



# **A Guide to Maintaining Ability in Multiple Sclerosis:**

Understanding treatment options



# What's the right choice for you?

You may have just been diagnosed with multiple sclerosis (MS), or have been living with this disease for a while and now it's time to start treatment with the aim of preserving your quality of life and ability for as long as possible.

Having MS does not necessarily mean giving up your dreams. Understanding what MS is and how it affects your body is the first step in making an educated decision about managing the disease, and understanding how a potential treatment may affect you, your symptoms, and your future.

There are five disease-modifying therapies available for relapsing-remitting MS (RRMS) and each have certain benefits, and appropriate uses, but which therapy is right for you? This booklet will give you the information you need to evaluate the different treatments available, ultimately, helping you make the right choice for your long-term health.



# What is Multiple Sclerosis?

What is MS and how does it affect your body?

MS is a chronic condition that, over time, may worsen. It is not well understood what causes MS. Most experts believe that MS is an autoimmune disease. This means that the immune system mistakenly attacks healthy cells, organs, or tissues in the body.

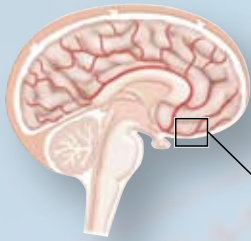
MS affects the central nervous system (CNS). Together, the brain and spinal cord are known as the CNS. Inside the CNS there are billions of nerve cells called neurons. These nerve cells communicate by sending electrical signals. These signals travel along a part of the nerve cell called an axon (nerve fibre).

The axons convey messages throughout the CNS allowing you to perform functions such as walking, hearing, and seeing. Axons are covered with a protective fatty substance called the myelin sheath. Myelin is similar to the coating around electrical wires. Myelin is crucial in sending messages along the axon at a rapid rate.

In MS, a type of immune cell known as a “T cell” becomes activated and starts to multiply. These immune cells cross the blood-brain barrier into the CNS. The blood-brain barrier is a layer of cells that surrounds and protects the CNS from large molecules, immune cells, and potentially damaging substances passing from the blood stream into the CNS.

Once inside the CNS, these immune cells attack the myelin causing inflammation and axon damage, leaving scar tissue called lesions or plaques.

