

A painting of a woman walking away from the viewer on a winding, golden-yellow path that leads towards a bright sun in a hazy, orange sky. The landscape is a lush green field with rolling hills. The woman is wearing a white long-sleeved shirt and red shorts, carrying a brown bag. The overall style is impressionistic with visible brushstrokes.

You & MS

Considering Your Treatment Choices

Prepared with technical assistance from the MS Society of Canada, which operates as an independent, voluntary health agency and does not approve, endorse or recommend any specific product or therapy but provides information to assist individuals in making their own decisions.

The content in this resource provides information based on Health Canada's product monographs, although the practice of your own neurologist may be different. You may wish to speak with your neurologist before making any changes to your treatment course.

Introduction

When your doctor first tells you that you have multiple sclerosis, the news can feel overwhelming. A thousand questions crowd your mind: *How will this affect my life? Will I be able to do all the things I've planned?* Other important questions that will need to be addressed are: *Should I start a treatment for my MS? And if so – how do I choose the right treatment for me?*

This booklet has been prepared to help answer some of your questions. It explains what may happen to you during the course of the disease, why you have symptoms, and the medications that are available to treat your MS.

Only two decades ago, there were no effective therapies for MS. Now there are several medications – which can be a challenge as you and your doctor decide which is the best option for you. Our hope is that the information in this booklet will help you take that all-important first step: learning about the different medications so you can make an informed decision about what is right for you.

Starting treatment provides a way of controlling your disease. Amid the many uncertainties of living with MS, it can provide reassurance that you are doing everything you can to fight MS – and to live your life as you have imagined it.



What is MS?

The immune system is part of the body's defences against bacteria, viruses and other things that can cause disease or tissue injury. Immune cells are able to distinguish between substances that are part of your body ("self") from substances that belong to these foreign invaders ("not-self").

This highly complex system involves millions of immune cells. In some cases the system can fail, causing immune cells to attack tissues in the person's own body. This autoimmune response is believed to be the underlying problem in multiple sclerosis.

In autoimmune disorders, immune cells often attack a certain type of tissue, such as the insulin-producing cells in Type 1 diabetes. In MS, the principal target of the attack is myelin, a substance that surrounds and protects nerve fibres much as insulation protects electrical wires. As part of this process, inflammation breaks down myelin and produces lesions in the central nervous system (the brain, spinal cord and optic nerves). These lesions are visible with magnetic resonance imaging (MRI).

Inflammatory damage can "short circuit" normal nerve function, which you experience as MS symptoms. These can include:

- Nerve tingling, "pins and needles" sensations or numbness
- Blurred vision, loss of vision, eye pain
- Muscle weakness, stiffness or muscle spasms
- Pain
- Poor coordination, dizziness or nausea
- Impaired bladder or bowel function.

