

Disease-Modifying Therapies for MS



MS

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For some people, a diagnosis of multiple sclerosis (MS) is a relief, giving a name and a reason for a parade of strange symptoms. For others, a diagnosis of MS brings frightening images of a challenging future. Regardless of one's initial reactions, the diagnosis of MS is a life-changing event.

Even before the news can be fully absorbed, people with MS face decisions about taking a disease-modifying medication, including when to start treatment and which one of the many available options is best suited to their individual needs. Early and ongoing treatment with a U.S. Food and Drug Administration (FDA)-approved therapy can make a difference for people with MS. Learn about your options by talking to your healthcare professional and contacting the National MS Society at nationalMSSociety.org or 1-800-344-4867. This booklet outlines the issues to consider with one's healthcare provider when choosing a treatment and describes the resources available to support a person's efforts to start and continue treatment.

Disease-modifying therapies

Disease-modifying therapies (also called DMTs, disease-modifying medications or disease-modifying treatments) are a key component of comprehensive MS care, along with managing MS relapses (also called exacerbations or attacks), treating symptoms, and paying attention to one's overall health and wellness. The disease-modifying medications are the best strategy currently available to slow the natural course of MS. Even though these medications don't generally make a person feel better, they can be looked upon as an investment in the future.

Clinical studies have demonstrated that all of these medications:

- Reduce the frequency and severity of clinical attacks (also called relapses or exacerbations). An attack is defined as the worsening of an MS symptom or symptoms, and/or the appearance of new symptoms, which lasts at least 24 hours and is separated from a previous exacerbation by at least one month. In clinical trials comparing treatment versus inactive placebo, these agents reduced MS attacks by 28-68 percent.
- Reduce the development of new lesions (damaged/scarred or active disease areas) within the brain and spinal cord as seen on MRI

(magnetic resonance imaging). In clinical trials, most people receiving the active treatment were also found to have fewer, smaller or no new lesions on MRI scans.

- Appear to slow down the accumulation of disability. In clinical trials, some of these medications have been shown to delay disability progression.

Subsequent clinical investigation and clinical experience have indicated that early intervention with disease-modifying therapies may help to prevent permanent damage in the central nervous system (which is made up of the brain, spinal cord and optic nerves). Permanent damage to nerve fibers (axons) occurs early in MS in association with the destruction of myelin. Overall brain atrophy (shrinkage) can occur early in the disease, and damage can be ongoing even when a person has no symptoms and feels well.

For all of these reasons, the MS Coalition consensus on disease-modifying therapy emphasizes the importance of early and ongoing treatment as follows:

- Starting treatment with an FDA-approved disease-modifying therapy **as soon as possible** is recommended:
 - When a person has been diagnosed with relapsing MS
 - If a person has had a first episode of neurologic symptoms, MRI findings consistent with MS, and other possible causes have been ruled out
 - When an individual has been diagnosed with secondary progressive MS (SPMS) or primary progressive MS (PPMS) but experiences active disease (relapses and/or inflammatory changes on MRI)
- Treatment with any disease-modifying therapy should be continued indefinitely, **unless** any of the following occur (in which case a different disease-modifying therapy should be considered):
 - The individual and his or her healthcare provider determine that the treatment is not controlling the disease adequately
 - The side effects are intolerable
 - A person is unable to follow the recommended treatment regimen
 - A more appropriate treatment becomes available

None of these medications is approved by the FDA for women who are pregnant or plan to become pregnant, or who are breastfeeding. It is important for women to discuss their plans for pregnancy with their healthcare provider so that they can decide together the best and safest treatment plan. To read the MS Coalition consensus paper, visit <http://ntl.ms/coalitionDMTsummary>

Options

There are currently 14 disease-modifying medications approved by the FDA for use in relapsing forms of MS (which include secondary progressive MS for those people who continue to experience relapses and primary progressive MS for those people who experience one or more relapses following their diagnosis). Of these, one is also approved specifically for secondary-progressive MS. None of these medications is a cure and none will prevent recurring symptoms, such as fatigue or numbness. However, each of them has a proven record of effectiveness.

Unfortunately, no disease-modifying medication has yet been approved to treat primary-progressive MS — the type of MS that shows steady progression from the onset of symptoms.

The decision to take a disease-modifying therapy is best made through careful consideration of the disease course you are experiencing, your lifestyle and the known side effects and potential risks and benefits of each of the therapies. A full discussion with a knowledgeable healthcare professional is the best guide for your choice among the available options. Each person's body or disease can respond to these medications in different ways and the medication that is the best option for one person may not be the best option for another person. In addition, a medication that adequately controls your disease today may not do so in the future, and you may need to change to a different medication. Fortunately, today people have access to a variety of effective medications that work in different ways in the body.