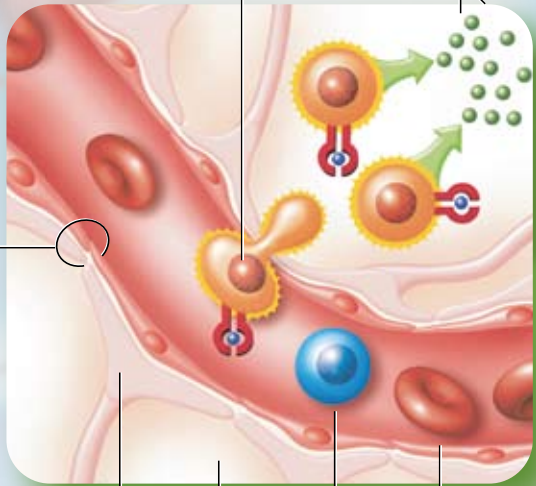




ACTIVATED  
T CELL  
PASSES  
THROUGH  
BLOOD-BRAIN  
BARRIER

RELEASE OF  
INFLAMMATORY  
SUBSTANCES,  
BRAIN TISSUE  
DAMAGE

BLOOD-BRAIN  
BARRIER



BRAIN CELL

T CELL

BRAIN TISSUE

RED BLOOD CELL

# What is Multiple Sclerosis?

## How MS progresses

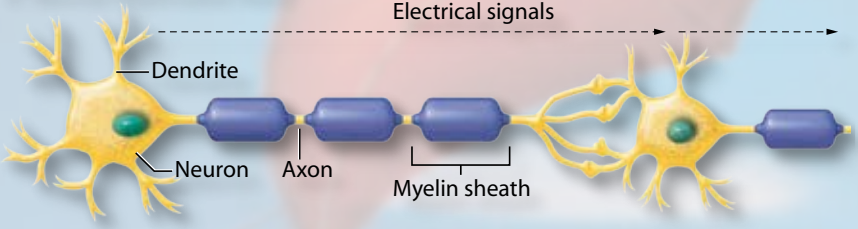
After each attack, the body works to repair the areas of damaged myelin. Over time, recovery and repair from each attack may be less and less complete. As the myelin is permanently damaged, or partially repaired, the axon becomes less effective at sending messages to the rest of the body. Not only is the myelin damaged, but the axon may also be destroyed. So messages either get through very slowly or not at all. Neuronal loss occurs naturally throughout our lifetime as part of aging, but it appears to be accelerated in MS. This permanent damage to the myelin and axons is thought to be the cause of disability in MS. By starting treatment early in the course of the disease, you have the best chance of maintaining your quality of life and level of ability.

The signs and symptoms of MS differ from person to person, depending on where lesions form in the brain or spinal cord. Some lesions are “silent,” meaning they cause no obvious symptoms, while other lesions can be directly associated with symptoms.

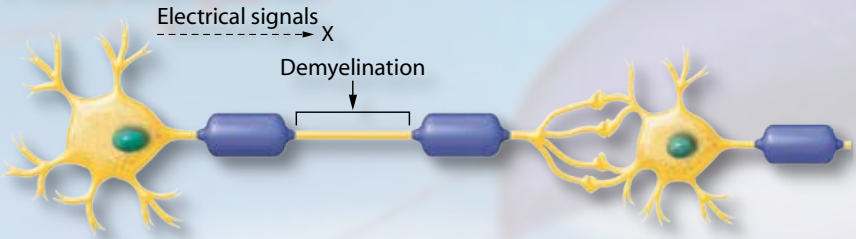
Research suggests that the greater the number of active lesions, the greater the risk of an attack (relapse). Unfortunately, the brain’s ability to compensate for neuronal damage and loss is finite. As nerve damage continues, there is a steady loss of ability, such as a permanent loss of sensation, chronic impairment to bowel or bladder function, or loss of mobility. Many researchers believe the risk of disability increases the more often you experience relapses. Therefore, choosing a treatment that reduces the number and severity of relapses could help protect and maintain a normal and healthy lifestyle.



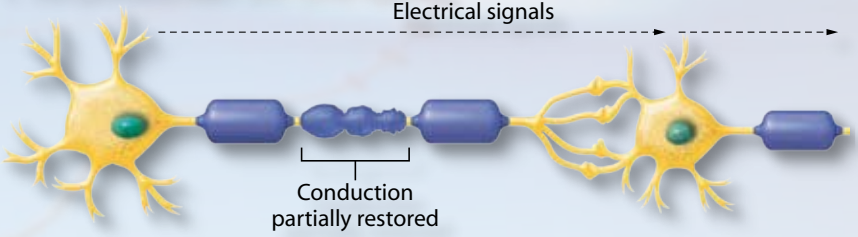
A Normal Myelinated Axon



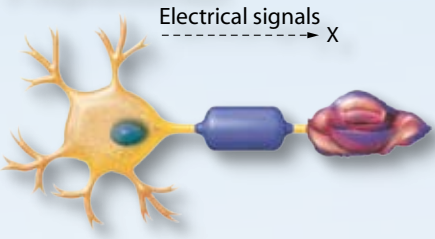
B Acutely Demyelinated Axon



C Demyelinated Axon with some repair



D Degenerated Axon



# Relapsing-remitting MS

## What is a relapse?

A relapse is any new or recurring symptom that lasts longer than 24 hours, in the absence of fever or infection. A fever or infection may temporarily worsen your symptoms, resulting in a flare-up of existing symptoms. This is temporary, and these symptoms disappear once you feel better.

