, and Vogt-Koyanagi-Harada syndrome).

How is uveitis treated?

Uveitis is a condition that needs careful medical care in order to control the inflammation and to prevent other problems such as glaucoma, cataract or macular oedema, which could lead to vision loss. Steroid drops, tablets, or injections are usually the first form of treatment for uveitis, however stronger immunosuppressive medicines such as cyclosporin and methotrexate are often needed.

CYCLOSPORIN

What is Cyclosporin used for?

Cyclosporin is a strong immunosuppressant drug that works by reducing the activity of the immune system. Cyclosporin inhibits a group of cells (T-lymphocytes), which play an important role in the immune system and contribute to the development of autoimmune diseases.

Cyclosporin is commonly used in organ transplants to reduce the risk of graft rejection however it can be used in other conditions such as psoriasis, severe atopic dermatitis, rheumatoid arthritis and other related diseases. Cyclosporin is also used to treat patients with ulcerative colitis who do not respond to treatment with steroids and is used to treat ocular inflammatory disease such as uveitis. Cyclosporin is



commonly used in the treatment in severe uveitis including Behcets Disease, pars planitis, sympathetic ophthalmia, where there are intolerable side effects due to the dose of corticosteroid that is used to control inflammation. The dosage of corticosteroid can be lowered with the addition of cyclosporin to the treatment regimen.

Note: The effect of cyclosporin takes several weeks. The drug is used in the long-term management of the condition rather than for immediate management of the condition.

Adverse Effects

Cyclosporin reduces the ability of the body to fight illnesses and diseases and therefore may increase the risk of developing an infection or cancer (particularly lymphoma or skin cancer). Treatment can be associated with a number of potentially serious adverse effects and adverse drug interactions. With careful use and monitoring, cyclosporin can be safe and effective.

The most common and potentially serious side effects are high blood pressure and kidney problems. The risk of developing these problems increases with higher dose and greater duration of treatment. Other side effects include headache, fatigue, nausea, fever, abdominal pain, chest pain, breathing difficulty, tremor, cramp, anaemia, discolouration of skin, swelling, numbness or tingling of the hands or feet, swelling of the gums, pancreatitis and increased risk of opportunistic fungal and viral infections.

Careful monitoring of several small laboratory tests (e.g. kidney function tests, blood tests, and liver function tests) is important to identify any toxic effects and to assess the response of the body to cyclosporin.

Drug Interactions

Cyclosporin interferes with a wide variety of other drugs and other substances. It is important to mention to your doctor all prescription and non-prescription medications that you are taking, including over-the-counter drugs and natural medication. The following is a list of some medications that may interfere with cyclosporin:

Antibiotics and antifungals: erythromycin, fluconazole (Diflucan), itraconazole (Sporanox), ketoconazole (Nizoral) and rifampin (Rifadin)

Antidepressants: fluoxetine (Prozac) and sertraline (Zoloft)

Anti-seizure medications: carbamazepine (Tegretol) and phenytoin (Dilantin)

Cholesterol lowering medications: simvastatin (Zocor)

Heart and blood pressure medications: amiloride (Midamor) diltiazem (Cardizem), spironolactone (Aldactone) and verapamil (Covera-HS, Isoptin, Verelan)



Human immunodeficiency virus (HIV) medications : indinavir (Crixivan), ritonavir (Norvir), nelfinavir (Viracept) and saquinavir (Fortovase, Invirase)
Others: allopurinol (Zyloprim), bromocryptine (Parlodel), danazol (Danocrine), androgens (male hormones), estrogens (female hormones), metoclopramide (Reglan), methylprednisolone, octreotide, ticlopidine (Ticlid), cimetidine (Tagamet), methoxsalen (OxSORALEN)

METHOTREXATE

What is Methotrexate?

