The information in this edition of Volume 2 was last updated in August 2015. The treatments described are: Aubagio®, Avonex®, Betaseron®, Copaxone®, Extavia®, Gilenya®, Glatopa™ (a generic equivalent of Copaxone), Lemtrada®, Novantrone®, Plegridy®, Rebif®, Tecfidera® and Tysabri®. Check nationalMSsociety.org/treatments for the most up-to-date list.

The Multiple Sclerosis Emerging Therapies Collaborative — which includes the MS Coalition, the American Academy of Neurology, the Veterans Administration (VA) Multiple Sclerosis Centers of Excellence East and West, and Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) — provides timely, evidence-based information about emerging therapies for people affected by multiple sclerosis (MS) and healthcare professionals. The Collaborative’s goal is to promote optimal, personalized treatment by facilitating effective doctor-patient communication and collaborative decision-making. ms-coalition.org/EmergingTherapies.
Most people recently diagnosed with MS are interested in learning as much as possible about the types of treatments that are available. Later in this series, Volume 4 (Treating Yourself Well) will talk about ways to manage symptoms and support your overall health. Your physician may already have recommended some of these strategies to you. This volume includes information about the disease-modifying agents for MS: those treatments that have been shown to alter the rate and/or extent of disease activity and progression.

While you may be alarmed to hear that some of these medications require injections or infusions, we hope that this volume will help alleviate your fears and provide you with the information you need to be an informed partner in making treatment decisions with your physician. Although this volume of Knowledge Is Power cannot tell you which medication is best for you, it will provide basic information to help you talk more comfortably with your healthcare providers.

“What can I expect from these medications? Will I feel better? How do I know which is best for me?”
Changing the Course of MS

Since 1993, the U.S. Food and Drug Administration (FDA) has approved many medications for use in multiple sclerosis. These medications make it possible to change the course of MS by reducing the frequency of relapses, reducing inflammation in the central nervous system and — to some degree — delaying the progression of disability.

These medications do not cure MS, and they’re not designed to provide relief from current symptoms — in fact, the effects on the disease may not be immediately apparent. However, each of these medications has been shown in placebo-controlled, double-blind clinical trials to provide significant benefit for people with relapsing forms of MS (including relapsing-remitting MS, progressive-relapsing MS and secondary-progressive MS in those individuals who continue to have relapses). To date, no medications have yet been shown to be effective for the treatment of primary-progressive MS.

Most of the medications are delivered by self-injection, three are oral, and three are delivered by intravenous (into the vein) infusion.

All of the available disease-modifying medications are approved by the FDA for use in relapsing forms of MS. None of these medications are approved for use during
pregnancy or breastfeeding. It is important to discuss with one’s healthcare provider how long before trying to conceive a woman must stop each of these medications.

**Injectable Medications**

All of the injectable medications are considered first-line treatment options — which means that the FDA has approved them for use in MS without requiring or recommending that other medications be tried first.

Interferon beta, which is one of several kinds of interferon, was the first type of disease-modifying treatment to be approved for use in MS. Interferons are proteins that are normally produced by cells in the immune system in response to viral infections and other conditions. They were named for their ability to interfere with viruses that are multiplying in the body. Interferon beta has a variety of effects on the immune system, including a reduction in those immune responses that cause inflammation in MS. The interferon beta medications that have been approved by the FDA are Avonex®, Betaseron®, Extavia®, Plegridy® and Rebif®. Each is manufactured through the use of recombinant DNA technology.

All of the interferon medications should be used with caution by any person with a history of depression, liver
or heart problems, epilepsy, thyroid problems, or blood problems, so be sure to discuss your medical history with your physician before starting any of these medications. Because of the potential of the interferon medications to affect the functioning of the liver and thyroid gland, and to alter the levels of white blood cells, red blood cells and platelets in a person’s system, periodic blood tests are recommended to monitor for these problems.

**Avonex® (interferon beta-1a)**

**Approval by the FDA**

Avonex (Biogen) is approved by the FDA for the treatment of relapsing forms of MS. In addition, Avonex has been shown to be an effective treatment for people who have experienced their first clinical episode of MS-like symptom(s) and have brain lesions on magnetic resonance imaging (MRI) that are consistent with MS (referred to as clinically isolated syndrome) but have not yet met the criteria for a definite MS diagnosis.

Avonex is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.
Clinical Outcomes

Avonex has been shown in clinical trials to slow progression of disability and to reduce the number of relapses and the number of new lesions on MRI. Avonex has also been shown to delay the time to a second clinical episode (and therefore a confirmed diagnosis of MS) in people with a first neurological event consistent with central nervous system inflammation/demyelination also known as clinically-isolated syndrome.

Route of Delivery and Side Effect Profile

This medication is given by intramuscular (directly into the muscle) injection once a week. An autoinjector device is available for injections.

The most common side effects of Avonex are flu-like symptoms that gradually diminish over time for most people. Injection site reactions are rare.

Betaseron®; Betaferon® in Canada and Europe (interferon beta-1b)

Approval by the FDA

Betaseron (Bayer HealthCare Pharmaceuticals Inc.) is approved for the treatment of relapsing forms of multiple sclerosis.
In addition, Betaseron has been shown to be an effective treatment for individuals who have experienced their first clinical episode and have MRI-detected brain lesions that are consistent with MS (clinically-isolated syndrome), but have not yet met the criteria for a diagnosis of MS.