Most people with MS have relapsing-remitting MS (RRMS). RRMS is characterized by clearly defined relapses followed by complete or partial recovery (remission). RRMS is the most common form of MS; 75% of people are diagnosed with RRMS.<sup>1</sup>

## Common MS symptoms:

- Vision Problems
- Fatigue
- Tingling / Numbness
- Muscle Weakness
- Discomfort / Pain
- Loss of Balance
- Spasticity
- Memory or Cognitive Problems
- Sexual Dysfunction
- Bladder and Bowel Problems



## How is MS treated?

Right now, there is no cure for MS, but there are treatments that have been found to alter the course of the disease and some may even delay the loss of ability. These are called disease-modifying drugs (DMDs). DMDs\* have been shown to impact MS in three ways, by:

1. Slowing the progressive loss of ability common in MS (by helping to prevent nerve damage).
2. Reducing the number and severity of relapses.
3. Reducing MRI activity\*\* (the number and/or size of lesions seen on MRI scans).

\* Not all DMDs have been proven equally effective on all three measures listed above.

\*\* The exact relationship between MRI findings and the clinical status of patients is unknown.

## When should I start treatment?

In 1999, the Canadian MS Clinics Network published a consensus statement advising early treatment with DMDs.\*<sup>2</sup>

### **Early treatment may:**

- Delay the progressive loss of ability
- Reduce the number and severity of relapses
- Reduce the number of brain lesions

\* This publication refers to Rebif<sup>®</sup>, Avonex<sup>®</sup>, Betaseron<sup>®</sup> and Copaxone<sup>®</sup>. Tysabri<sup>™</sup> was not approved for use by Health Canada at the time of publication.

Tysabri<sup>™</sup> is generally recommended for MS patients who have had an inadequate response to, or are unable to tolerate, other therapies for multiple sclerosis.<sup>3</sup>

**Don't delay treatment –  
aim to maintain ability in MS**

# Treating your MS

## Making the right choice

When deciding which medication is right for you, it helps to know the facts about the DMDs available.

Currently, there are two classes of MS therapies available: Immunomodulators and Selective Adhesion Molecule (SAM) Inhibitors.

## Classes of MS Therapies

### Immunomodulators

Rebif<sup>®</sup>  
Avonex<sup>®</sup>  
Betaseron<sup>®</sup>  
Copaxone<sup>®</sup>

### Selective Adhesion Molecule (SAM) Inhibitors

Tysabri<sup>™</sup>



## Immunomodulators

### Currently available DMDs

### What is the drug made of?

### How does it work?

Rebif®  
(interferon beta-1a)  
Approved by Health Canada  
February 5, 1998

Interferon beta-1a is a protein that exists naturally in the body. Interferon beta-1a medications are produced in mammalian cells.<sup>4,5</sup>

The precise mechanism of action is still unknown. It is thought interferon beta works to decrease the number of harmful immune cells outside the CNS that cause inflammation. As well, interferon beta “strengthens the blood-brain barrier (BBB),” which helps prevent harmful immune cells from entering the CNS and causing damage.<sup>4,5,6</sup>

Avonex®  
(interferon beta-1a)  
Approved by Health Canada  
April 6, 1998

Betaseron®  
(interferon beta-1b)  
Approved by Health Canada  
July 19, 1995

Interferon beta-1b is a slightly modified form of interferon beta that is produced in bacterial cells.<sup>6</sup>

Copaxone®  
(glatiramer acetate)  
Approved by Health Canada  
September 4, 1997

Glatiramer acetate is a synthetic compound which does not occur naturally in the body. It contains 4 naturally occurring amino acids (amino acids are the smallest units of protein) lined up in random order.<sup>7</sup>

The precise mechanism of action is still unknown. It is thought that glatiramer acetate works outside and inside the CNS to change the way the immune system reacts.<sup>7</sup>

## Selective Adhesion Molecule (SAM) Inhibitors

Tysabri™  
(natalizumab)  
Approved by Health Canada  
September 28, 2006

Natalizumab is a monoclonal antibody that does not occur naturally in the body. It is produced in a mouse cell line.<sup>3</sup>

The precise mechanism of action is still unknown. Natalizumab is an immunosuppressant that may act to prevent harmful immune cells from crossing the blood-brain barrier.<sup>3</sup>

# DMDs – Immunomodulators

## How do the DMDs compare?

Not all DMDs have been proven equally effective on all three important disease measures (delaying the progressive loss of ability, reducing the number and severity of relapses, and reducing MRI lesions). Furthermore, not all medications are used in the same way. Reviewing the effectiveness, administration and potential side effects of each DMD with your healthcare professional will help you make the right decision for you.

