DISEASE-MODIFYING THERAPIES FOR MS

National Multiple Sclerosis Society
A multiple sclerosis (MS) diagnosis can bring a sense of relief by giving a name and explanation for a parade of strange symptoms. It can also bring frightening images of a challenging future. Regardless of your initial reactions, a diagnosis is a life-changing event.

Even before the news can be fully absorbed, you 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 your 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 your healthcare provider when choosing a treatment, and describes the resources available to support your 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, relapses or clinical attacks), treating symptoms, and paying attention to your overall health and wellness. Disease-modifying medications are the best strategy currently available to slow the natural course of MS. Even though these medications don’t generally make you feel better, they can be looked upon as an investment in your future.

Clinical studies have demonstrated that all of the medications for relapsing forms of MS:

- Reduce the frequency and severity of clinical attacks in people with relapsing forms of MS. An attack is defined as a new neurological symptom or symptoms (such as a change in vision, weakness in a limb, new numbness or tingling or coordination difficulties), or the worsening of an old symptom, which lasts at least 24 hours and is not due to another cause (such as a fever). In clinical trials comparing treatment versus inactive placebo or another disease-modifying therapy (referred to as an “active comparator”), these agents reduced MS attacks by 28 to 68 percent.

- Reduce the development of new areas of damage in 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.

- Slow the accumulation of disability. In clinical trials, most of these medications have been shown to delay disability progression.
Subsequent research and clinical experience indicate that early treatment 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 nerves (axons) occurs in MS. Overall brain atrophy (shrinkage) can occur early in the disease, and damage can continue 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. To read the MS Coalition consensus paper, visit ntl.ms/coalitionDMTsummary.

The American Academy of Neurology (AAN) has developed guidelines for starting, switching and stopping disease-modifying therapies for adults with clinically isolated syndrome, relapsing-remitting MS and progressive forms of MS. To read those guidelines, visit: aan.com/Guidelines/home/GuidelineDetail/898

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.

**Options**

There are currently over a dozen disease-modifying medications approved by the FDA for use in relapsing forms of MS. Of these, one is also approved specifically for secondary-progressive MS, one is the first and only to be approved for primary progressive MS, and one is the only medication approved for use in children age 10 and older. 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.

The decision to take a disease-modifying therapy should be one made jointly between you and your healthcare provider. Your healthcare provider should inform you of all of your options, including how well each drug worked in clinical trials, and the side effects and risks of each. You should tell your healthcare provider what’s most important to you in terms of managing your disease. Explain your values, lifestyle and the quality of life you would like to maintain. Together you will decide on the treatment that is best for you. This is called shared decision making.

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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## Important Information

