

lupus  **FACT SHEET**

Lupus Canada

Immunosuppressive drugs used in treating lupus

Immunosuppressive drugs can be of great value in the treatment of systemic lupus erythematosus (SLE or lupus). They may help to reduce disease symptoms, prevent damage to vital organs (such as the kidneys and lungs), and help put the disease into remission.

Immunosuppressive drugs are used only when lupus is active, especially if there are severe kidney problems. They are almost always taken along with corticosteroids and, in fact, are often used to help gradually reduce the dose of corticosteroids. (Ideally, they eventually allow the corticosteroids to be discontinued.)

Like any medication, these agents may have adverse effects. Because they suppress the over-active immune system, most of these drugs can make you more susceptible to infection. Some of the drugs can cause bone marrow suppression. Cells are produced in the bone marrow, so the interference of these drugs can lead to decreased numbers of red blood cells (the cells that carry oxygen in your blood), white blood cells (the cells that fight infection) and platelets (the cells that aid in blood clotting).

If you are taking an immunosuppressive drug that may suppress the bone marrow, regular blood tests must be done to monitor your blood cell levels. Because the development of infection is more likely when you are taking an immunosuppressive, it is important to notify your doctor if you develop a fever or any other new symptoms.

Some believe that immunosuppressive drugs may increase the risk of certain cancers. The most common problem is a precancerous abnormality that, if undetected, could lead to cervical cancer. In fact, this condition is quite common even in women without lupus. For this reason, regular

gynecological check-ups with pap smear testing are recommended for all women, and is especially important for women with lupus. Fortunately, with regular checks to ensure that there is no precancerous changes in the cervix, the more serious consequences related to cervical cancer can be avoided, even if you take

immunosuppressive drugs.

Other cancers that are more common in people with lupus are lymphoma and lung cancer. However, there is no clear evidence that this increased risk is primarily caused by drug exposures. Though some lymphomas may be related to medication use, research suggests that lymphoma risk may also be increased by uncontrolled lupus. It is important to know that, though they occur more often in people who have lupus than in the general population, lymphomas still only arise in a very small number of people with lupus. Thus, when they are required to control lupus, the benefits of immunosuppressive drugs are generally believed to outweigh the risks.

Finally, don't forget that some of the greatest risk factors for cancer are ones that you can modify. These risk factors include smoking, a high-fat diet and obesity. Paying attention to these factors (especially

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quitting smoking) is the best cancer-preventing strategy that you can take.

Types of immunosuppressive drugs

Various types of immunosuppressive drugs are available to treat lupus. Although they have different mechanisms of action, each drug works to decrease the body's over-active immune response.

It is important that you understand exactly how and when to take your medications, and what the potential side effects are. You need to work with your doctor to make sure that the dosage delivers benefits with as few side effects as possible. The effects of these drugs build up gradually, so you may not notice the benefits for several months.

These are the immunosuppressive drugs most frequently used in the treatment of lupus:

Azathioprine (Imuran): One of the most widely used immunosuppressive drugs for lupus, azathioprine works by blocking immune cell function. Side effects can include nausea, lowered blood cell counts, and liver inflammation. If you are receiving this drug, you should have regular blood tests to determine that your cell counts and liver remain normal. If the tests indicate a problem, your doctor will adjust the drug dose.



PREGNANCY AND LACTATION

The use of many immunosuppressive drugs may present risks to an unborn baby. If you are beginning these drugs, talk to your doctor about your long-term plans for pregnancy. Your doctor will be able to suggest contraceptive measures during treatment. If you have uncontrolled lupus, pregnancy should be avoided until the lupus is controlled, as outcomes will be better for the baby and for you. Your doctor may also suggest delaying pregnancy for several months after stopping certain drugs to allow them to be cleared from your system and avoid affecting your unborn baby.

Some drugs may pass into breast milk. Expectant mothers who plan to breastfeed and who take any medications should consult their lupus specialists to ensure that breastfeeding is safe for the baby.

Cyclophosphamide

(Cytoxan): This agent inhibits cell division and growth, and it is a strong immunosuppressive drug. Cyclophosphamide in lupus treatment is reserved for very serious kidney disease or other internal organ involvement. It has the potential for severe side effects, including the risk of serious infection. Although well tolerated by most people, cyclophosphamide

may cause nausea and vomiting, and its use may decrease blood cell counts. Hair loss may also be a problem.

Additional side effects can include temporary or permanent sterility in both women and men. There may be options for limiting this risk, so discuss with your specialist. This drug can also damage a developing fetus if a woman becomes pregnant while being treated with the drug, so using contraception is very important.