## Immunomodulators – Efficacy in RRMS





Therapies	Rebif <sup>®5</sup> (interferon beta-1a)	Avonex <sup>®4</sup> (interferon beta-1a)	Betaseron <sup>®6</sup> (interferon beta-1b)	Copaxone <sup>®7</sup> (glatiramer acetate)
Slows the progressive loss of ability	●	●		
Reduces the number of relapses	●	●	●	●
Reduces the severity of relapses	●			
Reduces the number of hospitalizations	●			
Reduces the need for steroids	●			
Reduces disease activity as measured by MRI*	●	●		●

\*The exact relationship between MRI findings and the clinical status of patients is unknown.

Efficacy may not be the only factor when selecting a therapy. Maintaining your lifestyle is also a very important consideration. Part of that consideration is how convenient and easy a DMD is to administer.



## Administration

Therapies	Rebif® <sup>5</sup>	Avonex® <sup>4</sup>	Betaseron® <sup>6</sup>	Copaxone® <sup>7</sup>
Dose	44 mcg/0.5 mL or 22 mcg/0.5 mL	30 mcg/0.5 mL	0.25 mg/1.0 mL	20 mg/1.0 mL
Route of injection	Injected under the skin (subcutaneous injection)	Injected into the muscle (intramuscular injection)	Injected under the skin (subcutaneous injection)	Injected under the skin (subcutaneous injection)
Injection frequency	3 times a week	Once a week	Every other day	Every day
Needle gauge ††	29 gauge †† 	23 gauge †† 	30 gauge †† 	27 gauge †† 
Needle length	½ inch	1-¼ inch	½ inch	½ inch
Autoinjector available	Yes	Yes	Yes	Yes
Preparation required for injection	No. Supplied as pre-filled, preassembled syringes.	No. Supplied as pre-filled, preassembled syringes.	Yes. Medication must be mixed (reconstituted) prior to injection. Some assembly required.	No. Supplied as pre-filled, preassembled syringes.
Patient Support Program	Yes. Multiple Support Program® <a href="http://www.msprogram.ca">www.msprogram.ca</a>	Yes. Avonex® Alliance™ <a href="http://www.msalliance.ca">www.msalliance.ca</a>	Yes. BETAPLUS® <a href="http://www.betaplus.ca">www.betaplus.ca</a>	Yes. Shared Solutions® <a href="http://www.mswatch.ca">www.mswatch.ca</a>

†† The higher the gauge, the thinner the needle.

# Possible side effects

## What side effects might I experience?

All immunomodulator therapies available for the treatment of MS have side effects. In general, most side effects are manageable and resolve with continued treatment over time.

**Interferon-beta:** The most common side effects are:

- Flu-like symptoms, such as fever, chills, muscle aches, and fatigue.<sup>4,5,6</sup>
- Injection-site reactions, such as soreness, redness, pain, bruising, or swelling may occur at the place of the injection.<sup>4,5,6</sup>

## Incidence of the most common side effects of interferon-beta products

Therapies	Rebif <sup>®5</sup> (HSA* & FBS** free formulation)	Avonex <sup>®4</sup> (HSA* free formulation)	Betaseron <sup>®6</sup>
Flu-like symptoms	71.5%	88%	76%
Injection site reactions	30.8%	25%	85%

\*HSA – Human Serum Albumin

\*\*FBS – Foetal Bovine Serum

Other possible side effects may include changes in white blood cell count, thyroid function or liver enzymes. A very rare, but potentially serious side effect of interferon beta treatment is liver injury.<sup>4,5,6</sup> Periodic blood tests will monitor any of these potential changes.<sup>4,5,6</sup> Your healthcare provider will discuss the frequency of these tests with you.