### Injectable Treatments

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<th>Manufacturer</th>
<th>Dose/Administration</th>
<th>FDA approval</th>
<th>Most common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Avonex®</strong> (interferon beta-1a)</td>
<td>Biogen</td>
<td>30 mcg intramuscularly (into a large muscle) once weekly</td>
<td>For the treatment of adults with relapsing forms of MS to slow the accumulation of physical disability and reduce the frequency of clinical exacerbations, and for adult patients who have experienced a first clinical episode and have MRI features consistent with MS</td>
<td>Headache, flu-like symptoms (chills, fever, muscle pain, fatigue weakness), injection site pain and inflammation See warnings on page 11</td>
</tr>
<tr>
<td><strong>Betaseron®</strong> (interferon beta-1b)</td>
<td>Bayer Healthcare Pharmaceuticals Inc.</td>
<td>0.25 mg subcutaneously (under the skin) every other day</td>
<td>For the treatment of adults with relapsing forms of MS to reduce the frequency of clinical exacerbations; and for adult patients who have experienced a first clinical episode and have MRI features consistent with MS</td>
<td>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 12</td>
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<tr>
<td><strong>Copaxone®</strong> (glatiramer acetate)</td>
<td>Teva Neuroscience</td>
<td>20 mg subcutaneously every day, or 40 mg subcutaneously three times per week</td>
<td>For the treatment of adults with relapsing forms of MS Approval: 1996 US; 1997 CAN Pregnancy Category B (see footnote, page 7)</td>
<td>Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain See warnings on <a href="#">page 13</a></td>
</tr>
<tr>
<td><strong>Extavia®</strong> (interferon beta-1b)</td>
<td>Novartis Pharmaceuticals</td>
<td>0.25 mg subcutaneously every other day</td>
<td>For the treatment of adults with relapsing forms of MS to reduce the frequency of clinical exacerbations; and for adult 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 7)</td>
<td>Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness) following injection, headache, injection site reactions (swelling redness, pain) See warnings on <a href="#">page 12</a></td>
</tr>
<tr>
<td><strong>Glaterimer Acetate</strong> (therapeutic equivalent to Copaxone)</td>
<td>Mylan Pharmaceuticals</td>
<td>20 mg subcutaneously every day, or 40 mg subcutaneously three times per week</td>
<td>For the treatment of adults with relapsing forms of MS Approval: 2017 US Pregnancy Category B (see footnote, page 7)</td>
<td>Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain See warnings on <a href="#">page 13</a></td>
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</table>
| **Glatopa®** (glatiramer acetate, generic equivalent of Copaxone) | Sandoz – a Novartis company | 20 mg subcutaneously every day, or 40 mg subcutaneously three times per week | For the treatment of adults with relapsing forms of MS  
Approval: 2015 US  
Pregnancy Category B (see footnote below) | Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain  
See warnings on page 13 |
| **Plegridy®** (pegylated interferon beta-1a) | Biogen | 125 mcg subcutaneously every 14 days | For the treatment of adults with 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 11 |
| **Rebif®** (interferon beta-1a) | EMD Serono, Inc / Pfizer, Inc | 22 mcg or 44 mcg subcutaneously three times per week | For the treatment of adults with 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 11 |

**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.

**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.
<table>
<thead>
<tr>
<th>Oral Treatments</th>
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<tbody>
<tr>
<td><strong>Treatment (chemical name)</strong></td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
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<tr>
<td><strong>Aubagio® (teriflunomide)</strong></td>
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<tr>
<td>Sanofi Genzyme</td>
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<tr>
<td><strong>Gilenya® (fingolimod)</strong></td>
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<tr>
<td>Novartis Pharmaceuticals</td>
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<td></td>
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<tr>
<td><strong>Tecfidera® (dimethyl fumarate)</strong></td>
</tr>
<tr>
<td>Biogen</td>
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<td></td>
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</tbody>
</table>

**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.
<table>
<thead>
<tr>
<th>Treatment (chemical name)</th>
<th>Dose/Administration</th>
<th>FDA approval</th>
<th>Most common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lemtrada®</strong> (alemtuzumab)</td>
<td>12 mg per day for five consecutive days, followed by 12 mg per day on three consecutive days one year later</td>
<td>For the treatment of adults 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</td>
<td>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 16</td>
</tr>
<tr>
<td><strong>Novantrone®</strong> (mitoxantrone)</td>
<td>12 mg/m² every 3 months. Lifetime cumulative dose limit of approximately 8–12 doses over 2–3 years (140 mg/m²).</td>
<td>For reducing neurologic disability and/or the frequency of clinical relapses in adult patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting MS</td>
<td>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 17</td>
</tr>
</tbody>
</table>

