

DISEASE-MODIFYING THERAPIES FOR MS



**National
Multiple Sclerosis
Society**

Updated June 2020. Please visit nationalMSSociety.org/DMT for the most current version of this publication.

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 28-68%.
- 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 nationalMSSociety.org/DMTConsensus.

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 a shared decision 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 potential side effects and risks of each. You should tell your healthcare provider what's most important to you in terms of managing your disease and 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.

Each person's body or disease can respond to these medications differently, and the medication that is the best option for one person may not be the best choice 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.

Table of Contents

Important information	5
Injectable treatments	5
Oral treatments.....	8
Intravenous infusion treatments	11
Managing side effects of disease-modifying therapies	13
Understanding the warnings in the FDA labeling information	13
Injectable medications	13
Interferon beta-1a (Avonex [®] and Rebif [®]) and Pegylated Interferon beta-1a (Plegridy [®]) warnings	13
Interferon beta-1b (Betaseron [®] and Extavia [®]) warnings.....	14
Glatiramer acetate, (Copaxone [®] , glatiramer acetate, and Glatopa [®]) warnings	15
Oral medications	15
Teriflunomide (Aubagio [®]) warnings.....	15
Fingolimod (Gilenya [®]) warnings	16
Cladribine (Mavenclad [®]) warnings	18
Siponimod (Mayzent [®]) warnings	19
Dimethyl fumarate (Tecfidera [®]) warnings.....	21
Diroximel fumarate (Vumerity [®]) warnings.....	22
Ozanimod (Zeposia [®]) warnings.....	22
Infused medications	24
Alemtuzumab (Lemtrada [®]) warnings.....	24
Mitoxantrone (Novantrone [®]) warnings.....	26
Ocrelizumab (Ocrevus [®]) warnings.....	26
Natalizumab (Tysabri [®]) warnings.....	27
Work with your healthcare provider to optimize your treatment	29
The bottom line	29
Paying for a disease-modifying therapy: Help is available	30
Industry-sponsored sites for patient information and/or financial assistance.....	31
Help with the cost of medications for symptom management	32
A recommended resource	32

Important information

Injectable treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Avonex® (interferon beta-1a)</p> <p>Biogen</p>	<p>30 mcg intramuscularly (into a large muscle) once weekly</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approved: 1996 US; 1998 CAN</p> <p>Pregnancy: Data do not suggest a clear relationship between use and major congenital malformations, but may cause fetal harm based on animal data.</p>	<p>Headache, flu-like symptoms (chills, fever, muscle pain, fatigue weakness), injection site pain and inflammation (see warnings, page 13)</p>
<p>Betaseron® (interferon beta-1b)</p> <p>Bayer Healthcare Pharmaceuticals Inc.</p>	<p>0.25 mg subcutaneously (under the skin every other day)</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approved for RRMS: 1993 US; 1995 CAN Approved for SPMS: 1995 CAN</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>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, page 14)</p>

Injectable treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Copaxone® (glatiramer acetate)</p> <p>Teva Neuroscience</p>	<p>20 mg subcutaneously every day, or 40 mg subcutaneously three times per week</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 1996 US; 1997 CAN</p> <p>Pregnancy: Available human data are not sufficient to support conclusions about drug-associated risk for major birth defects and miscarriage</p>	<p>Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain (see warnings, page 15)</p>
<p>Extavia® (interferon beta-1b)</p> <p>Novartis Pharmaceuticals</p>	<p>0.25 mg subcutaneously every other day</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2009 US; 2009 CAN</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness) following injection, headache, injection site reactions (swelling, redness, pain) (see warnings, page 14)</p>
<p>Glaterimer Acetate (therapeutic equivalent to Copaxone)</p> <p>Mylan Pharmaceuticals</p>	<p>20 mg subcutaneously every day, or 40 mg subcutaneously three times per week</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2017 US</p> <p>Pregnancy: Available human data are not sufficient to support conclusions about drug-associated risk for major birth defects and miscarriage</p>	<p>Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain (see warnings, page 15)</p>