It is not uncommon for symptoms to temporarily worsen while your body adjusts to your medication. For most people, side effects appear in the first months of treatment and tend to diminish or disappear with time and continuous use. These side effects can be easily managed using simple strategies. Your doctor, nurse or the Multiple Support Program can offer tips for preventing and managing these common side effects.

Your body naturally produces interferon, so it usually accepts interferon medications as natural substances. In some people the body starts to think the medication is a foreign substance. In these instances, the body reacts by producing antibodies, some of which may impact the effectiveness of your medication.<sup>9</sup> These are called Neutralizing Antibodies (NAbs).

It is important to note that the majority of people treated with interferon beta do not develop NAbs. Moreover, study results on the effects of NAbs are inconclusive.

For more information on NAbs, contact your health care provider.



# Possible side effects

**Glatiramer acetate:** The most common side effects are:

- Injection-site reactions, such as redness, swelling, itchiness or hives surrounding the injection site.<sup>7</sup>
- An immediate post-injection reaction can occur immediately after self-injecting. Some people experience flushing, breathlessness, chest pain, palpitations, throat constriction, laboured breathing, and hives as if having a heart attack or an anxiety attack. While frightening, these symptoms usually go away within 15 minutes and do not have any lasting consequences.<sup>7</sup>

Incidence of the most common side effects of glatiramer acetate

Therapy	Copaxone <sup>®7</sup>
Injection site reactions	66%
Immediate post-injection reaction	10%

Another possible side effect is the occurrence of lipoatrophy, often this is an irreversible skin condition. This is described as the loss of subcutaneous (under the skin) fatty tissue. When this occurs it may be similar in appearance to cellulite and accompanied by the hardening of skin at the injection site.<sup>7,10</sup>



The other class of MS therapy available is:

## Selective Adhesion Molecule (SAM) Inhibitors Efficacy in RRMS:

Tysabri™ is generally recommended for MS patients who have had an inadequate response to, or are unable to tolerate, other therapies for multiple sclerosis.<sup>3</sup>

<b>Treatment:</b>	<b>Tysabri™<sup>3</sup> (natalizumab)</b>
Slows the progressive loss of ability	●
Reduces the number of relapses	●
Reduce the severity of relapses	
Reduces the number of hospitalizations	
Reduces the need for steroids	
Reduces disease activity as measured by MRI*	●

\* The exact relationship between MRI findings and the clinical status of patients is unknown

There are many factors to consider when selecting a therapy. Lifestyle considerations are one of those factors to consider. Part of that consideration is how convenient and easy a DMD is to administer.

## Administration

<b>Therapy:</b>	<b>Tysabri™<sup>3</sup> (natalizumab)</b>
Dose	300 mg
Route of injection	Intravenous (IV) infusion by a healthcare professional
Injection frequency	Every 4 weeks
Injection time and monitoring	Medication is infused over 1 hour at a certified infusion clinic. The individual must be observed for 1 hour after the infusion is complete.
Preparation required for administration	Yes. Must be administered by a healthcare professional at a certified infusion clinic.

# Possible side effects

## What side effects might I experience?

Like other treatments for MS, natalizumab can have side effects. Some of the associated side effects are manageable with the correct education and support, while other potential side effects may require supervision by your physician.

**Natalizumab:** The most common side effects are:

- Infusion-related reactions including headache, dizziness, fatigue, itchiness or hives.<sup>3</sup>

## Incidence of the most common side effects of natalizumab

Therapy:	Tysabri™ <sup>3</sup>
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Infusion-related reactions	23%
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Other possible side effects are urinary tract infections, pneumonia and hypersensitivity reactions such as anaphylaxis.<sup>3</sup>

Natalizumab is generally recommended for MS patients who have had an inadequate response to, or are unable to tolerate, other therapies for MS, due to reports of a rare brain infection called progressive multifocal leukoencephalopathy (PML) occurring in patients who have been given natalizumab. PML can cause disability or death. The absolute risk for PML in patients treated with natalizumab cannot be precisely estimated and factors that might increase an individual's risk for PML have not been identified.<sup>3</sup>