*Manufacturer: Sanofi Genzyme*
## Intravenous Infusion Treatments

<table>
<thead>
<tr>
<th>Treatment (chemical name)</th>
<th>Manufacturer</th>
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<th>FDA approval</th>
<th>Most common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ocrevus®</strong> (ocrelizumab)</td>
<td>Genentech (a member of the Roche Group)</td>
<td>600 mg every 6 months (first dose: 300 mg IV on day one and 300 mg IV 2 weeks later)</td>
<td>For the treatment of adults with relapsing MS or primary progressive MS Approval: 2017 US; 2013 CAN Pregnancy Category: 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. (see footnote below)</td>
<td>Infusion reactions (most commonly itchy skin, rash, throat irritation, flushed face or fever, headache), which in rare instances may be life-threatening; increased risk of infections, including respiratory tract infections and herpes infections; possible increase in malignancies, including breast cancer See warnings on page 18</td>
</tr>
<tr>
<td><strong>Tysabri®</strong> (natalizumab)</td>
<td>Biogen</td>
<td>300 mg once every 28 days. Must take place in an approved infusion facility</td>
<td>Used as a monotherapy (not in combination with any other MS disease-modifying treatment or other immune suppressant drugs) for the treatment of adult patients with relapsing forms of multiple sclerosis. Tysabri increases the risk of PML, a rare and potentially fatal brain infection. Approval: 2006 US; 2006 CAN Pregnancy Category C (see footnote below)</td>
<td>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 18</td>
</tr>
</tbody>
</table>

**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 side effect listed. Some adverse effects are common, while others occur less frequently but may be serious. All the side effects listed here occurred in at least 2 to 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 treatment he or she recommends and can guide you on how to manage any side effects that occur. The manufacturers’ websites (page 27) also give information about the side effects you may experience. It is important that you follow your healthcare provider’s instructions if you experience any side effects or reactions to a medication.

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 on the medication’s label to call attention to it.

Injectable medications

Interferon beta-1a (Avonex® and Rebif®) and Pegylated Interferon beta-1a (Plegridy®) warnings

The FDA prescribing information for Avonex, Rebif and Plegridy includes the following warnings and precautions:

- Depression and suicide have been reported to occur with increased frequency in those receiving interferon beta-1a medications.
- Some people taking Avonex and Plegridy developed heart problems. If you have a history of heart problems, these medications could make those problems worse. You should be monitored while on Avonex or Plegridy for worsening of your heart problems.
- Liver problems or worsening liver problems can occur from receiving interferon beta-1a medications. You should have periodic blood tests to check for this while on interferon beta-1a medications.
- Interferon beta-1a medications can cause decreased peripheral blood counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising. You should have blood tests to check for a possible reduction in white blood cells, red blood cells, and cells that help blood clot while on treatment.
- Serious allergic reactions can happen quickly with these medications.
Injection site reactions can occur on Rebif and Plegridy, including skin infections and severe skin damage. Rotate injection sites on a regular basis and contact your healthcare provider right away if the site looks infected or does not heal within a few days.

Increased risk of drug-induced autoimmune disorders has been reported in some people using these medications.

Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in some people taking interferon medications.

Seizures have occurred in some people taking interferon beta-1a.

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

The FDA prescribing information for Betaseron and Extavia includes the following warnings and precautions:

- Depression and suicide have been reported to occur with increased frequency in those receiving interferon beta-1b medications.
- Interferon beta-1b medications can cause liver problems including liver failure. You should have periodic blood tests to monitor for this while taking interferon beta-1b medications.
- Serious allergic reactions can happen quickly and may happen after your first dose of these medications or after you have taken interferon beta-1b medications many times.
- Some people taking interferon beta-1b medications developed heart problems. If you have a history of heart problems, these medications could make those problems worse. You should be monitored while on them for worsening of your heart problems.
- Serious skin reactions can happen in some people, including areas of severe damage to skin and the tissue below the skin (necrosis). Change your injection site each time you inject interferon beta-1b medications.
- Interferon beta-1b medications can cause decreased white blood counts. Blood test monitoring while taking interferon beta-1b medications is recommended.
- Clots in small blood vessels (thrombotic microangiopathy – TMA) have been reported in some people taking interferon medications.
- Seizures have occurred in some people taking interferon beta-1b.
- Some cases of drug-induced autoimmune disorders have been reported with these medications.