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The following table presents important information about each of the medications, which are grouped by route of administration: injectable (intramuscular or subcutaneous), oral and intravenous (into the vein) infusion.

INJECTABLE TREATMENTS			
Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Avonex® (interferon beta-1a) Biogen	30 mcg intramuscularly (into a large muscle) once weekly	For the treatment of relapsing forms of MS to slow the accumulation of physical disability and reduce the frequency of clinical exacerbations, and for patients who have experienced a first clinical episode and have MRI features consistent with MS Approved: 1996 US; 1998 CAN Pregnancy Category C (see footnote, page 8)	Headache, flu-like symptoms (chills, fever, muscle pain, fatigue weakness), injection site pain and inflammation See warnings on page 12
Betaseron® (interferon beta-1b) Bayer Healthcare Pharmaceuticals Inc.	0.25 mg subcutaneously (under the skin) every other day	For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; and for patients who have experienced a first clinical episode and have MRI features consistent with MS Approved for RRMS: 1993 US; 1995 CAN Approved for SPMS: 1995 CAN Pregnancy Category C (see footnote, page 8)	Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness) following injection, headache, injection site reactions (swelling redness, pain), injection site skin breakdown, low white blood cell count See warnings on page 13

INJECTABLE TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Copaxone® (glatiramer acetate) Teva Neuroscience	20 mg subcutaneously every day, or 40 mg subcutaneously three times per week	For the treatment of relapsing forms of MS Approval: 1996 US; 1997 CAN Pregnancy Category B (see footnote, page 8)	Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain See warnings on page 13
Extavia® (interferon beta-1b) Novartis Pharmaceuticals	0.25 mg subcutaneously every other day	For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; and for patients who have experienced a first clinical episode and have MRI features consistent with MS Approval: 2009 US; 2009 CAN Pregnancy Category C (see footnote, page 8)	Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness) following injection, headache, injection site reactions (swelling redness, pain) See warnings on page 14
Glatopa™ (glatiramer acetate, generic equivalent of Copaxone 20 mg) Sandoz – a Novartis company	20 mg subcutaneously every day	For the treatment of relapsing forms of MS Approval: 2015 US Pregnancy Category B (see footnote, page 8)	Injection site reactions (redness, pain, swelling) See warnings on page 14

INJECTABLE TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Plegridy® (pegylated interferonbeta-1a) Biogen	125 mcg subcutaneously every 14 days	For the treatment of relapsing forms of MS Approval: 2014 US Pregnancy Category C (see footnote below)	Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness, headache, itching). Injection site reactions (swelling, redness, pain) See warnings on page 14
Rebif® (interferon beta-1a) EMD Serono, Inc / Pfizer, Inc	22 mcg or 44 mcg subcutaneously three times per week	For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations and delay the accumulation of physical disability Approval: 1998 US; 2002 CAN Pregnancy Category C (see footnote below)	Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness, headache), injection site reactions (redness, pain, swelling) See warnings on page 15

INJECTABLE TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Zinbryta™ (daclizumab) Biogen	150 mg once a month	<p>For the treatment of adult patients with relapsing forms of MS. The FDA indication includes a statement that this medication should generally be reserved for people who have had an inadequate response to two or more disease-modifying therapies</p> <p>Approval: 2016 US</p> <p>Pregnancy Category: None. (Pregnancy categories are not designated for drugs approved after 1/1/16) No adequate data in pregnant women; animal data suggest that use of this medication during pregnancy may pose risks to the developing fetus.</p>	<p>Colds, upper respiratory tract infections, rash, flu, rash, throat pain, bronchitis, eczema, depression, swollen lymph nodes, elevated liver enzymes</p> <p>See warnings on page 15</p>
<p>Category B: Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.</p> <p>Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</p>			