Methotrexate is an immunosuppressive medication that belongs to a class of medicines known as antimetabolites. It is capable of blocking the metabolism of cells and therefore interferes with the normal division and functions of cells. Due to this effect, it has been helpful in treating certain diseases associated with abnormally rapid cell growth, such as in cancer. It has also been found to be helpful in treating several inflammatory diseases such as severe psoriasis, rheumatoid arthritis and rare cases of sarcoidosis. Methotrexate has been used to treat a variety of inflammatory eye diseases. It is used in the treatment of severe uveitis, but may also be used for certain cases of scleritis and vasculitis. Treatment with methotrexate has shown to maintain or improve vision and reduce signs and symptoms of inflammation. Methotrexate is usually considered after treatment with other medications has been unsuccessful in controlling the condition.

Note: Methotrexate is used as the long-term management and the effect of treatment with methotrexate takes several weeks.

Adverse effects

Close monitoring is required while taking this medicine. Methotrexate is generally well tolerated, but can cause severe toxicity. The incidence and severity of the side effects are generally related to the dose and frequency of use. The most commonly reported side effects include swollen gums, mouth ulcers, nausea, vomiting, diarrhoea, loss of appetite, headache, unusual tiredness and dizziness. Methotrexate can also reduce the levels of white, red and platelet blood cells in the blood, which can increase the risk of infection, anaemia or bleeding.

Methotrexate can cause severe toxicity of the liver, lungs, kidneys and bone marrow. Some side effects can be serious and include blood in the urine, lung toxicity or poor lung function (chest pain, dry cough and shortness of breath), inflammation of the pancreas (stomach tenderness, nausea, vomiting, fever, increased pulse rate), anaemia, irregular heartbeat, persistent sore throat, serious infection (herpes, hepatitis, blood infection, pneumonia), fatigue, mental changes, difficulty speaking or slurred speech. muscle weakness, fainting, rashes, skin ulcers or blistered skin, unusual bleeding or bruising and vision changes.

Drug Interactions



Methotrexate can interact with other medications. If methotrexate is taken along with other medications, it can affect the way some of them work and may cause harmful side effects. It is important to mention all of the medications you are taking, including prescription and nonprescription medications, vitamin supplements, and herbal products. The following is a list of medications that may interact with methotrexate and cause an increased risk of adverse effects:

Sulfonamides such as co-trimoxazole (Bactrim, Septra), sulfadiazine, sulfamethizole (Urobiotic), and sulfisoxazole (Gantrisin)

Tetracyclines (Brodspec, Panmycin, Tetracap)

Cyclosporine and oral anticoagulants (eg, warfarin)

Steroids (prednisone and others)

Use of penicillins with high and low dose methotrexate should be carefully monitored.

Antibiotics: certain oral antibiotics such as tetracycline and chloramphenicol may decrease absorption of methotrexate or suppress metabolism of the drug.

Non-steroidal antiinflammatory drugs (NSAIDs): The use of methotrexate can be affected by NSAIDs and the risk of side effects may be increased. Severe bone marrow suppression, anaemia, and gastrointestinal toxicity have been reported with administration of methotrexate along with some NSAIDs such as ibuprofen (Advil), naproxen (Naprosyn), diclofenac (Voltaren), diflunisal (Dolobid), etodolac (Lodine), flurbiprofen (Ansaid), indomethacin (Indocin), ketoprofen (Orudis), ketorolac (Toradol), meloxicam (Mobic), piroxicam (Feldene), and others.

Other important points

Before having any surgery tell your doctor that you are taking methotrexate.

Talk to your doctor before having any vaccinations during your treatment with methotrexate.

Avoid taking methotrexate if you are pregnant or planning to become pregnant.

It is very important to follow-up regularly with your doctor to monitor your condition so that harmful effects are detected without delay. Baseline assessments include a complete blood count, hepatic enzymes, renal function tests, and a chest X-ray. Lab tests are required before, during, and following treatment to assess the response of the body to methotrexate and to treat side effects before they become severe.



Note: This information is a summary only and does not provide a complete list of all the side effects and drug interactions that may occur. If you would like further information, talk with your doctor or pharmacist.