Betaseron is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

**Clinical Outcomes**

Betaseron has been shown in clinical trials to reduce the frequency and severity of relapses and the number of new lesions on MRI, as well as to slow the progression of disability. Betaseron has also been shown to delay the time to a second clinical episode (and therefore a confirmed diagnosis of MS) in those with a clinically-isolated syndrome.

**Route of Delivery and Side Effect Profile**

This medication is injected *subcutaneously* (under the skin) every other day. An autoinjector device is available for the injections.

The most frequent side effects are flu-like symptoms that gradually diminish over time for most people. Some patients also experience injection site reactions consisting of pain, redness, inflammation and occasional tissue breakdown.
Extavia® (interferon beta-1b)

Approval by the FDA

Extavia (Novartis Pharmaceuticals) is identical to Betaseron, however it is sold under a different brand name. Like Betaseron, it is approved for use in all relapsing forms of MS and has been shown to be an effective treatment for individuals who have experienced a clinically-isolated syndrome.

Extavia is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

Clinical Outcomes

Because Extavia is the same formulation as Betaseron, no additional clinical trials were required. The expected benefits are identical.

Route of Delivery and Side Effect Profile

Identical to Betaseron

Plegridy® (peginterferon beta-1a)

Approval by the FDA

Plegridy (Biogen) is approved for the treatment of relapsing forms of MS.
Plegridy is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

**Clinical Outcomes**

Plegridy has been shown in a clinical trial to reduce the rate of relapses and the number of new lesions on MRI, as well as to reduce the risk of disability progression.

**Route of Delivery and Side Effect Profile**

Plegridy is a pegylated form of interferon beta-1a, which means that it has been chemically modified to allow its effects to last longer in the body and to reduce the frequency of injections. The medication is injected subcutaneously every 14 days. An autoinjector device is available for the injections.

The most frequent side effects are flu-like symptoms. Some patients also experience injection site reactions consisting of pain, redness, inflammation and occasional tissue breakdown.

**Rebif® (interferon beta-1a)**

**Approval by the FDA**

Rebif (EMD Serono, Inc./Pfizer, Inc.) is approved by the FDA for the treatment of relapsing forms of MS.

Rebif is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.
Clinical Outcomes

Rebif has been shown to reduce the number and frequency of relapses and the number of new lesions on MRI, as well as to slow the progression of disability.

Route of Delivery and Side Effect Profile

This medication is injected subcutaneously three times per week. An autoinjector device is available for the injections.

The most frequent side effects are flu-like symptoms (fever, chills, fatigue, achiness) that gradually diminish over time for most people. Some patients also experience injection site reactions consisting of pain, redness, inflammation and occasional tissue breakdown.

Additional information about the interferon medications (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from each manufacturer’s patient support line (see pages 36-42), or by linking to the FDA Medication Guide found on each medication’s website: **Avonex.com, Betaseron.com, Extavia.com, Plegridy.com, Rebif.com**. Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.
Copaxone® (glatiramer acetate)

Copaxone (Teva Neuroscience), and a generic equivalent of this medication called Glatopa™ (Sandoz, a Novartis company) are the only non-interferon injectable medications. Glatiramer acetate is a synthetic compound made up of the four amino acids (the building blocks of protein) that are found in myelin. Both Copaxone and Glatopa are thought to decrease the immune system’s production of harmful, pro-inflammatory cells and increase the production of beneficial or anti-inflammatory cells that work to reduce inflammation in the central nervous system (CNS).

Approval by the FDA

Copaxone and Glatopa are both approved by the FDA for the treatment of relapsing forms of MS.

Neither Copaxone nor Glatopa is recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

Clinical Outcomes

Copaxone has been shown to reduce the frequency of MS relapses, as well as the number and volume of brain lesions on MRI. Copaxone has also been shown to delay the time to a second clinical episode (and therefore a confirmed diagnosis of MS) in those with a clinically isolated syndrome.
The FDA has determined that Glatopa is equivalent to the 20 mg dose of Copaxone that is taken daily; Glatopa is not equivalent to the 40 mg dose of Copaxone that is taken three times per week.

**Route of Delivery and Side Effect Profile**

Copaxone is delivered daily (20 mg) or three times per week (40 mg) by subcutaneous injection. Glatopa is delivered daily (20 mg) by subcutaneous injection.

Injection site reactions including pain, redness, inflammation and occasional tissue breakdown are the most common side effects of Copaxone and Glatopa. Some people taking these medications also develop tissue loss (lipoatrophy) around injection sites, which is usually permanent and may limit the long-term use of this medication.

On rare occasions, some people taking Copaxone or Glatopa also experience a brief post-injection reaction involving shortness of breath, flushing and chest tightening that subsides spontaneously after a few minutes. This post-injection reaction is believed to have no lasting consequences.

Additional information about Copaxone (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 38), or at [Copaxone.com](http://Copaxone.com) (see page 6 of the FDA Prescribing Information). Since new
trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.

All of the injectable medications except Glatopa and Plegridy are also approved by Health Canada.

**Oral Medications**

Three oral disease-modifying therapies are now available to treat MS. Like the injectable medications, these oral medications are also considered first-line treatment options by the FDA. However, prescribers (physicians and nurse practitioners) may differ in their use of injectable or oral options for people who are newly-diagnosed with MS. The optimal first-line therapy is best decided after a thorough discussion between each patient and prescriber of the person’s individual’s needs and circumstances, and including the coverage offered by the person’s insurance provider.