Glatiramer acetate, (Copaxone®, glatiramer acetate, and Glatopa®) warnings

The FDA prescribing information for Copaxone, glatiramer acetate and Glatopa includes the following warnings and precautions:

- Post-injection reaction that includes at least two of the following: flushing, chest pain, palpitations, increased heart rate, anxiety, shortness of breath, constriction of the
throat and rash may happen within minutes of injection. These symptoms generally resolve quickly on their own and have no long-term effects. Although it can happen any time, it is more likely to occur after the first few months of treatment and may occur more than once.

- Chest pain may occur as part of the post-injection reaction or by itself. It typically lasts a few minutes and has no long-term effects.
- Permanent depressions under the skin at injection sites (lipoatrophy) can happen because of damage to the fatty tissue under your skin. Areas of skin tissue death (necrosis), although rare, may occur. You can reduce your chance of developing these problems by choosing a different injection area each time you administer these medications.

**Oral medications**

**Teriflunomide (Aubagio®) warnings**

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

- Aubagio may cause serious liver problems that may lead to death. Your risk of liver problems may be higher if you take other medicines that also affect your liver. Your healthcare provider should do blood tests to check your liver within 6 months before you start taking Aubagio and 1 time a month for 6 months after you start taking Aubagio. Continued blood tests after 6 months on therapy might be necessary if you are taking other medications that can affect your liver.

- Aubagio may cause harm to your unborn baby. Do not take Aubagio if you are pregnant. Do not take Aubagio unless you are using effective birth control. A woman should be given a pregnancy test prior to starting the medication. If you become pregnant while taking Aubagio or during the 2 years after you stop taking it, tell your healthcare provider right away. Men who plan to father a child should stop taking the medication and undergo treatment to remove the medication rapidly from the body before trying to conceive.

The prescribing information also contains the following additional warnings:

- Aubagio may stay in your blood for up to 2 years after you stop taking it. Your healthcare provider can prescribe a medicine to help lower your blood levels of Aubagio more quickly. Talk to your healthcare provider if you want more information about this.

- Aubagio can cause allergic reactions, including serious skin problems.

- Aubagio can decrease your white blood cell count. When you have a low white blood cell count, you may have more frequent infections. You should have a complete blood count prior to starting treatment and may need to continue this monitoring while on treatment.

- You should be tested for tuberculosis before starting treatment. If you test positive for tuberculosis you should not begin taking Aubagio until the treatment for tuberculosis has been successfully completed.
You should not receive live vaccines while taking Aubagio and for 6 months after you stop taking it.

Aubagio can cause numbness or tingling (peripheral neuropathy) in your hands or feet that is different from your MS symptoms.

Aubagio may cause acute kidney failure and elevated potassium levels in the blood. These increases are temporary but your healthcare provider might monitor for them with blood tests.

Aubagio can cause high blood pressure. You should have your blood pressure checked by your healthcare provider before starting Aubagio and while you are taking it.

Aubagio can cause a painful red or purplish rash with peeling or blisters.

Aubagio can cause new or worsening breathing problems.