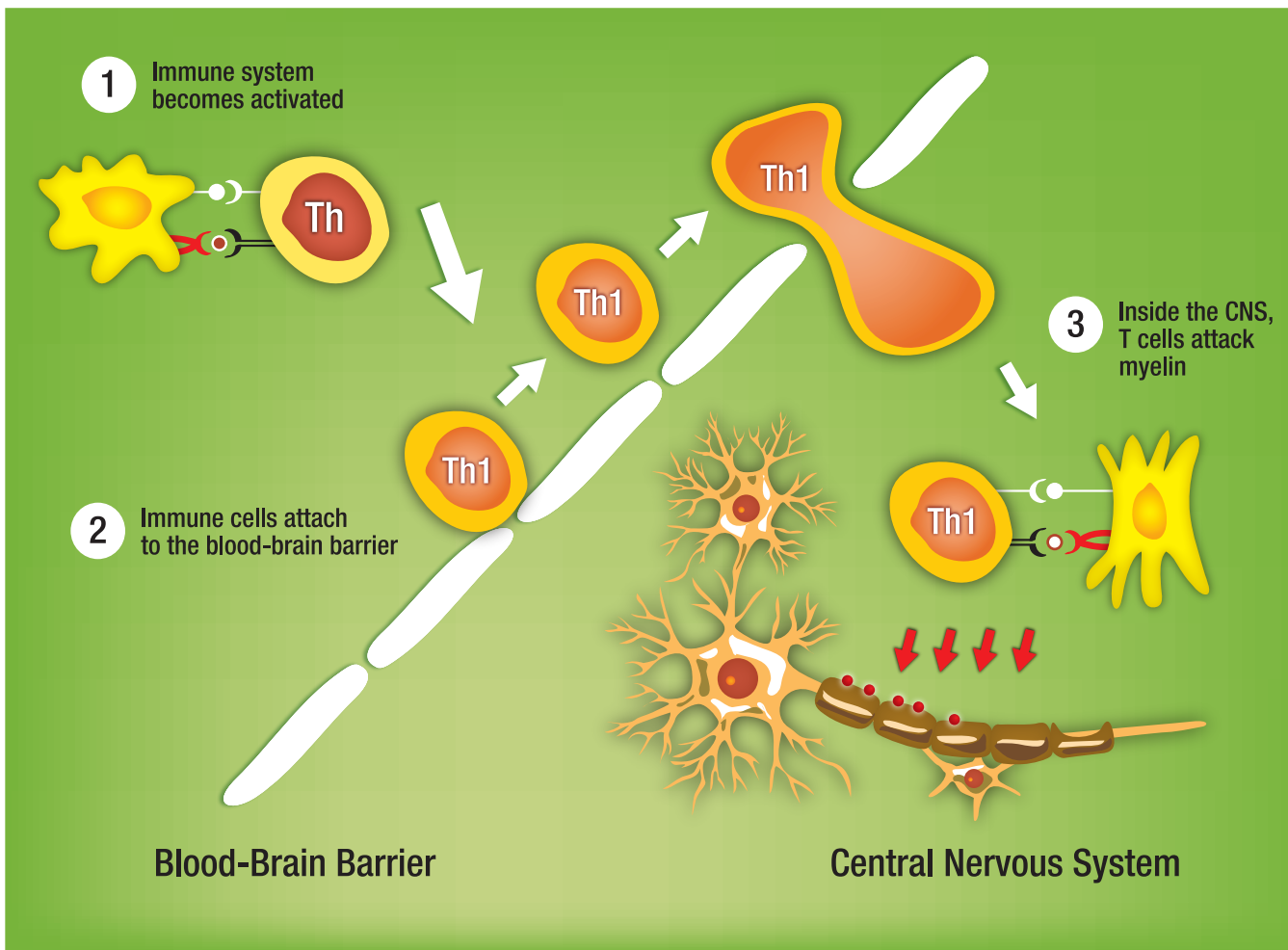
Initial symptoms may not meet all the criteria that doctors use to diagnose MS but may indicate that you have a “clinically isolated syndrome” suggestive of MS (called CIS). This may be an early warning sign as many people with CIS will later be diagnosed as having MS.

Following an MS attack (a “relapse”), inflammation subsides and the body tries to repair the damage, nerve function is restored to some degree and MS symptoms improve (“remission”). This pattern of worsening symptoms following by periods of relative wellness is characteristic of *relapsing-remitting MS*. This is the type of MS that most people have when they are diagnosed.

Unfortunately, during the course of MS, the body's ability to repair the damage becomes increasingly impaired. Nerve cells deteriorate and become permanently severed, a process called neurodegeneration. So over time there is a steady accumulation of disability. At first, this may mean that your symptoms don't fully go away during periods of remission. Later on, you may find that a problem (such as muscle weakness or bladder control) steadily worsens from year to year. This phase of the disease is called *secondary-progressive MS*. A minority of people experience increasing disability from the outset, which is called *primary-progressive MS*.

In relapsing forms of MS, medication combats this process, reducing the frequency and severity of relapses and slowing the disease progression that often culminates in disability. MS is a life-long disease so long-term treatment is necessary. Regular treatment gives your body the help it needs to control the disease. Stopping treatment early, or not taking the medication as often as your doctor prescribes, can mean that MS will get out of control again.

UNDERSTANDING MS



How do MS Medications Work?

The picture illustrates what happens during an MS relapse.

1. The immune system gets “turned on” and immune cells (called T cells) become activated.
2. Activated T cells attach to the blood-brain barrier (BBB), a layer of tightly-packed cells that normally blocks harmful substances from entering the central nervous system (the CNS: the brain, spinal cord and optic nerves). This attachment enables the T cells to squeeze through the gaps and enter the CNS.
3. Once inside the CNS, activated T cells attack the myelin covering the delicate nerve fibres.