Because this medication is cleared by the kidneys and excreted in the urine, it can cause inflammation and bleeding in the bladder. One way to try to prevent this is to drink extra fluids, as directed by your doctor. The drug is usually given by injection in lupus, often with another intravenous medication

(Mesna or Uromitexan[®]) to limit adverse effects on the bladder.

Blood tests to determine cell counts should be done regularly. If your cell counts are seriously decreased, your doctor will adjust the drug dosage, which generally allows the blood counts to rise. Monitoring of urine tests is important. After stopping the drug, you should continue urine tests to check for abnormalities in the bladder. Bladder cancer is a possible side effect of high doses of cyclophosphamide, although it appears to be a very rare occurrence in lupus.

Methotrexate (Rheumatrex): Methotrexate may be useful for certain types of lupus activity when other drugs (e.g., nonsteroidal anti-inflammatory drugs (NSAIDs) or anti-malarials) do not adequately control the symptoms. In fact, methotrexate is often used in combination with these drugs. Some people like this drug because it is only taken once a week. Methotrexate is generally not chosen for very severe lupus, however.

Side effects of methotrexate may include liver and lung reactions, as well as lowered cell counts. Stomach upset or hair loss may also be a problem. If you are receiving this drug, you should have blood tests to monitor your cell counts and liver regularly; your doctor will modify the dosage if you experience side effects. To reduce toxicity, a supplement (folic acid) is prescribed.

Cyclosporine (Neoral): Originally developed to prevent rejection of kidney and other organ transplants, cyclosporine has been used to treat rheumatic diseases, including lupus. This medication modifies the immune system without decreasing cell counts. However, it may elevate blood pressure and reduce kidney

function. For these reasons, its use in lupus treatment has decreased.

Mycophenolate mofetil (CellCept): Developed to prevent the rejection of transplanted organs, mycophenolate is increasingly used as an alternative to cyclophosphamide for lupus with kidney involvement. It may be useful for other forms of lupus activity also. Mycophenolate works by curbing excessive activity of lymphocytes (a type of white blood cell). It is often well tolerated, although it can cause nausea and diarrhea. When you take this drug, regular lab tests, including cell counts, are required.

Leflunomide (Arava): Leflunomide is an anti-inflammatory medication that can help to reduce the pain and swelling of arthritis and can decrease damage to joints. Like cyclosporine, this medication is not used very often in lupus treatment.

Rituximab (Rituxan) is a cancer drug that works by decreasing the activity of white blood cells known as lymphocytes. Studies of people with severe lupus who did not respond to initial treatment with other drugs and were then treated with rituximab have shown great promise. Because this drug is relatively new, must be given by injection, and is very expensive, it is reserved for very severe cases. Recently, reports of a rare but serious complication have arisen, related to a brain infection causing death. However, this drug has been used safely in many people with severe lupus who did not respond to other treatment; thus, rituximab is an option for difficult cases.

New treatments

Researchers continue to look for more effective lupus treatments. Some studies have focused on blocking the

expression of genes that may cause some of the symptoms of lupus. Many advances have been made, and trials of such agents are underway, although it may be some time before they are routinely used in lupus treatment.

Risks and benefits

When considering cytotoxic drug therapy, it is important to weigh the benefits against the risks. Doctors use the term "risk-benefit ratio" to describe the comparison of a medication's side effects and beneficial effects.

While cytotoxic medications are generally not used if your lupus is mild, these drugs may be very helpful and even life-saving if your lupus is quite active and symptomatic or if you have major organ involvement.

Your doctor may order a kidney biopsy or other tissue biopsy before recommending one of these drugs.



FOR MORE INFORMATION

- Lupus Canada: www.lupuscanada.org. This site includes electronic versions of the *Living Well with Lupus* fact sheets.
- *Lupus: The Disease with a Thousand Faces*, edited by Dr. Sasha Bernatsky and Dr. Jean-Luc Senécal, Key Porter Books (2004) ISBN 1-55263-603-8. Contact Lupus Canada to order this book.
- The Arthritis Foundation: www.arthritis.ca
- Lupus Foundation of America: www.lupus.org

Disclaimer

Systemic lupus erythematosus is an autoimmune disease that affects thousands of Canadians, mostly women in their childbearing years. Symptoms vary greatly from person to person and treatment is highly individualized. Patients are urged to contact their physician or healthcare professional with any questions or concerns they might have.

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