**Fingolimod (Gilenya®) warnings**

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

- Gilenya may cause allergic reactions.
- Gilenya may cause slow heart rate (bradycardia or bradyarrhythmia) when you start taking it, especially after the first dose. You will have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose of Gilenya. You will be observed by a healthcare professional for at least 6 hours after taking your first dose of Gilenya and have another ECG at the end of that 6-hour observation. If your ECG shows any heart problems or if your heart rate is still too low or continues to decrease, you will continue to be observed. Your slow heart rate will usually return to normal within 1 month after you start taking Gilenya. If you have certain types of heart problems, or if you are taking certain types of medicines that can affect your heart, you will be observed overnight after you take your first dose of Gilenya. If you miss 1 or more doses of Gilenya, you may need to be observed by a healthcare professional when you take your next dose.
- When Gilenya is stopped, symptoms of MS can return and become worse compared to before or during treatment. Many people who have worsening of MS symptoms after stopping Gilenya do not return to the level of function that they had before stopping Gilenya. This worsening happens most often within 12 weeks after stopping Gilenya, but can happen later. Always talk to your doctor before you stop taking Gilenya for any reason. Tell your doctor if you have worsening symptoms of MS after stopping Gilenya.
- Gilenya can increase blood pressure. Your healthcare provider should check your blood pressure while you are on Gilenya.
- Gilenya can increase your risk of serious infections that can be life-threatening and cause death.
- Gilenya lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 2 months of stopping treatment. Your
healthcare provider may do a blood test to check your white blood cells before you start taking Gilenya and while you are on it.

- You should not receive live vaccines while on Gilenya or up to two months after stopping Gilenya.
- If you have not had chicken pox (varicella), your healthcare provider may recommend the varicella vaccine prior to starting Gilenya.
- Gilenya may cause progressive multifocal leukoencephalopathy (PML), a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with weakened immune systems but has happened in people who do not have weakened immune systems.
- Gilenya can cause breathing problems.
- Gilenya may cause a problem with your vision called macular edema. If macular edema happens, it usually starts in the first 3 to 4 months after you start taking Gilenya. Your healthcare provider should test your vision before you start taking Gilenya, 3 to 4 months after you start taking Gilenya or any time you notice vision changes during treatment with Gilenya.
- Gilenya may cause liver problems. Your healthcare provider should do blood tests to check your liver before you start Gilenya.
- Gilenya may cause types of skin cancer called basal cell carcinoma and melanoma. You should have your skin checked while taking Gilenya.
- Gilenya can cause swelling and narrowing of the blood vessels in your brain, a condition called Posterior Reversible Encephalopathy Syndrome (PRES). This happens rarely and usually gets better after you stop taking Gilenya.

**Dimethyl fumarate (Tecfidera®) warnings**

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

- Tecfidera can cause allergic reactions. An allergic reaction can occur after the first dose or at any time during treatment.
- Progressive multifocal leukoencephalopathy (PML), a rare brain infection that usually leads to death or severe disability, has been reported in people taking Tecfidera. If PML happens, it usually happens in people with weakened immune systems but has happened in people who do not have weakened immune systems.
- Tecfidera may cause decreases in your white blood cell count. Your healthcare provider should do a blood test before you start treatment with Tecfidera and while on therapy.
- Tecfidera can cause liver problems. Your healthcare provider should do blood tests to check your liver function before you start taking Tecfidera and during treatment if needed.
Infused medications
All medications delivered by IV infusion are given directly into a vein through a small catheter or needle. This poses 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.

Alemtuzumab (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 impacts the kidneys).
- Lemtrada can cause serious and life-threatening infusion reactions that may happen while you receive it or up to 24 hours or longer after the infusion.
- Lemtrada may increase your chance of getting certain cancers, including thyroid cancer, skin cancer (melanoma), blood cancers and lymphoma.
- Serious and life-threatening stroke has been reported within 3 days of LEMTRADA administration.

The prescribing information also includes the following additional warning:

- Lemtrada may cause thyroid problems.
- Lemtrada may cause a decrease in some types of blood cells. Some people with low blood counts have increased infections. Your healthcare provider will do blood work to check for low blood cell counts.
- Lemtrada may cause serious infections, specifically herpes viral infections, human papilloma virus (HPV) (females only), tuberculosis, fungal infections and listeria.
- Lemtrada can cause inflammation of the gallbladder without gallstones.
- Lemtrada can cause pneumonitis, the swelling of lung tissue.