This chain of events can be interrupted at several points – which is how different MS medications work.

1. Modify the response of T cells. This can be accomplished in several ways.

An MS medication can:

- Make the T cells less harmful – which is what glatiramer acetate (Copaxone®) and the beta-interferons (Avonex®, Betaseron®, Extavia* and Rebif®) do.
- Reduce the number of harmful T cells that are available to attack myelin – which is what fingolimod (Gilenya*) does.
- Destroy T cells – which is what immunosuppressant drugs do.

2. Interact with the BBB so activated T cells can’t get into the CNS. One way this can be accomplished is by:

- Preventing T cells from sticking to the BBB so they can’t squeeze into the CNS – which is what natalizumab (Tysabri®) does.

As you can see, these medications act in different ways to reduce the inflammation seen in MS and to make the autoimmune attack less harmful to the nerve fibres in the CNS.

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What are my Treatment Options?

The following pages summarize the MS medications that are currently available in Canada.

Beta-Interferons

Beta-interferon is a synthesized form of a protein produced by cells in the body. This class of medication comprises four drugs that have similar effects on the body. All are administered by injection.

- *Avonex® (beta-interferon-1a)*
- *Betaseron® (beta-interferon-1b)*
- *Extavia* (beta-interferon-1b)*
- *Rebif® (beta-interferon-1a)*

Avonex® and Rebif® are comparable drugs that are administered at different doses by different types of injection. Betaseron® and Extavia are the same drug sold under different brand names.*

Avonex® (beta-interferon-1a)

How is it taken?

By injection into the muscle 1 time per week.

What is it used to treat?

- CIS (clinically isolated syndrome)
- Relapsing MS.

Why is it used?

To reduce the frequency of MS relapses, reduce inflammatory activity on MRI and slow the progression of disability.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Avonex® reduces the frequency of MS relapses by about one-third, reduces the number of lesions on MRI, and delays the time to disability. In people with CIS, Avonex® reduces the chance of having a second attack.

What are the possible side effects?

The most common side effects are flu-like symptoms (e.g. fatigue, chills, fever, muscle aches, and sweating) and skin reactions at the injection site (pain). Some people may also develop liver, blood and thyroid problems, allergic reactions and depression.

What tests are needed?

Periodic blood tests are recommended to ensure that your liver and bone marrow are functioning normally.



Betaseron® and Extavia* (beta-Interferon-1b)

How is it taken?

By injection under the skin 1 time every other day.

What is it used to treat?

- CIS (clinically isolated syndrome)
- Relapsing MS.

Why is it used?

To reduce the frequency of MS relapses, reduce inflammatory activity on MRI and slow the progression of disability.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Betaseron®/Extavia* reduces the frequency of MS relapses by about one-third, reduces the number of lesions on MRI, and delays the time to disability. In people with CIS, Betaseron®/Extavia* reduces the chance of having a second attack.

What are the possible side effects?

The most common side effects are flu-like symptoms (fatigue, chills, fever, muscle aches, and sweating) and skin reactions at the injection site (swelling, redness, discolouration and pain). Some people may also develop liver, blood and thyroid problems, allergic reactions and depression.

What tests are needed?

Periodic blood tests are recommended to ensure that your liver and bone marrow are functioning normally.

Rebif® (beta-interferon-1a)

How is it taken?

By injection under the skin three times per week. The medication is available in two dosage strengths.

What is it used to treat?

- Relapsing MS.

Why is it used?

To reduce the frequency of MS relapses, reduce inflammatory activity on MRI and slow the progression of disability.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Rebif® reduces the frequency of MS relapses by about one-third, reduces the number of lesions on MRI, and delays the time to disability.

What are the possible side effects?

The most common side effects are flu-like symptoms (fatigue, chills, fever, muscle aches, and sweating) and skin reactions at the injection site (swelling, redness, discolouration and pain). Some people may also develop liver, blood and thyroid problems, allergic reactions and depression.

What tests are needed?

Periodic blood tests are recommended to ensure that your liver and bone marrow are functioning normally.