**Aubagio® (teriflunomide)**

Aubagio (Genzyme, a Sanofi company) is a novel oral compound that inhibits the function of rapidly dividing immune cells that have been implicated in MS. It can inhibit a key enzyme that is needed by white blood cells (lymphocytes)
— which reduces the proliferation of T and B immune cells that are active in MS and inhibits the production of immune messenger chemicals by T cells. Reducing immune activity in this way reduces damage to nerve cells.

**Approval by the FDA**

Two doses of Aubagio — 7 mg and 14 mg daily — are approved by the FDA for adults with relapsing forms of MS.

Aubagio is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing. Before conceiving a child, both men and women who are taking Aubagio should stop taking the medication and undergo a rapid elimination protocol to remove the medication from their bodies (See Managing the Risks Associated with Aubagio on page 14).

**Clinical Outcomes**

Aubagio has been shown to reduce the average number of MS relapses and disease activity on MRI scans in comparison to placebo. The higher dose has also been shown to slow progression of disability.

**Route of Delivery and Side Effect Profile**

Aubagio (at either the 7 mg or 14 mg dose) is taken orally in pill form, once daily. The most common side effects in
the clinical trials of Aubagio were abnormal liver tests, hair thinning (alopecia), diarrhea, flu, nausea, and burning or prickling feelings in the skin (paresthesias).

Aubagio can cause serious side effects, including:

- Severe liver problems that may lead to death
- Damage to a developing fetus or fetal death
- A decrease in white blood cells that can increase a person’s risk of infection and make it unsafe to receive certain types of vaccination during treatment and for six months after stopping the medication
- Kidney problems and related elevation of potassium in the blood
- Skin problems such as redness and peeling
- New or worsening breathing problems
- High blood pressure

Managing the Risks Associated with Aubagio

Aubagio remains in the blood for up to two years after treatment is stopped. If necessary, procedures are available to remove the medication from the body more rapidly.

Before starting Aubagio, a person should be given a blood test (or have had one within the previous six months) to detect levels of liver enzymes and levels of blood cells. The FDA also
recommends a screening test for tuberculosis (tuberculin skin test) and a check of blood pressure. Women of childbearing age should also be given a pregnancy test.

Before conceiving a child, women and men should stop taking Aubagio, follow the recommended procedure to remove the medication from the body, and consult with their neurologist about when it is considered safe to attempt conception.

After treatment has been started, blood tests to detect liver enzymes should be done monthly for six months, followed by monitoring for any signs of liver damage. A person should also be monitored for signs of infection and have a periodic blood pressure check.

A person who develops symptoms of kidney problems (pain in the side or flank) or of elevated potassium levels (persistent nausea or a racing heartbeat) should have their kidney functions monitored.

Additional information about Aubagio (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 43), or by linking to the FDA Medication Guide found at Aubagio.com. Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.
**Gilenya® (fingolimod)**

Gilenya (Novartis Pharmaceuticals) is a new class of medication called a sphingosine 1-phosphate receptor modulator, which is thought to act by retaining certain white blood cells (lymphocytes) in the lymph nodes, thereby preventing them from circulating in the bloodstream and crossing the blood-brain barrier into the central nervous system (CNS). Preventing the entry of these cells into the CNS reduces inflammatory damage to nerve cells.

**Approval by the FDA**

Gilenya is approved by the FDA for adults with relapsing forms of MS.

Gilenya is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

**Clinical Outcomes**

Gilenya has been shown in clinical trials to reduce the relapse rate and the risk of disability progression in comparison to placebo, and to reduce brain lesion activity as measured by MRI. Gilenya has also been shown to be more effective in reducing the relapse rate and lesion activity on MRI compared to Avonex®.
Route of Delivery and Side Effect Profile

Gilenya is taken orally in capsule form, once daily. The most common side effects in the clinical trials of Gilenya were headache, influenza, diarrhea, back pain, abnormal liver tests and cough.

Gilenya may cause serious side effects, including:

- A slowed heart rate, particularly right after the first dose, which generally reaches the lowest point six hours after the dose is taken.
- An increased risk of infections, particularly infections caused by herpes viruses, caused by the lowering of the person’s white blood cell count.
- A problem with vision caused by swelling of the macula, which is located in the back of the eye.

Managing the Risks Associated with Gilenya

Any person who has experienced significant heart problems or a stroke within the past six months or who currently has an irregular or abnormal heartbeat should not take Gilenya. People with a past history of heart problems should be evaluated by their cardiologist before starting this medication. People who are taking heart medications or blood pressure medicines should review these with their MS provider prior to taking Gilenya.
The FDA has recommended that all patients be given an electrocardiogram (EKG) before starting treatment. They should be monitored in their doctor’s office for the first six hours after the initial dose of Gilenya to check for a decrease in heart rate, and then be given another EKG at the end of the six-hour period. If a significant decrease in heart rate occurs, monitoring should continue until the problem is resolved. In addition, patients are encouraged to contact their physician if they experience dizziness, unusual tiredness, or a slowed or irregular heartbeat. A person’s heart rate generally returns to normal after one month on treatment.