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

- Your healthcare provider should determine if you have adequate immunity to the varicella zoster virus (chicken pox/shingles). If you do not, your healthcare provider should consider giving you the varicella vaccine. The vaccine should be administered at least 6 weeks prior to starting Lemtrada.
- Your healthcare provider should check you for tuberculosis before you receive Lemtrada. If you test positive you should complete treatment for tuberculosis prior to starting Lemtrada.
- If you have an active infection your healthcare provider should consider delaying treatment with Lemtrada until it is fully controlled.
- Your healthcare provider will prescribe an antiviral agent to reduce your chance of getting herpes viral infections.
You will be given corticosteroids immediately before the infusion on the first three days of each treatment course to minimize the risks associated with infusion reactions.

Women taking Lemtrada should have an annual HPV (human papillomavirus) screening.

You should have thyroid function blood tests before treatment and every 3 months until 48 months after the last infusion.

You should have blood tests looking at different types of white and red blood cells prior to treatment and monthly thereafter until 48 months after the last infusion.

You should have blood tests to assess kidney function prior to treatment and monthly thereafter until 48 months after the last infusion.

You should have a urinalysis with urine cell counts prior to treatment and monthly thereafter until 48 months after the last infusion.

You should have a skin exam before starting treatment and yearly thereafter to monitor for melanoma (a type of skin cancer).

You should avoid eating foods that may be a source of a food borne infection known as listeria (for example, deli meat, unpasteurized milk and cheese products, or undercooked meat, seafood or poultry) or make sure the food you eat is heated well.

You should not have a live virus vaccine after a course of Lemtrada. Talk to your healthcare provider before getting any vaccinations after you receive Lemtrada.

You should call your healthcare provider right away if you have stomach pain, fever, nausea or vomiting.

You should call your healthcare provider right away if you have shortness of breath, cough, wheezing, chest pain or tightness or are coughing up blood.

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 correctly and in a timely way.

Mitoxantrone (Novantrone®) warnings

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

- Novantrone is a chemotherapy medication that should only be administered under the supervision of a physician experienced in the use of cytotoxic chemotherapy agents.
- Secondary acute myeloid leukemia (AML), a type of cancer, has been reported in MS patients and cancer patients treated with Novantrone. AML can be fatal.
- Cardiotoxicity, specifically heart failure that can be fatal, has occurred during treatment with Novantrone or months to years after stopping treatment. The risk for cardiotoxicity increases with the number of treatments with Novantrone and can occur even if you do not have any heart risk factors prior to starting therapy. Once someone has received Novantrone, yearly monitoring of heart function should occur indefinitely.
Novantrone is rarely prescribed for MS. To learn more about the warnings for Novantrone, review the medication guide available at ntl.MS/mitoxantrone.

Ocrelizumab (Ocrevus®) warnings

The FDA prescribing information for Ocrevus (ocrelizumab) includes the following warnings and precautions:

- Ocrevus can cause infusion reactions that can be serious and require you to be hospitalized. You will be monitored during your infusion and for at least 1 hour after each infusion of Ocrevus for signs and symptoms of an infusion reaction. These infusion reactions can happen for up to 24 hours after your infusion.
- Ocrevus increases your risk of getting upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes infections. Infections can happen during treatment or after you have received your last dose of Ocrevus. If you have an active infection, your healthcare provider should delay your treatment with Ocrevus until your infection is gone.
- Ocrevus may cause hepatitis B virus (HBV) reactivation. Before starting treatment with Ocrevus, your healthcare provider will do blood tests to check for HBV infection. If you have ever had HBV infection, it may become active again during or after treatment with Ocrevus. HBV becoming active again (called reactivation) may cause serious liver problems including liver failure or death. Your healthcare provider will monitor you if you are at risk for HBV reactivation during treatment and after you stop receiving Ocrevus.
- Although no cases of progressive multifocal leukoencephalopathy (PML) were seen in the clinical trials for Ocrevus, it may happen with this medication. PML is a rare brain infection that usually leads to death or severe disability.
- Ocrevus may cause a weakened immune system. Ocrevus taken before or after other medicines that weaken the immune system could increase your risk of getting infections.
- You should receive any required live or live-attenuated vaccines at least 4 weeks before you start treatment with Ocrevus. You should not receive ‘live’ or ‘live attenuated’ vaccines while you are being treated with Ocrevus and until your healthcare provider tells you that your immune system is no longer weakened.
- When possible, you should receive any non-live vaccines at least 2 weeks before you start treatment with Ocrevus. If you would like to receive any non-live (inactivated) vaccines, including the seasonal flu vaccine, while you are being treated with Ocrevus, talk to your healthcare provider.
- If you are pregnant or planning to become pregnant, talk to your healthcare provider about vaccinations for your baby, as some precautions may be needed.
- An increased risk of certain types of cancers, including breast cancer, may exist with Ocrevus. The recommendation is for women to follow standard breast cancer screening guidelines.
Natalizumab (Tysabri®) warnings