Copaxone® (glatiramer acetate)

Unlike the beta-interferons, Copaxone® is a synthetic protein made from an assortment of amino acids.

How is it taken?

By injection under the skin 1 time per day.

What is it used to treat?

- CIS (clinically isolated syndrome)
- Relapsing-remitting MS.

Why is it used?

To reduce the frequency of MS relapses, reduce inflammatory activity on MRI and slow the progression of disability.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Copaxone® reduces the frequency of MS relapses by about one-third and reduces the number of lesions on MRI. In people with CIS, Copaxone® reduces the chance of having a second attack.

What are the possible side effects?

The most common side effects are skin reactions at the injection site, such as redness, pain, injection site mass and itching. Some people may also experience an immediate post-injection reaction (flushing, chest pain, palpitations, anxiety and difficulty breathing) that is self-limited. Injections may also cause a loss of tissue at the injection site (called lipoatrophy) that results in skin dimpling or pitting.

What tests are needed?

No specific monitoring is required.



New MS Treatments

Two additional medications are available to treat people with relapsing-remitting MS. Both are typically used in people who have not responded adequately to a beta-interferon or glatiramer acetate or who can't tolerate one of the injectable drugs. These medications are generally considered to be more potent, but may be associated with a small risk of serious side effects.

Gilenya (fingolimod)*

Gilenya* is the first oral MS medication available in Canada. It is an agent that affects the immune system such that white blood cells tend to stay in lymph nodes rather than going into the central nervous system, which leads to the inflammation seen in MS.

How is it taken?

As a capsule by mouth 1 time per day.

What is it used to treat?

- Relapsing-remitting MS.

Why is it used?

To reduce the frequency of relapses and to delay the progression of physical disability. Gilenya* is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, one or more therapies for MS.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Gilenya* reduces the frequency of MS relapses by about one-half and reduces the number of lesions on MRI compared to placebo or an active control.

What are the possible side effects?

The most common side effects are headache, influenza, diarrhea, back pain, elevated liver enzymes and cough. Less common side effects may include lower respiratory tract infections (e.g. bronchitis), and swelling in a structure of the eye (called the macula, reported to occur with higher doses). A slowing of the heart rate may occur when taking the first dose of Gilenya*; this generally does not cause symptoms and does not persist after the first dose. Blood pressure may be slightly elevated during long-term treatment.

What tests are needed?

People who have not had chickenpox or have not been vaccinated for chickenpox will need a blood test to determine their level of antibodies to the chickenpox virus (varicella zoster virus [VZV]); a vaccination for chickenpox is recommended in people who do not have antibodies to VZV. An electrocardiogram (ECG) will be needed if you have not had one in the past 6 months. A 6-hour observation period is required when you take the first dose. Blood tests are needed every 3 months in the first year of treatment and periodically thereafter to ensure that your liver and bone marrow are functioning normally. Eye exams will also be needed after 3-4 months on treatment or if you develop visual disturbances. An eye exam is needed before starting treatment if you have diabetes or certain other conditions affecting the eyes.



Tysabri® (natalizumab)

Tysabri® is a type of antibody that targets a protein involved in MS. It is administered by infusion as an outpatient in a clinic. For the infusion, a needle is inserted into a vein and the drug is slowly dripped into your body. This takes about one hour. Another hour is needed for observation to ensure that you don't have a reaction to the infusion.

How is it taken?

By infusion into the vein 1 time every 4 weeks.

What is it used to treat?

- Relapsing-remitting MS.

Why is it used?

To reduce the frequency of relapses, to reduce the number and volume of brain lesions on MRI, and to delay the progression of physical disability. Tysabri® is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, other therapies for MS.

What are the possible benefits?

In relapsing-remitting MS, studies have shown that Tysabri® reduces the frequency of MS relapses by about two-thirds and reduces the number of lesions on MRI.

What are the possible side effects?

The most common side effects are infections such as urinary tract infection and hypersensitivity reactions (rash, headache). Other side effects may include fatigue and depression.

Tysabri® may be associated with a potentially fatal condition called PML (progressive multifocal leukoencephalopathy). This is caused by reactivation of the JC virus, which most people have been exposed to during their lifetime. The JC virus is normally dormant, but can develop into a fatal or debilitating brain infection during treatment with Tysabri®. The risk of developing PML is estimated to be 1 in 1000 in the first 18 months of treatment. This risk increases with longer treatment to perhaps as high as 2 in 1000.