In some people taking natalizumab, the body may identify the medication as a foreign substance, and react by producing antibodies to defend itself against this foreign substance. These antibodies are called anti-natalizumab antibodies. Anti-natalizumab antibodies are associated with decreased effectiveness of the medication and increase the incidence of hypersensitivity reactions.<sup>3</sup>

The majority of people treated with natalizumab do not develop anti-natalizumab antibodies.<sup>3</sup>

## Depression

Depression is common in people with MS; individuals may experience depression before diagnosis. Therefore, it is important to remember that because depression is common in MS, it may not be related to DMD treatment. Regardless of the cause, if you have symptoms of depression, you should tell your doctor or nurse right away.

## Taking control of MS

Early treatment with immunomodulators is recommended to alter the course of MS and maintain ability.<sup>2</sup> Those who begin treatment early and remain on treatment can minimize the risk of disability and increase their chances of maintaining a more normal and healthy lifestyle.<sup>11</sup> Be a partner in your own care, ask questions, get informed and take control of your treatment and your life.

# Glossary

**Antibody** – Any of a large number of proteins of high molecular weight that are produced normally by specialized B cells after stimulation by an antigen and act specifically against the antigen in an immune response.

**Inflammation** – A tissue's response to injury, characterized by the mobilization of immune cells, swelling, and fluid accumulation.

**Monoclonal** – produced by, being, or composed of cells derived from a single cell.

**MRI (Magnetic resonance imaging)** – A scanner that produces detailed pictures of the brain and spinal cord.

**Nerve fibre damage** – Damage to myelin and/or axons, which ultimately leads to disability.

**Pseudo-relapse** – A temporary flare-up of new or existing symptoms due to fever, infection, or acute illness, that disappears once the stressor is removed.

**Remission** – When symptoms of MS subside completely or partially for a period of time.

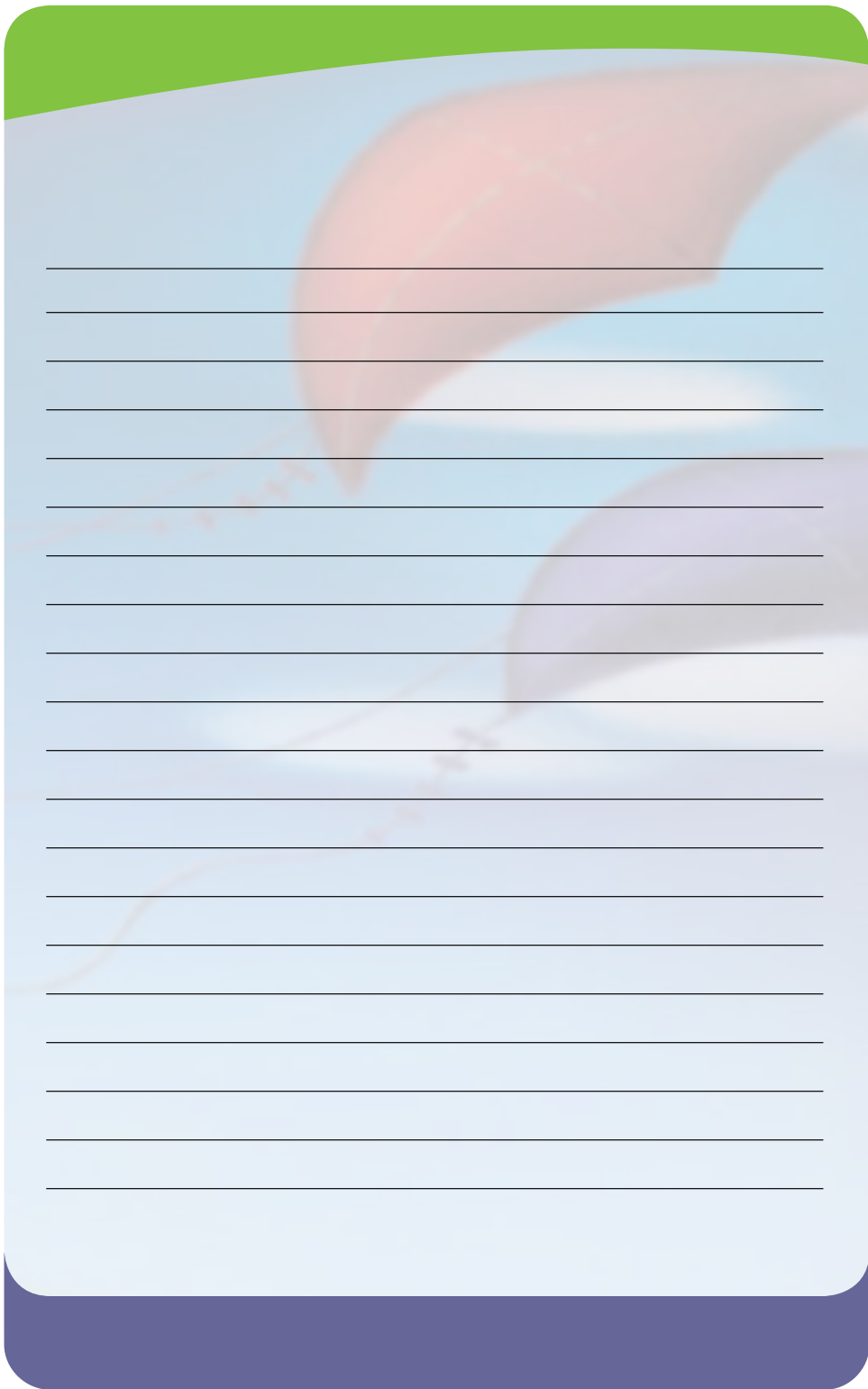
**Remyelination** – The repair of damaged myelin.