ORAL TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Aubagio [®] (teriflunomide) Sanofi Genzyme	7 mg or 14 mg pill once daily	For the treatment of relapsing forms of MS Approval: 2012 US; 2013 CAN Pregnancy Category X (see footnote below)	Headache, hair thinning, diarrhea, nausea, abnormal liver tests See warnings on page 16
Gilenya [®] (fingolimod) Novartis Pharmaceuticals	0.5 mg capsule once daily	For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability 2010 US; 2011 CAN Pregnancy Category C (see footnote below)	Headache, flu, diarrhea, back pain, liver enzyme elevations, sinusitis, abdominal pain, pain in extremities and cough See warnings on page 17
Tecfidera [®] (dimethyl fumarate) Biogen	120 mg capsule taken twice daily for one week, followed by 240 mg capsule taken twice daily thereafter	For the treatment of relapsing forms of MS 2013 US; 2013 CAN Pregnancy Category C (see footnote below)	Flushing (sensation of heat or itching and a blush on the skin), gastrointestinal issues (nausea, diarrhea, abdominal pain). See warnings on page 18

Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Category X: Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

INTRAVENOUS INFUSION TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Lemtrada® (alemtuzumab) Sanofi Genzyme	12 mg per day for five consecutive days, followed by 12 mg per day on three consecutive days one year later	For the treatment of relapsing forms of MS. The FDA indication includes a statement that this medication should generally be reserved for people who have had an inadequate response to two or more disease-modifying therapies Approval: 2014 US; 2014 CAN Pregnancy Category C (see footnote, page 11)	Rash, headache, fever, nasal congestion, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infections, hives, itching, thyroid gland disorders, fungal Infection, pain in joints, extremities and back, diarrhea, vomiting, flushing. 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 while the medication is being administered and for 24 hours or more after the infusion is over See warnings on page 19
No brand name available (mitoxantrone) Available only as a generic medication	12 mg/m ² every 3 months. Lifetime cumulative dose limit of approximately 8–12 doses over 2–3 years (140 mg/m ²).	For reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting MS Approval: 2000 US Pregnancy Category D (see footnote, page 11)	Nausea, hair loss, menstrual change, upper respiratory infection, urinary tract infection, mouth sores, irregular heartbeat, diarrhea, constipation, back pain, sinusitis, headache, blue-green urine See warnings on page 21

INTRAVENOUS INFUSION TREATMENTS

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA Approval	Most Common Side Effects
Tysabri® (natalizumab) Biogen	300 mg once every 28 days. Must take place in an approved infusion facility	Used as a monotherapy (not in combination with any other MS disease-modifying treatment or other immune suppressant drugs) for the treatment of patients with relapsing forms of multiple sclerosis. Tysabri increases the risk of PML, a rare and potentially brain infection Approval: 2006 US; 2006 CAN Pregnancy Category C (see footnote below)	Headache, fatigue, joint pain, chest discomfort, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea, and rash. See warnings on page 21

Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Category D: There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Managing side effects of disease-modifying therapies

Not everyone will experience every one of the side effects listed. Some adverse effects are common, and others are very infrequent — but may be serious. All of the side effects listed here occurred in at least 2-5 percent of participants in the clinical trials and were more frequent in the treatment groups than in the groups receiving placebo. Your healthcare provider can give you a better sense of how frequently problems occur with the specific agent he or she recommends for you and can guide you on how to manage any side effects that occur. The manufacturers' websites (page [25](#)) also give you information about the side effects you may experience.

Understanding the warnings in the FDA labeling information

In addition to the common side effects listed for each medication, the FDA lists Warnings and Precautions. In some instances, a warning is printed in a black box in the medication's label in order to call particular attention to it.

Injectable Medications

Avonex[®] warnings

The FDA prescribing information for Avonex (interferon beta-1a) includes the following warnings and precautions:

- Individuals with a history of depression, a seizure disorder or cardiac problems should be closely monitored while on this medication.
- All patients on this medication should have periodic liver function testing.
- Periodic blood testing is recommended to check for a possible reduction in infection-fighting blood cells, red blood cells, and cells that help blood to clot.
- Rare but significant allergic reactions have been reported to this medication.

- Increased risk of drug-induced autoimmune disorders has been reported with this medication.
- Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in people taking interferon medications. ([back to table, page 5](#))

Betaseron® warnings

The FDA prescribing information for Betaseron (interferon beta-1b) includes the following warnings and precautions:

- Individuals with a history of depression or a seizure disorder should be closely monitored while on this medication.
- Patients with congestive heart failure should be monitored for worsening of their cardiac symptoms.
- All patients on this medication should have baseline liver function testing and periodic testing thereafter.
- Rare but significant allergic reactions have been reported with this medication.
- Because skin infections or areas of severe skin damage can occur, injection sites should be rotated on a regular basis.
- Because this medication can lower the white blood cell count, monitoring with a complete blood count is recommended.
- Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in people taking interferon medications. ([back to table, page 5](#))

Copaxone® warnings

The FDA prescribing information for Copaxone (glatiramer acetate) includes the following warnings and precautions:

- Approximately 16 percent of people will experience an immediate post-injection reaction that includes at least two of the following: flushing, chest pain, palpitations, anxiety, shortness of breath, constriction of the throat and transient skin eruptions. These symptoms generally disappear spontaneously after about 15 minutes and have no long-term effects.