What tests are needed?

Continued vigilance is required for early detection of PML should it occur. This may include periodic MRIs. If PML is suspected, a lumbar puncture may be performed to test the cerebrospinal fluid for the presence of JC virus DNA.



Comparing Your Treatment Options

The decision to start treatment represents an important commitment on your part since the medication will have to be taken regularly. So it is important to choose the medication that you will be most comfortable taking, can be accommodated into your lifestyle, and which offers the right balance of benefits and risks.

The choice of a specific treatment is not “right” or “wrong”. The right choice will be the one that most suits your preferences, your life situation and your MS. The worksheet below will help you in your discussions with your doctor and MS nurse as you decide which is the best option for your situation.

If you have the right information, know what’s important to you, and get the support you need from your MS team, family and friends – you are certain to make the best choice for you.

Questions	Answers	My thoughts
Which medication do you think would best control my MS?		
Are there any reasons why I shouldn't take a specific drug?		
What are the advantages and disadvantages of injecting/infusing my medication?		
What are the advantages and disadvantages of an oral treatment?		

Questions	Answers	My thoughts
How will the different medications affect my lifestyle?		
What problems have other people had on a specific medication?		
What tests and procedures will be needed?		
What is involved with these tests and procedures?		
What side effects am I most likely to have?		
What side effects are the hardest to cope with?		
Are there any factors that might make it difficult for me to stay on the medication?		
What are my options if the treatment doesn't work or I can no longer take it?		



Frequently Asked Questions (FAQ)

Is treatment really necessary for MS?

Treatment is generally advised for people with MS who have relapses to reduce the frequency of inflammatory relapses and to slow the progression of disabilities. Left untreated, MS can cause significant tissue damage in your brain and spinal cord. During the lifetime course of MS, this damage can cause permanent physical and mental disability.

When do I have to start treatment?

While it is best to start therapy for relapsing-remitting MS as soon as possible, it is important that you take the time to consider your options carefully and then begin once you have committed yourself to the treatment course you have decided on.

Should I start treatment if I'm planning to become pregnant?

Talk to your doctor if you are planning a pregnancy. Taking an MS medication during pregnancy is not recommended since some medications have the potential to cause birth defects. If you want to become pregnant soon, it may be best to wait until after the baby is born before you start treatment. If your plans are less definite, medications will not affect your fertility so you can always interrupt treatment in the months or years ahead when you are ready to become pregnant.

How will I know if my treatment is working?

You have already experienced a number of symptoms, but MS is generally a “silent disease”. While MS lesions in your brain and spinal cord cause relapses, these inflammatory lesions actually occur 10-20-fold more often than relapse symptoms. So even when you are feeling well, the inflammation and neurodegeneration that are the hallmarks of MS are continuing to cause tissue damage. Much of this inflammation will be controlled by the medication you take – but you may not feel very different than before. However, as you continue to take your medication, you may realize that your relapses are not as frequent or are less severe. When you see your MS doctor, he/she will perform a neurological exam and other tests as necessary to assess how well you are doing.

What do I do if I experience side effects?

Your doctor or MS nurse will tell you about the possible side effects of the medication you are taking. If you think you are experiencing a side effect – report it to your doctor as soon as possible. Your MS team can explain how to lessen some of the side effects, or provide you with some tips on how to cope with them. Some side effects don’t cause symptoms – but that doesn’t mean they aren’t potentially serious. That is why periodic tests (e.g. blood tests) are needed to ensure that you are not having a bad reaction to the drug. Testing also enables your doctor to respond quickly if a problem does arise.

Can I change medications if I don’t like the one I’m taking?

For a treatment to be successful, it must be taken on a long-term basis as prescribed by your doctor. This can be difficult, so it’s important to choose a medication that you can live with. If you decide at some point that you don’t like the choice you’ve made and you find it difficult to maintain the treatment regimen – talk to your doctor about trying another medication. Most medications can be started soon after stopping another one, or after only a brief interruption in therapy. The important thing is to continue on therapy – to control MS for the rest of your life.

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