The physician may test a person’s blood prior to starting treatment in order to evaluate the level of white blood cells. A person with no history of chicken pox may be given a blood test for antibodies to determine if she or he has ever been exposed to the varicella zoster virus. If the test indicates no previous exposure, the FDA recommends that the varicella zoster vaccination be considered at least one month before starting treatment.

The FDA has also recommended vision testing prior to the first dose of Gilenya, after three to four months of treatment, and any time a person notices significant vision changes, including blurriness, shadows or a blind spot in the center of his or her vision, and/or sensitivity to light.
One case of progressive multifocal leukoencephalopathy (PML) has been confirmed in a person with MS who had been taking Gilenya for four years. Among people being treated for MS, PML has been most commonly reported in those taking Tysabri (see page 30 for more information about PML).

Additional information about Gilenya (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 44), or by linking to the FDA Patient Medication Guide found at Gilenya.com. Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.

**Tecfidera® (dimethyl fumarate)**

Tecfidera (Biogen), formerly known as BG-12, is dimethyl fumarate, a formulation that was developed specifically for use by people with multiple sclerosis. Although its exact mechanism of action is not known, Tecfidera is thought to inhibit immune cells and molecules, and may have antioxidant properties that could be protective against damage to the brain and spinal cord.
Approval by the FDA

Tecfidera is approved by the FDA for adults with relapsing forms of MS.

Tecfidera is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

Clinical Outcomes

Tecfidera has been shown to reduce the average number of MS relapses and the proportion of people who experience relapses, as well as reducing the number of lesions seen on MRI. Tecfidera may also slow disease progression.

Route of Delivery and Side Effect Profile

Tecfidera is an oral therapy contained in capsules taken two times per day. The most common side effects in the clinical trials of Tecfidera were flushing (which can create a sensation of heat or itching and a red blush on the skin) and gastrointestinal events (such as bloating, diarrhea, nausea and upper abdominal pain). These side effects usually begin during the first month of treatment, decreasing thereafter. The risk of flushing may be reduced by taking the medication with food or by taking non-enteric coated aspirin (up to 325 mg) 30 minutes prior to eating, and then taking Tecfidera.
Less common side effects in the clinical trials included rash, leakage of protein into the urine and elevation of liver enzymes. However, no cases of liver failure or kidney failure were reported in the clinical trials.

Tecfidera also reduced blood lymphocyte (white blood cell) counts (see Managing the Risks Associated with Tecfidera).

**Managing the Risks Associated with Tecfidera**

Tecfidera should not be taken by anyone with a known sensitivity to dimethyl fumarate or to any of the inactive ingredients used in this medication. Some people taking Tecfidera have experienced severe allergic reaction including anaphylaxis (itchy rash, difficulty breathing, and swelling of the throat) and angioedema (swelling under the skin in the throat and tongue).

Tecfidera may reduce lymphocyte counts significantly. Although no increase in serious infections was seen in the people with low lymphocyte counts in the clinical trials, one clinical trial participant who had been on the medication for four years developed progressive multifocal leukoencephalopathy (PML) after the trial’s completion and died. Among people being treated for MS, PML has been most commonly reported in those taking Tysabri (see page 30 for more information about PML).
Prior to starting this medication, the healthcare provider should check a recent (within six months) blood cell count to ensure that the person’s lymphocyte (white blood cell) count is within the normal range. The blood cell count should be repeated six months after the start of treatment and then every six months to a year thereafter — or more often if the doctor determines that it is necessary.

It is also recommended that healthcare providers consider withholding treatment for any person with a serious infection until the infection has resolved.

Additional information about Tecfidera (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 45), or by linking to the FDA Medication Guide found at Tecfidera.com (click on the link to “Patient Information”). Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.

All of the oral medications are also approved by Health Canada.
Infused Medications

Three of the approved disease-modifying medications are delivered by intravenous (into the vein) infusion. Of these, Tysabri is the only one considered to be a first-line treatment option. Although Novantrone is approved by the FDA to treat secondary progressive MS and worsening relapsing-remitting MS, it is seldom used today.

Lemtrada® (alemtuzumab)

Lemtrada (Genzyme, a Sanofi company) is a humanized monoclonal antibody that causes depletion of lymphocytes (types of white blood cells) that are known to play a key role in the MS disease process.

Approval by the FDA

Lemtrada is approved by the FDA to treat relapsing forms of MS, but because of the risks associated with this medication, the FDA recommends that it generally be reserved for people who have had an inadequate response to at least two other disease-modifying therapies.

Lemtrada is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.
Clinical Outcomes

Lemtrada has been shown in comparison trials with Rebif (interferon beta 1-a, subcutaneous) to be significantly more effective in reducing relapse rates than Rebif (interferon beta-1a) and in keeping a person relapse-free over a two-year period. Lemtrada may also reduce worsening of disability.

Route of Delivery and Side Effects Profile

Lemtrada is given by intravenous infusion for five consecutive days initially and for three consecutive days one year later.

The most common side effects include rash, headache, fever, nasal congestion, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, hives, itching, thyroid gland disorders, fungal infection, pain in joints, extremities and back, diarrhea, sinusitis, sore mouth and throat, tingling, dizziness, abdominal pain, flushing and vomiting. Infusion reactions (including nausea, hives, itching, insomnia, chills, flushing, fatigue, shortness of breath, changes in the sense of taste, indigestion, dizziness, pain) are also common during the infusion and for 24 hours or longer after the infusion is completed.