This post-injection reaction generally occurs after the first few months of treatment and may occur more than once in a given individual. Transient chest pain — without any long-term effects — may also occur one or more times, either as part of the post-injection reaction or separately.

- Permanent depressions under the skin at injection sites (lipoatrophy) can occur because of destruction of the fatty tissue. In addition, areas of severe skin damage can occur. For these reasons, careful rotation of injection sites is recommended so that no single area is injected more than one time per week. ([back to table, page 6](#))

Extavia® warnings

Because Extavia (interferon beta-1b) is identical to Betaseron® (interferon beta-1b), the FDA prescribing information for Extavia includes the same warnings. ([see Betaseron, page 13](#))

Glatopa™ warnings

Because Glatopa is the generic equivalent of Copaxone® (glatiramer acetate), the FDA prescribing information for Glatopa includes the same warnings. ([see Copaxone, page 13](#))

Plegridy® warnings

The FDA prescribing information for Plegridy (pegylated interferon beta-1a) includes the following warnings and precautions:

- All patients on this medication should have periodic liver function testing.
- Individuals with a history of depression, a seizure disorder, or cardiac problems should be closely monitored while on this medication.
- Periodic blood testing is recommended to check for a possible reduction in infection-fighting blood cells, red blood cells, and cells that help blood to clot.
- Because skin infections or areas of severe skin damage can occur, injection sites should be rotated on a regular basis.
- Rare but significant allergic reactions have been reported to this medication.

- Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in people taking interferon medications.
- Increased risk of drug-induced autoimmune disorders has been reported in people taking this medication. ([back to table, page 7](#))

Rebif® warnings

The FDA prescribing information for Rebif (interferon beta-1a) includes the following warnings and precautions:

- Individuals with a history of depression or a seizure disorder should be closely monitored while on this medication.
- All patients on this medication should have baseline liver function testing and periodic testing thereafter.
- Periodic blood testing is recommended to check for a possible reduction in infection-fighting blood cells, red blood cells, and cells that help blood to clots.
- Because injection site reactions and areas of severe skin damage can occur, injection sites should be rotated on a regular basis and the medication should not be injected into an affected area until the skin is completely healed.
- Rare but significant allergic reactions have been reported to this medication.
- Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in people taking interferon medications.
- Increased risk of drug-induced autoimmune disorders has been reported in people taking this medication. ([back to table, page 7](#))

Zinbryta™ warnings

The FDA prescribing information for Zynbryta (daclizumab) includes the following warnings and precautions:

- This medication can cause severe liver injury, including life threatening events. Liver function testing is recommended prior to starting treatment, monthly during treatment and for up to six months after the last dose.

- Immune-mediated disorders, including severe skin reactions, swollen lymph glands, non-infectious colitis, can occur.

Because of the risks associated with this medication, Zinbryta is only available through a Risk Evaluation and Mitigation Strategy (REMS) program called the Zinbryta REMS Programs. Prescribing physicians and nurse practitioners must be enrolled and trained; patients must be enrolled and comply with ongoing monitoring requirements; pharmacies must be certified and dispense only to enrolled patients. ([back to table, page 8](#))

Additional information about each of the injectable 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 page [25](#)), or by linking to the FDA Medication Guide found on each medication's website: [Avonex.com](#), [Betaseron.com](#), [Copaxone.com](#), [Extavia.com](#), [Glatopa.com](#), [Plegridy.com](#), [Rebif.com](#), [Zinbryta.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.

Oral Medications

Aubagio® warnings

The FDA prescribing information for Aubagio (teriflunomide) includes the following black box warnings and precautions:

- Aubagio can cause liver damage. A blood test to detect levels of liver enzymes should be given before starting the medication and then repeated monthly for six months, followed by monitoring for damage to the liver. In the event of significant liver problems, people should stop taking Aubagio immediately. Because Aubagio is known to remain in the blood for as long as two years after a person stops taking it, treatment regimens are available to remove the medication rapidly from the body.
- Aubagio can cause major birth defects for up to two years after the medication is discontinued. A woman should be given a pregnancy test prior to starting the medication and should use effective birth control while taking the medication. If she becomes pregnant accidentally, she should stop taking Aubagio immediately and undergo treatment to remove the medication rapidly from the body. Men who plan to father a

child should stop taking the medication and undergo treatment to remove the medication rapidly from the body before they and their partners try to conceive.