## For More Information

For more information about your MS, the following resources may be of interest:

1. Holland, Nancy J. *Multiple Sclerosis: A Guide for the Newly Diagnosed* (2<sup>nd</sup> Ed.) New York: Demos Medical Publishing Inc., 2002.
2. O'Connor, Paul. *Multiple Sclerosis: The Facts You Need* (3<sup>rd</sup> Ed.) Toronto: Key Porter Books, 2005.
3. Living with MS Website.  
Available at: [www.livingwithms.ca](http://www.livingwithms.ca)





To find out more about how you can  
live well with MS, visit [www.livingwithms.ca](http://www.livingwithms.ca)

1. MS Society of Canada. Accessible at [www.mssociety.ca](http://www.mssociety.ca).
2. Oger, J., Freedman, M. Consensus Statement of the Canadian MS Clinics Network on: The use of disease modifying agents in multiple sclerosis. *CJNS* 1999;26(4):274-275.
3. Tysabri™ Product Monograph. Biogen Idec Canada Inc. January 2009.
4. Avonex® Product Monograph. Biogen Idec Canada Inc. April 2006.
5. Rebif® Product Monograph. EMD Serono Canada Inc. October 2008.
6. Betaseron® Product Monograph. Bayer Canada Inc. November 2008.
7. Copaxone® Product Monograph. Teva Neuroscience. April 2009.
8. Giovannoni, G., Barbarash, O., Casset-Semanaz, F., et al. Safety and immunogenicity of a new formulation of interferon  $\beta$ -1a (Rebif® New Formulation) in a Phase IIIb study in patients with relapsing multiple sclerosis: 96-week results. *Mult Scler* 2009;15(2):219-228.
9. Sorensen, P.S., et al. Clinical importance of neutralizing antibodies against interferon beta in patients with relapsing remitting multiple sclerosis. *Lancet* 2003;362:1184-1191.
10. Edgar, C. et al. Lipoatrophy in patients with multiple sclerosis on glatiramer acetate. *CJNS* 2004;31(1):58-63.
11. Goodin, D.S., Frohman, E.M., Garmany, G.P. Jr, et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002;58(2):169-178