Managing the Risks Associated with Lemtrada

Lemtrada poses significant risks for serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia (ITP - a rare bleeding condition) and anti-glomerular basement
membrane disease (which can damage the kidneys) and thyroid disorders. Lemtrada also increases a person’s risk of malignancies (including thyroid cancer, melanoma, and blood cancers). To help minimize these risks as much as possible, the FDA has made the following recommendations for pre-treatment screening and careful monitoring during and after treatment:

- Ensuring that a person has been vaccinated for, or has antibodies to the varicella zoster virus
- Checking thyroid function before treatment and every three months until 48 months after the final infusion
- Testing blood counts, serum creatinine levels and urine before treatment and monthly thereafter until 48 months after the last infusion
- Examining the skin at the start of treatment and yearly thereafter to check for melanoma

In addition, people with an active infection should delay treatment until after the infection is controlled, and avoid any live-virus vaccine after a course of treatment with Lemtrada.

Serious and life-threatening infusion reactions (including swelling in the mouth or throat, trouble breathing, weakness, dizziness, fast, slow or irregular heartbeat, chest pain, rash) can occur with Lemtrada. To minimize the risks associated with infusion reactions, corticosteroids are given immediately before the infusion on the first three days of each treatment course.
Because of these risks, Lemtrada is only available from certified prescribers and pharmacies, and people taking the medication, as well as the healthcare facility administering the medication, must be enrolled in a Risk Evaluation and Mitigation Strategy (REMS) program to ensure that all the required screening and monitoring requirements are followed in a timely way.

Additional information about Lemtrada (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 46), or by linking to the FDA Medication Guide found at Lemtrada.com. Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.

**Novantrone® (mitoxantrone for injection concentrate)**

Novantrone (EMD Serono, Inc.) is a potent treatment that suppresses the immune system. It was previously approved only for use in one type of leukemia and certain forms of prostate cancer. Novantrone acts by slowing the division of cells and altering other immune cells and substances.
Approval by the FDA

Novantrone is approved by the FDA to reduce neurologic disability and/or the frequency of clinical relapses in patients with secondary-progressive MS (with or without relapses), progressive-relapsing MS or worsening relapsing-remitting MS. It is not approved for use in primary-progressive MS and is rarely, if ever, used as an initial treatment.

Novantrone is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

Clinical Outcomes

Novantrone has been shown to slow progression of disability, reduce frequency of relapses, and reduce accumulation of new brain lesions as shown on MRI.

Route of Delivery and Side Effects Profile

Novantrone is administered via intravenous infusion, once every three months. The short-term side effects, which can include nausea, hair loss, urinary tract infections and menstrual disorders, are manageable and reasonably well tolerated.

Novantrone may cause permanent infertility. In addition, Novantrone increases a person’s risk of heart damage and secondary acute myelogenous leukemia (AML). The risk of AML is higher for those people who have previously been treated with certain types of chemotherapy medications.
Managing the Risks Associated with Novantrone

Cardiac complications from Novantrone can occur at any time, but is more likely to be seen after multiple doses. Because of its potential long-term impact on cardiac function, the FDA cautions that the medication should be used only in those with normal heart function, and that cardiac monitoring should continue for the duration of the treatment and after the treatment is completed.

It is further recommended that the total lifetime dose of Novantrone be limited to minimize cardiac problems. As a result, most people will receive a maximum of 8 to 12 doses over two to three years. The FDA also recommends yearly cardiac evaluations after dosing of Novantrone is completed to monitor for late occurring cardiac problems.

Additional information about Novantrone (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867 or from the FDA Medication Guide for Novantrone at [http://ntl.MS/mitoxantrone](http://ntl.MS/mitoxantrone). Since new trials are announced periodically, and additional information becomes available as trials are completed, it is important to check these resources on a routine basis.
Tysabri® (natalizumab)

Tysabri (Biogen) is a laboratory-produced monoclonal antibody that is designed to block the movement of potentially damaging immune cells from the bloodstream, across the blood-brain barrier, and into the brain and spinal cord. The medication inhibits this movement by attaching to alpha 4-integrin, a protein on the surface of immune T-cells that normally enables them to adhere to and pass through the blood-brain barrier. Because of this mode of action, Tysabri is called a selective adhesion molecule (or “SAM”) inhibitor.

Approval by the FDA

Tysabri is approved for all relapsing forms of MS. Because of risks associated with Tysabri, the FDA instructs prescribers to weigh potential benefits of this medication against these possible risks. The FDA further recommends that Tysabri should be used as a stand-alone treatment, and not in combination with any other disease-modifying treatment.

Tysabri is not recommended for women who are pregnant or trying to become pregnant, or for women who are nursing.

Clinical Outcomes

Tysabri has been shown to reduce the number and frequency of relapses and the number of new lesions on MRI, as well as to slow the progression of disability.
Route of Delivery and Side Effect Profile

Tysabri is delivered by monthly intravenous infusion at approved infusion centers. The most common side effects associated with the monthly infusions include headache, pain in the arms or legs, fatigue, urinary tract infections, lung infections, vaginitis, joint pain, depression, diarrhea and pain in the stomach area.