The prescribing information also contains the following additional warnings:

- Aubagio® can decrease a person's white blood cell count and increase the risk of infections. People should have a complete blood count prior to starting treatment and be monitored for infection while on treatment. People should also be tested for latent tuberculosis before starting treatment. A person who tests positive for tuberculosis should not begin taking Aubagio until the treatment for tuberculosis has been successfully completed.
- Aubagio can cause damage to nerves in the peripheral nervous system (peripheral neuropathy); monitoring for symptoms of peripheral neuropathy should continue throughout treatment.
- Aubagio can cause acute kidney failure and elevated potassium in the blood. Renal function should be monitored in anyone who experiences symptoms of renal failure or elevated potassium levels.
- Aubagio can cause elevations in blood pressure; blood pressure should be monitored and managed during treatment.
- A person who develops a painful red or purplish rash with peeling or blisters should contact his or her healthcare provider.
- A person who experiences new or worsening breathing problems should contact his or her healthcare provider. ([back to table, page 9](#))

Gilenya® warnings

The FDA prescribing information for Gilenya (fingolimod) includes the following warnings and precautions:

- Because Gilenya can cause a person's heart rate to temporarily slow after the first dose, all patients should be given an electrocardiogram (ECG) prior to the first dose, monitored for six hours after the first dose with hourly pulse and blood pressure measurement, and then given a repeat ECG. If cardiac symptoms persist after the six-hour observation period, observation and continuous ECG monitoring should be maintained until the problems are resolved. In addition, any person with a history of cardiac problems should be carefully evaluated before starting treatment

with Gilenya. Anyone who has experienced a heart attack, unstable angina, a stroke or stroke warning, or certain types of heart failure within the past six months should not begin treatment with Gilenya. People who take a medication that affects their heart rhythm should not take Gilenya.

- Blood pressure should be monitored during treatment with Gilenya.
- Gilenya can increase a person's risk of infection, particularly infections caused by herpes viruses. Gilenya also poses a slightly increased risk of progressive multifocal leukoencephalopathy (PML). Because this medication reduces the number of white blood cells, a blood test to measure white blood cell count is recommended prior to starting treatment. PML has been most commonly reported in those taking Tysabri (to learn more, see page [21](#)).
- If a person has not had chicken pox (varicella), his or her doctor may recommend the varicella vaccine prior to starting this medication.
- Gilenya can affect respiratory function. Anyone who experiences changes in their breathing should be evaluated.
- A vision test is recommended prior to starting treatment and about 3 months later to look for evidence of macular swelling (swelling at the back of the eye that can cause blurred vision).
- Because Gilenya can cause liver problems, a liver function test is recommended prior to starting treatment. ([back to table, page 9](#))

Tecfidera® warnings

The FDA prescribing information for Tecfidera (dimethyl fumarate) includes the following warnings and precautions:

- Tecfidera (dimethyl fumarate) can cause severe allergic reactions, including anaphylaxis (a reaction that occurs very quickly and may include itchy rash, difficulty breathing and swelling of the throat, and angioedema (a swelling under the skin that typically occurs in the throat and tongue). An allergic reaction can occur after the first dose or at any time during treatment. A person who experiences any of these symptoms should stop the medication and seek medical care immediately.
- A few cases of progressive multifocal leukoencephalopathy (PML) have been reported in people taking Tecfidera. Symptoms of PML progress

over days to weeks and include progressive weakness on one side of the body, clumsiness, vision changes and changes in thinking, memory and orientation that lead to confusion and personality changes. Anyone experiencing changes of this kind while taking Tecfidera® should report them immediately to his or her healthcare provider. PML has been most commonly reported in those taking Tysabri (to learn more, see page [21](#)).

- Tecfidera may reduce blood lymphocyte counts significantly. Prior to starting this medication, a complete blood count (CBC), including lymphocyte count, should be done, followed by another CBC after six months of treatment, and every 6-12 months thereafter, or more often if the healthcare provider feels it is necessary. ([back to table, page 9](#))

Additional information about each of the oral 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 page [25](#)), or by linking to the FDA Medication Guide found on each medication's website: [Aubagio.com](#), [Gilenya.com](#), [Tecfidera.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.