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

- Tysabri increases the risk of a rare brain infection that usually leads to death or severe disability called progressive multifocal leukoencephalopathy (PML). If PML happens, it usually happens in people with weakened immune systems.

Your risk of getting PML is higher if you: have received Tysabri for a long time (especially longer than 2 years), have received certain medicines that can weaken your immune system before you start receiving Tysabri and have been infected by the John Cunningham Virus (JCV). JCV is a common virus that is harmless in most people but can cause PML in people who have weakened immune systems, such as people taking Tysabri. Most people who are infected by JCV do not know it or do not have any symptoms. This infection usually happens in childhood. Before you start receiving Tysabri or during your treatment, your doctor may do a blood test to check if you have been infected by JCV.

Your healthcare provider should discuss the risks and benefits of Tysabri treatment with you before you decide to receive Tysabri. If you are interested in learning more about the risk of PML see table 1 of the medication prescribing information.

If you test negative for anti-JCV antibodies you are still at risk for developing PML for two reasons: you can become infected by the JC virus at any time without knowing it; the laboratory test to detect antibodies to the JC virus may produce a false negative result. Therefore, testing should be done prior to starting treatment with Tysabri, and repeated periodically while you are on treatment.

Because of your risk of getting PML while you receive Tysabri, it is only available through a restricted distribution program called the TOUCH® program. Prescribers, patients and infusion centers that administer Tysabri must enroll in the TOUCH program.

The prescribing information also includes the following additional warnings:

- Tysabri may cause liver damage, even after the first dose. Liver failure requiring a liver transplant has also occurred. Blood tests can be done to check for liver damage.
- Tysabri may increase your risk of getting an infection of the brain or the covering of your brain and spinal cord (encephalitis or meningitis) caused by herpes viruses that may lead to death. Herpes infections of the eye, causing blindness in some patients, have also occurred.
Allergic reactions, including serious allergic reactions have occurred with this medication. Serious allergic reactions usually happen within 2 hours of the start of your infusion, but they can happen at any time after you receive Tysabri.

Tysabri may increase your chance of getting an unusual or serious infection because Tysabri can weaken your immune system. You have a higher risk of getting infections if you also take other medicines that can weaken your immune system.

Additional information about each medication, including results from clinical trials, can be obtained from the National MS Society by calling 1-800-344-4867 or visiting www.nationalmssociety.org/Treating-MS/Medications, or from each manufacturer (see page 28). 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 monitoring. 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.