Managing the Risks Associated with Tysabri

Tysabri increases a person’s risk for a rare brain infection called progressive multifocal leukoencephalopathy (PML), which usually results in severe disability or death. Over the past several years, research results have enabled clinicians to estimate the risk of PML. A blood test to detect antibodies to the virus that causes PML (JC virus) is available and recommended to be obtained at regular intervals while someone is on treatment with Tysabri. A positive JC virus antibody result increases one’s risk of developing PML. Additional risk factors for the development of PML include duration of Tysabri treatment beyond 2 years and previous use of chemotherapy drugs. Because of the risk of PML, Tysabri is available only through a special distribution program called the TOUCH® Prescribing Program.

The medication can only be prescribed and delivered by physicians, infusion centers and pharmacies that are registered with the program. And only those patients who are enrolled in
the program, and meet all the conditions set by the program, can receive this medication. Prior to starting treatment with Tysabri, and before each infusion, people will be evaluated at the infusion center to ensure that they are still appropriate candidates for this medication.

In rare instances, Tysabri has also been associated with severe liver damage, even after a single dose. It is recommended that any person taking this medication have periodic blood tests to monitor liver functions and any signs of liver damage (yellowing of the skin and eyes [jaundice] unusual darkening of the urine, nausea, feeling tired or weak, and vomiting) should be reported immediately to one’s physician.

Infections of the brain and spinal cord (encephalitis) and of surrounding tissues (meningitis), caused by herpes viruses, can also occur in people taking Tysabri. It is critical that any of the following be reported immediately to one’s physician – sudden fever, severe headache, confusion, drowsiness, vision change (especially light sensitivity), stiff neck or behavior change – so that treatment with an antiviral medication can be started.

Additional information about Tysabri (including results from clinical trials) can be obtained from the National MS Society by calling 1-800-344-4867, from the manufacturer’s patient support line (see page 49), or by linking to the FDA Medication Guide found at Tysabri.com. Since new trials are announced periodically, and additional information
becomes available as trials are completed, it is important to check these resources on a routine basis.

All of the infused medications except Novantrone are also approved by Health Canada.

The Importance of Early Treatment

Results from the clinical trials have led MS experts to conclude that early and ongoing treatment with a disease-modifying therapy can help prevent progression of disability and protect quality of life, thus prolonging a person’s ability to remain active, productive and engaged. Read more in a summary of the MS Coalition’s consensus at http://ntl.ms/coalitionDMTsummary. This means that any person who is having relapses or whose MRI scans show areas of inflammation should be considered a candidate for treatment with one of these medications.

Avonex®, Betaseron®, Copaxone® (and its generic form, Glatopa™), Extavia® and Rebif® have also been shown to delay the development of MS in people who have experienced their first clinical episode and have MRI-detected brain lesions consistent with MS. More information about the importance of early and ongoing treatment is available at nationalMSsociety.org/adherence.
The importance of early treatment has been reinforced by a growing understanding of the disease process in MS. Inflammation in the central nervous system causes damage not only to the protective coating (myelin) around the nerve fibers in the central nervous system, but also to the nerve fibers themselves.

This damage is visible on magnetic resonance imaging (MRI scans) as lesions or scars (also called plaques) and as damaged areas referred to as “black holes.” Since the damage to myelin and nerve fibers can be permanent, a primary goal of early treatment is to reduce the frequency and severity of relapses (also called attacks or exacerbations) during which inflammation and demyelination can occur.

Decisions concerning whether or when to begin treatment with one of the disease-modifying medications will best be made by you and your physician together. The factors to be taken into account in making these decisions include the disease course you are experiencing, each medication’s potential benefits and side effects, the route of delivery and frequency of dosing, and your personal priorities and lifestyle. The most important goal to keep in mind as you think through the various options is to find a treatment you can use comfortably and consistently until an even better treatment is identified.
Summary

The care and treatment of MS is in an exciting phase. Medications that have been shown to modify the course of the disease are shown in the tables below in alphabetical order. The tables on pages 36-42 list the injectable medications. The tables on pages 43-45 list the oral medications. The infusion options are shown in the tables on pages 46-49.

With treatment options comes the opportunity to educate yourself and participate with your physician in the decision-making process. Your best sources of additional information about these medications are your healthcare providers, the National MS Society and the pharmaceutical companies who distribute them. Most of these companies offer their customers information; training and support; and financial assistance for qualifying individuals who do not have prescription medication insurance coverage. See Patient Information and Financial Support Programs for each medication in the following tables.
Things to Think About

- According to MS experts, initiation of treatment is now advised for any person with a confirmed diagnosis of MS who has active symptoms or evidence of disease activity on his or her MRI scans. Treatment may also be considered for people who have experienced their first clinical episode and have MRI-detected brain lesions consistent with MS (clinically-isolated syndrome).

- By educating yourself about the route of delivery, possible benefits and potential side effects of each of these medications, you can be an informed partner in making treatment decisions.

- Your best sources of additional information about these medications are your healthcare providers, the National Multiple Sclerosis Society and the pharmaceutical companies who distribute the medications.