Infused Medications

All medications delivered by IV infusion pose risks of bruising, vein damage, blood clots and more. Infusions must be managed by a well-trained medical professional who is qualified to administer them.

Lemtrada® warnings

The FDA prescribing information for Lemtrada (alemtuzumab) includes the following black box warnings and precautions:

- Lemtrada causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia (ITP, a rare bleeding condition) and anti-glomerular basement membrane disease (which impact the kidneys).
- The medication can cause serious and life-threatening infusion reactions while the medication is being given and for 24 hours after each infusion.
- Lemtrada increases the risk of malignancies (thyroid cancer, melanoma, and blood cancers).

The prescribing information also includes the following additional warning:

- Thyroid disorders can occur with this medication.

To address these risks, the FDA recommends the following screening and monitoring strategies for anyone taking this medication:

- Prior to treatment, it should be determined whether the person has adequate immunity to the varicella zoster virus. If the person does not, the varicella vaccine should be administered 6 weeks prior to starting the medication.
- To minimize the risks associated with infusion reactions, corticosteroids are given immediately before the infusion on the first three days of each treatment course.
- An antiviral agent is started on the first day of each treatment course and continued for a minimum of 2 months.
- Thyroid function tests should be obtained before treatment and every 3 months until 48 months after the last infusion.
- Full blood count looking at different types of white and red blood cells should be obtained prior to treatment and monthly thereafter until 48 months after the last infusion.
- Blood tests to assess kidney function levels should be obtained prior to treatment and monthly thereafter until 48 weeks after the last infusion.
- Urinalysis with urine cell counts should be obtained prior to treatment and monthly thereafter until 48 months after the last Infusion.
- A skin exam should be done at the start of treatment and yearly thereafter to monitor for melanoma (a type of skin cancer).
- A person with an active infection should not start treatment until the infection is controlled.
- People should not have a live virus vaccine after a course of Lemtrada.

Because of the risks associated with Lemtrada, this treatment 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. ([back to table, page 10](#))

Mitoxantrone warnings

The FDA prescribing information for mitoxantrone includes the following black box warning and precautions:

- Acute myeloid leukemia (AML), a type of cancer, has been reported in MS patients and cancer patients treated with mitoxantrone. AML can be fatal.

The prescribing information also contains the following additional warning:

- Mitoxantrone) is a chemotherapeutic treatment originally developed to treat certain forms of cancer. The total lifetime dose is limited in order to avoid possible heart damage. People taking Novantrone should have tests of their heart function before each dose and periodically after treatment has ended. It cannot be used in people with pre-existing heart problems, liver disease, and certain blood disorders. ([back to table, page 10](#))

Tysabri® warnings

The FDA prescribing information for Tysabri (natalizumab) includes the following black box warnings and precautions:

- Tysabri increases the risk of a rare, often fatal brain disease called PML (progressive multifocal leukoencephalopathy, which is caused by the common JC virus.

There are no interventions that are known to cure PML once it occurs, but a course of plasma exchange to remove Tysabri from the bloodstream as quickly as possible may provide benefit.

For people taking Tysabri, three factors increase the risk of PML: longer treatment duration (particularly beyond two years), previous treatment with an immunosuppressant medication and testing positive for antibodies to the JC virus (which indicates that a person has previously been exposed to the JC virus). The availability of a laboratory test to test JC-antibody status has made it easier for people with MS and their physicians to weigh the risks and benefits of this therapy.

The medication label suggests that the risks and benefits of starting or continuing Tysabri should be carefully considered in patients who test positive for antibodies to the JC virus and have one or both of the other risk factors. Those found to be antibody positive, have used Tysabri for

less than two years, and have no prior use of immune suppressing drugs are estimated to have a risk of PML of less than 1/1000; those with all three known risk factors have an estimated risk of PML of 13/1000. In individuals who are antibody negative, have no prior history of immunosuppression, and take Tysabri for less than two years, the risk of PML is approximately 1/50,000.

A person who tests negative for anti-JCV antibodies is still at risk for the development of PML for two very important reasons. First, she or he can be infected by the JC virus at any time without knowing it. Second, the laboratory test to detect antibodies to the JC virus will produce a false negative result about three percent of the time. Therefore, testing should be done prior to starting treatment with Tysabri, and repeated every six months while a person is on treatment. For the purposes of risk evaluation, a person who tests positive for JC virus antibodies at any point in time is considered to be antibody-positive even if he or she tests negative on a later test. Careful monitoring for PML should continue for six months after treatment has ended.