Coverage of disease-modifying therapies will vary among insurance companies and individual insurance plans. Most insurance plans have a formulary, or lists of medication that they will cover. 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®, Ocrevus®, 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, 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 22). 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

<table>
<thead>
<tr>
<th>Brand</th>
<th>Program/Source</th>
<th>Phone Number</th>
<th>Website/Link</th>
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<tbody>
<tr>
<td><strong>AUBAGIO®</strong></td>
<td>MS One to One®</td>
<td>855-676-6326</td>
<td>MSOnetoOne.com</td>
</tr>
<tr>
<td><strong>AVONEX®</strong></td>
<td>MS ActiveSource®</td>
<td>800-456-2255</td>
<td>avonex.com or aboveMS.com</td>
</tr>
<tr>
<td><strong>BETASERON® and BETAPLUS®</strong></td>
<td></td>
<td>800-788-1467</td>
<td>betaseron.com</td>
</tr>
<tr>
<td><strong>COPAXONE®</strong></td>
<td>Shared Solutions®</td>
<td>800-887-8100</td>
<td>copaxone.com</td>
</tr>
<tr>
<td><strong>EXTAVIA®</strong></td>
<td>Extavia Go Program™</td>
<td>866-398-2842</td>
<td>extavia.com</td>
</tr>
<tr>
<td></td>
<td>Patient Assistance NOW</td>
<td>800-245-5356</td>
<td>patientassistanceon.com</td>
</tr>
<tr>
<td><strong>GILENYA®</strong></td>
<td>Gilenya Go Program™</td>
<td>800-445-3692</td>
<td>gilenya.com</td>
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<tr>
<td></td>
<td>Patient Assistance NOW</td>
<td>800-245-5356</td>
<td>patientassistanceon.com</td>
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<tr>
<td><strong>GLATOPA™</strong></td>
<td>GlatopaCare™</td>
<td>855-452-8672</td>
<td>glatopa.com/glatopa_care</td>
</tr>
<tr>
<td><strong>GLATIRAMER ACETATE</strong></td>
<td>Mylan Support Program</td>
<td>1-844-695-2667</td>
<td>glatirameracetate.com/en/patient-support</td>
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<tr>
<td><strong>LEMTRADA®</strong></td>
<td>MS One to One®</td>
<td>855-676-6326</td>
<td>MSOnetoOne.com</td>
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<tr>
<td><strong>MITOXANTRONE®</strong></td>
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<td>No patient support program at this time</td>
</tr>
<tr>
<td><strong>OCREVUS®</strong></td>
<td>Genentech Access Solutions</td>
<td>1-844-627-3887</td>
<td>Genentech-Access.com</td>
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<tr>
<td></td>
<td></td>
<td>1-866-422-2377</td>
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<tr>
<td><strong>PLEGRIDY</strong></td>
<td>MS ActiveSource®</td>
<td>800-456-2255</td>
<td>plegidy.com or aboveMS.com</td>
</tr>
<tr>
<td><strong>REBIF®</strong></td>
<td>MS LifeLines®</td>
<td>877-447-3243</td>
<td>rebif.com or mslifelines.com</td>
</tr>
<tr>
<td><strong>TECFIDERA®</strong></td>
<td>MS ActiveSource®</td>
<td>800-456-2255</td>
<td>tecfidera.com or aboveMS.com</td>
</tr>
<tr>
<td><strong>TYSABRI®</strong></td>
<td>MS ActiveSource®</td>
<td>800-456-2255</td>
<td>tysabri.com or aboveMS.com</td>
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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® Go Program™ is a trademark of Novartis AG Corporation.
Gilenya® is a registered trademark of Novartis AG Corporation.
Gilenya® Go Program™ is a trademark of Novartis AG Corporation.
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Glatiramer acetate is a trademark of Mylan Pharmaceuticals Inc.
GlatopaCare® is a trademark of Novartis AG.
MS ActiveSource® is a registered trademark Biogen.
MS Lifelines® is a registered trademark of EMD Serono, Inc.
MS One to One® is a trademark of Genzyme Corporation.
Lemtrada® is a registered trademark of Genzyme Corporation.
Ocrevus® is a registered trademark of Genentech.
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.
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.

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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 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 mobilizes people and resources so that everyone 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, collaborates with MS organizations around the world, and provides programs and services designed to help people with MS and their families move their lives forward.