- As with all medications, it is important for women who are pregnant or wish to become pregnant to consult with their physicians about the use of any of these medications.
### Injectable Options to Treat Relapsing Forms of MS

#### Avonex®

<table>
<thead>
<tr>
<th><strong>Chemical Name</strong></th>
<th>interferon beta-1a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manufacturer/Distributor</strong></td>
<td>Biogen</td>
</tr>
<tr>
<td><strong>Approval</strong></td>
<td>1996 US; 1998 Can</td>
</tr>
<tr>
<td><strong>Frequency/Route of Delivery</strong></td>
<td>Weekly; intramuscular injection</td>
</tr>
<tr>
<td><strong>Common Side Effects</strong>*</td>
<td>Flu-like symptoms following injection, which lessen over time for many people</td>
</tr>
<tr>
<td><strong>Less Common Side Effects</strong></td>
<td>Depression, mild anemia, elevated liver enzymes, liver toxicity</td>
</tr>
</tbody>
</table>

#### Patient Information and Financial Support Programs

MS ActiveSource®
800-456-2255
avonex.com
msactivesource.com
Betaseron®

Chemical Name
interferon beta-1b

Manufacturer/Distributor
Bayer Healthcare Pharmaceuticals Inc.

Approval

Frequency/Route of Delivery
Every other day; subcutaneous injection

Common Side Effects*
Flu-like symptoms following injection, which lessen over time for many people; injection site reactions

Less Common Side Effects
Depression, elevated liver enzymes, low white blood cell counts

Patient Information and Financial Support Programs
BETAPLUS®
800-788-1467
betaseron.com/betaplus
**Copaxone®**

**Chemical Name**
glatiramer acetate

**Manufacturer/Distributor**
Teva Neuroscience

**Approval**
1996 US; 1997 Can

**Frequency/Route of Delivery**
Daily (20mg) OR three times per week (40mg); subcutaneous injection

**Common Side Effects***
Injection site reactions

**Less Common Side Effects**
A reaction immediately after injection which includes anxiety, chest tightness, shortness of breath, and flushing. This lasts 5–10 minutes and has no known long-term effects.

**Patient Information and Financial Support Programs**
Shared Solutions®
800-887-8100
copaxone.com/AboutSharedSolutions.aspx
Extavia®

Chemical Name
interferon beta-1b

Manufacturer/Distributor
Novartis Pharmaceuticals

Approval
2009 US; 2009 Can

Frequency/Route of Delivery
Every other day; subcutaneous injection

Common Side Effects*
Flu-like symptoms following injection, which lessen over time for many people; injection site reactions

Less Common Side Effects
Depression, elevated liver enzymes, low white blood cell counts

Patient Information and Financial Support Programs
Extavia® Go Program™
866-398-2842
extavia.com
Patient Assistance NOW
patientassistancenow.com
800-245-5356
### Glatopa™

**Chemical Name**
glatiramer acetate

**Manufacturer/Distributor**
Sandoz – a Novartis company

**Approval**
2015 US

**Frequency/Route of Delivery**
Daily (20mg); subcutaneous injection

**Common Side Effects***
Injection site reactions

**Less Common Side Effects**
A reaction immediately after injection which includes anxiety, chest tightness, shortness of breath, and flushing. This lasts 5–10 minutes and has no known long-term effects.

**Patient Information and Financial Support Programs**
GlatopaCare™
855-452-8672
glatopa.com/glatopa_care
### Plegridy®

**Chemical Name**
peginterferon beta-1a

**Manufacturer/Distributor**
Biogen

**Approval**
2014 US

**Frequency/Route of Delivery**
Every 14 days; subcutaneous injection

**Common Side Effects**
Flu-like symptoms following injection, injection site reactions

**Less Common Side Effects**
Depression, mild anemia, elevated liver enzymes, liver toxicity

**Patient Information and Financial Support Programs**
MS ActiveSource®
800-456-2255
plegridy.com
msactivesource.com
**Rebif®**

**Chemical Name**
interferon beta-1a

**Manufacturer/Distributor**
EMD Serono, Inc./Pfizer, Inc.

**Approval**
1998 US; 2002 Can

**Frequency/Route of Delivery**
Three times per week; subcutaneous injection

**Common Side Effects***
Flu-like symptoms following injection, which lessen over time for many people; injection site reactions

**Less Common Side Effects**
Depression, elevated liver enzymes, low white blood cell counts

**Patient Information and Financial Support Programs**
MS Lifelines®
877-447-3243
rebif.com
mslifelines.com
Oral Options to Treat Relapsing Forms of MS

Aubagio®

Chemical Name
teriflunomide

Manufacturer/Distributor
Genzyme, a Sanofi company

Approval
2012 US; 2013 Can

Frequency/Route of Delivery
Every day; pill taken orally

Common Side Effects*
Diarrhea, abnormal liver tests, nausea, flu, hair thinning, burning or tingling sensations

Less Common Side Effects
Lowered levels of white blood cells, which can increase the risk of infections; increase in blood pressure; severe liver damage; See page 14 for warnings.

Patient Information and Financial Support Programs
MS One to One®
855-676-6326
MSOnetoOne.com
Gilenya®

Chemical Name
fingolimod

Manufacturer/Distributor
Novartis Pharmaceuticals

Approval
2010 US; 2011 Can

Frequency/Route of Delivery
Every day; capsule taken orally

Common Side Effects*
Headache; flu, diarrhea, back pain, liver enzyme elevations, cough

Less Common Side Effects
Slowed heart rate following first dose, infections, swelling in the eye; See page 17 for warnings.