Because of the risk of PML, Tysabri® is only available under a restricted distribution program, referred to as the TOUCH® program, which was created to monitor patients for PML and other adverse effects. Prescribing physicians and patients must enroll in this mandatory registry program. Infusion centers must also be enrolled in the TOUCH program. Patients using Tysabri should promptly report any continuously worsening symptoms to their prescriber.

The prescribing information also includes the following additional warnings:

- Tysabri has been found to increase the risk of liver damage, even after the first dose. Liver failure requiring a liver transplant has also occurred. Any person experiencing symptoms of liver injury, including yellowing of the skin and eyes (jaundice) unusual darkening of the urine, nausea, feeling tired or weak, and vomiting, should contact his or her physician immediately. Blood tests can be done to check for liver damage.
- Infections of the brain and spinal cord (encephalitis) and of surrounding tissues (meningitis) caused by herpes viruses can also occur. The following symptoms should be reported immediately to one's healthcare provider — sudden fever, severe headache, vision change (especially light sensitivity, stiff neck, behavior change or change in cognition — so that treatment with an antiviral medication can be started.

- Serious hypersensitivity reactions, including anaphylaxis, have occurred with this medication. Anaphylaxis occurs very quickly and may include itchy rash, difficulty breathing and swelling of the throat, and angioedema (a swelling under the skin that typically occurs in the throat and tongue). A person who experiences a hypersensitivity reaction of this kind should permanently discontinue this medication.
- Tysabri is **not** recommended for use by any person whose immune system is weakened by disease or by the use of medications that alter the immune system, including other disease-modifying therapies. ([back to table, page 11](#))

Additional information about Lemtrada and Tysabri (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 page [25](#)), or by linking to the FDA Medication Guide on each medication's website: [Lemtrada.com](#), [Tysabri.com](#). Additional information about mitoxantrone is available at <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.

Work with your healthcare provider to optimize your treatment

All of the disease-modifying therapies described in this booklet have been shown to be effective in treating MS. After choosing the medication that you and your healthcare provider feel would offer the greatest benefit for you at this time, there are steps you can take to optimize your treatment and manage the potential side effects and risks:

- Take your medication according to the instructions you have been given. If you find that you are having difficulty being consistent with your treatment, be sure to let your healthcare provider know so that you can work together to address whatever challenges you are having. No medication can offer optimal benefit unless it is taken as prescribed.
- Each of these medications requires some type(s) monitoring to ensure a person's health and safety. Talk with your healthcare provider about the monitoring that is required for the medication you are taking and be consistent with it.

- Report any unusual symptoms or changes you experience to your healthcare provider.
- If you have questions about your treatment, any side effects you may be experiencing, or risks that may be involved with the medication you are taking, do not hesitate to ask your healthcare provider about them.

The bottom line

Many factors will influence the decision that you and your physician make about your choice of medication. One of them will be lifestyle issues that could affect your ability to stay with a treatment over time. Another factor is your response to the therapy, which should be carefully tracked. If your MS is not responding, you and your physician should discuss what other options might work for you.

Paying for a disease-modifying therapy: Some help is available

Disease-modifying medications are costly. The actual cost to an individual or an insurance company will vary depending on a variety of factors. Because cost information is subject to frequent change, we recommend that you contact your healthcare plan and/or your pharmacy for cost information.

Some private insurance plans do not cover prescription medications, although they may cover procedures such as IV infusions in a medical facility. Plans that do cover prescription medications often have a list of the specific medications covered by the plan (known as a formulary). It is possible that some disease-modifying medications are covered by a plan and some are not. In addition, many formularies now distinguish between “preferred” and “non-preferred” medications, or put medications on different tiers. The co-insurance amounts you may have to pay as a result can vary significantly.

Because Novantrone[®], Tysabri[®] and Lemtrada[®] must be infused in a medical facility, they are covered under Medicare Part B. If Avonex[®] is administered in a physician’s office or clinic, it will be covered by Medicare Part B under most circumstances. For more detailed information, contact MS ActiveSource[®] at 800-456-2255.

Medicare Part D covers prescription medications through private plans approved by Medicare. For more information on Medicare prescription coverage, go to [nationalMSSociety.org/medicare](https://www.nationalMSSociety.org/medicare), or call 1-800-344-4867.

Medicaid includes prescription coverage. However, the list of specific medications covered may vary from state to state. Call your state Medicaid office for more information.

Each of the pharmaceutical companies offers a program designed to help people apply for and use all the state and federal programs for which they are eligible.