Patient Information and Financial Support Programs
Gilenya® Go Program™
800-445-3692
gilenya.com
patientassistancecom
**Tecfidera®**

**Chemical Name**
dimethyl fumarate

**Manufacturer/Distributor**
Biogen

**Approval**
2013 US; 2013 Can

**Frequency/Route of Delivery**
Twice daily; capsule taken orally

**Common Side Effects***
Flushing (sensation of heat or itching and a blush on the skin), gastrointestinal issues (nausea, diarrhea, abdominal pain)

**Less Common Side Effects**
Rash, protein in the urine, elevated liver enzymes; reduction in blood lymphocyte (white blood cell) counts; See page 21 for warnings.

**Patient Information and Financial Support Programs**
MS ActiveSource®
800-456-2255
tecfidera.com
msactivesource.com
Additional Approved Treatment Options

**Lemtrada®**

**Chemical Name**
alemtuzumab

**Manufacturer/Distributor**
Genzyme, a Sanofi company

**Approval**
2014 US; 2014 Can

**Frequency/Route of Delivery**
Five days in a row initially and three consecutive days one year later, by infusion in a medical facility.

**Common Side Effects***
Rash, headache, fever, nasal congestion, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, hives, itching, thyroid gland disorders, fungal infection, pain in joints, extremities and back, diarrhea, sinusitis, sore mouth and throat, tingling, dizziness, abdominal pain, flushing and vomiting. Infusion reactions (during infusions and for 24 hours or longer following an infusion) are also common; See page 24 for warnings.
Less Common Side Effects
Cough, chills, influenza, skin inflammation, indigestion, blood in the urine, shortness of breath, racing heartbeat, anxiety, muscle weakness, bronchitis, chest pain, muscle spasms, muscle pain, decreased lymphocyte (types of white blood cell) count, redness of the skin, swelling in upper or lower extremities, nosebleeds, neck pain and abnormal uterine bleeding.
In addition serious and life-threatening side effects can occur with Lemtrada; See page 24 for warnings.

Patient Information and Financial Support Programs
MS One to One®
855-676-6326
MSOnetoOne.com
Novantrone®

**Chemical Name**
mitoxantrone

**Manufacturer/Distributor**
EMD Serono, Inc.

**Approval**
2000 US

**Frequency/Route of Delivery**
Four times a year by IV infusion in a medical facility. Lifetime cumulative dose limit of approximately 8–12 doses over two to three years

**Common Side Effects***
Blue-green urine 24 hours after administration, infections, bone marrow suppression (fatigue, bruising, low blood cell counts), nausea, hair thinning, bladder infections, mouth sores. Patients must be monitored for serious liver and heart damage; See page 28 for more information on side effects and risks.

**Patient Information and Financial Support Programs**
No patient support program at this time
**Tysabri**

**Chemical Name**
natalizumab

**Manufacturer/Distributor**
Biogen

**Approval**
2006 US; 2006 Can

**Frequency/Route of Delivery**
IV infusion every four weeks in a registered infusion facility

**Common Side Effects**
Headache, fatigue, urinary tract infections, depression, lower respiratory tract infections, joint pain and chest discomfort

**Less Common Side Effects**
Allergic or hypersensitivity reactions within two hours of infusion (dizziness, fever, rash, itching, nausea, flushing, low blood pressure, difficulty breathing, chest pain); See page 30 for more information on side effects and risks associated with PML.

**Patient Information and Financial Support Programs**
MS ActiveSource®
800-456-2255
tysabri.com
msactivesource.com
Additional Resources

Thousands of resources, pieces of information and shared experiences about MS are available in print and on the internet. Some of the information you come across may be strictly experiential, anecdotal, unsupported or even inaccurate. Always consider the source; ask your healthcare provider or the National MS Society to help you identify credible resources.

From the National MS Society

For answers to questions about MS and its management, contact the National MS Society at 1-800-344-4867 or visit the Society’s website at nationalMSsociety.org or the following topic-specific pages:

- Information for Those Newly Diagnosed
  nationalMSsociety.org/newlydiagnosed

- General Information about MS
  nationalMSsociety.org/aboutMS
Treatments Used in MS  
nationalMSsociety.org/treatments

MS Clinical Trials  
nationalMSsociety.org/clinicaltrials

Medications Used in MS  
nationalMSsociety.org/meds

Educational Videos  
nationalMSsociety.org/educationalvideos

The Society publishes many other resources about various aspects of MS. These resources are available online or call 1-800-344-4867 to request.

See the Publications Catalog that was mailed with Volume 1 of this series or visit nationalMSsociety.org/brochures

Books

Books from Demos Medical Publishing

Call 1-800-532-8663 or visit demoshealth.com 
(Enter titles in the search bar or click on “Shop for Health Books” and shop by condition at top of page.)


> Ch. 6: Miller A: Considering Options for Managing Relapses and the Disease Course.
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Early and ongoing treatment with an FDA-approved therapy can make a difference for people with multiple sclerosis. Learn about your options by talking to your healthcare professional and contacting the National MS Society at nationalMSsociety.org or 1-800-344-4867.
The National MS Society mobilizes people and resources so people affected by MS can live their best lives as we stop MS in its tracks, restore what has been lost and end MS forever. To fulfill this mission, the Society funds cutting-edge research, drives change through advocacy, facilitates professional education, and provides programs and services designed to help people with MS and their families move their lives forward.

nationalMSsociety.org

1-800-344-4867