They also help some people who are uninsured or under-insured through patient assistance programs. The companies invite physicians and people with MS who might be deterred by the cost from considering a disease-modifier to call the toll-free numbers listed in “Industry-Sponsored Sites” (see page [255](#)). Ask for information on available assistance.

For additional information on specific industry assistance, visit: nationalMSSociety.org/DMTassistance.

Industry-Sponsored Sites for Patient Information and/or Financial Assistance

AUBAGIO®

MS One to One®

855-676-6326

MSOnetoOne.com

AVONEX®

Above MS™

800-456-2255

avonex.com

abovems.com

BETASERON®

BETAPLUS®

800-788-1467

betaseron.com

COPAXONE®

Shared Solutions®

800-887-8100

copaxone.com

EXTAVIA®

Extavia Go Program™

866-398-2842

extavia.com

Patient Assistance NOW

800-245-5356

patientassistancenow.com

GILENYA®

Gilenya Go Program™

800-445-3692

gilenya.com

Patient Assistance NOW

800-245-5356

patientassistancenow.com

GLATOPA™

GlatopaCare™

855-452-8672

glatopa.com/glatopa_care

LEMTRADA®
MS One to One®
855-676-6326
MSOnetoOne.com

MITOXANTRONE®
No patient support program
at this time

PLEGRIDY
Above MS™
800-456-2255
plegridy.com
abovems.com

REBIF®
MS LifeLines®
877-447-3243
rebif.com
mslifelines.com

TECFIDERA®
Above MS™
800-456-2255
tecfidera.com
abovems.com

TYSABRI®
Above MS™
800-456-2255
tysabri.com
abovems.com

ZINBRYTA™
800-456-2255
zinbryta.com

Help with the cost of medications for symptom management

In addition to the disease-modifying therapies discussed, there are many other medications, treatments and strategies to help manage specific MS symptoms such as bowel and bladder function, spasticity, and pain. Symptom management medications make important contributions to keeping people with MS well and active.

“Finding Lower-Priced Prescription Drugs” is a useful resource focused on making medications more affordable. Visit nationalMSSociety.org/insurance for more information.

For detailed information on patient assistance programs from their manufacturers, visit needymeds.org.

A recommended resource

The Multiple Sclerosis Emerging Therapies Collaborative — which includes the MS Coalition, the American Academy of Neurology, the VA Multiple Sclerosis Centers of Excellence East and West, and ACTRIMS — provides timely, evidence-based information about emerging therapies for people affected by multiple sclerosis and healthcare professionals. The Collaborative’s goal is to promote optimal, personalized treatment by facilitating effective doctor-patient communication and collaborative decision-making. Visit ms-coalition.org/EmergingTherapies.

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Extavia® is a registered trademark of Novartis AG Corporation.

Extavia® Go Program™ is a trademark of Novartis AG Corporation.

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MS One to One® is a trademark of Genzyme Corporation.

Lemtrada® is a registered trademark of Genzyme Corporation.

Plegridy® is a registered trademark of Biogen.

Rebif® is a registered trademark of EMD Serono, Inc.

Shared Solutions® is a registered trademark of Teva Neuroscience, Inc. Corporation.

Tecfidera® is a registered trademark of Biogen.

Tysabri® is a registered trademark of Biogen.

TOUCH® is a registered trademark of Biogen.

Zinbryta™ is a trademark of Biogen.

The National Multiple Sclerosis Society (“Society”) is proud to be a source of information on multiple sclerosis related topics. The information provided is based on professional advice, published experience, and expert opinion, but does not constitute medical or legal advice. For specific medical advice, consult a qualified physician. For specific legal advice, consult a qualified attorney.

The Society does not endorse products, services or manufacturers. Such names appear here solely because they are considered helpful information. The Society assumes no liability for the recipient’s use of any product or service mentioned. The Society does not independently verify whether the information provided by each service provider is accurate. The Society undertakes no responsibility to verify whether the service provider is appropriately licensed and certified and has applicable insurance coverage.

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 Society publishes many other resources about various aspects of MS. Visit nationalMSsociety.org/brochures or call 1-800-344-4867.

Other popular resources include:

- Fatigue: What You Should Know
- Managing MS through Rehabilitation
- Multiple Sclerosis and Your Emotions
- Taming Stress in Multiple Sclerosis

The National MS Society’s mission is for people affected by MS to 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, collaborates with MS organizations around the world, and provides services designed to help people with MS and their families move their lives forward.



nationalMSsociety.org

1-800-344-4867