Injectable treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Glatopa® (glatiramer acetate, generic equivalent of Copaxone)</p> <p>Sandoz – a Novartis company</p>	<p>20 mg subcutaneously every day, or 40 mg subcutaneously three times per week</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2015 US</p> <p>Pregnancy: Available human data are not sufficient to support conclusions about drug-associated risk for major birth defects and miscarriage</p>	<p>Injection site reactions (redness, pain, swelling), flushing, shortness of breath, rash, chest pain (see warnings, page 15)</p>
<p>Plegridy® (pegylated interferonbeta-1a)</p> <p>Biogen</p>	<p>125 mcg subcutaneously every 14 days</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2014 US</p> <p>Pregnancy: Data do not suggest a clear relationship between use and major congenital malformations, but may cause fetal harm based on animal data.</p>	<p>Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness, headache, itching), injection site reactions (swelling, redness, pain) (see warnings, page 13)</p>
<p>Rebif® (interferon beta-1a)</p> <p>EMD Serono, Inc / Pfizer, Inc</p>	<p>22 mcg or 44 mcg subcutaneously three times per week</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 1998 US; 2002 CAN</p> <p>Pregnancy: Data do not suggest a clear relationship between use and major congenital malformations, but may cause fetal harm based on animal data.</p>	<p>Flu-like symptoms (chills, fever, muscle pain, fatigue, weakness, headache), injection site reactions (redness, pain, swelling) (see warnings, page 13)</p>

Oral treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Aubagio® (teriflunomide)</p> <p>Sanofi Genzyme</p>	<p>7 mg or 14 mg pill once daily</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2012 US; 2013 CAN</p> <p>Pregnancy: Contraindicated for use in pregnant women and in females of reproductive potential who are not using effective contraception because of the potential for fetal harm</p>	<p>Headache, hair thinning, diarrhea, nausea, abnormal liver tests (see warnings, page 15)</p>
<p>Gilenya® (fingolimod)</p> <p>Novartis Pharmaceuticals</p>	<p>0.5 mg capsule once daily</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older.</p> <p>Approval: 2010 US; 2011 CAN</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>Headache, flu, diarrhea, back pain, abnormal liver tests, sinusitis, abdominal pain, pain in extremities, cough (see warnings, page 16)</p>

Oral treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Mavenclad® (cladribine)</p> <p>EMD Serono, Inc.</p>	<p>Tablet given in two treatment courses, once per year for two years. Each treatment course has two cycles, which are 4-5 days long and about one month apart. The exact dose will depend on your weight.</p>	<p>For the treatment of relapsing forms of MS, to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use is generally recommended for those who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS.</p> <p>Approval: 2019 US; 2017 CAN</p> <p>Pregnancy: Contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the risk of fetal harm</p>	<p>Upper respiratory infection, headache, low white blood cell count (see warnings, page 18)</p>
<p>Mayzent® (siponimod)</p> <p>Novartis Pharmaceuticals</p>	<p>Increases each day over 4-5 days to the ongoing (maintenance) dose of a 1 mg or 2 mg pill once daily. Your healthcare provider will do a blood test to determine whether you will take the 1 mg or 2 mg maintenance dose and give you specific instructions for increasing the dose each day to reach the maintenance dose.</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2019 US</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>Headache, high blood pressure, abnormal liver tests (see warnings, page 19)</p>

Oral treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
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, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Approval: 2013 US; 2013 CAN Pregnancy: May cause fetal harm based on animal data	Flushing (sensation of heat or itching and a blush on the skin), gastrointestinal issues (nausea, diarrhea, abdominal pain) (see warnings, page 21)
Vumerity® (diroximel fumarate) Biogen	231 mg capsule taken twice daily for one week, followed by two 231 mg capsules taken twice daily thereafter	For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Approval: 2013 US Pregnancy: May cause fetal harm based on animal data	Flushing (redness, itching, rash) and stomach problems (nausea, vomiting, diarrhea, stomach pain, indigestion) (see warnings, page 22)
Zeposia® (ozanimod) Bristol Myers Squibb	0.23 mg capsule once daily for days 1-4, followed by 0.46 mg capsule once daily for days 5-7, then increased to 0.92 mg capsule once daily on day 8 and thereafter.	For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Approval: 2020 US Pregnancy: May cause fetal harm based on animal data	Upper respiratory tract infections, elevated liver enzymes, low blood pressure when you stand up (orthostatic hypotension), painful and frequent urination (signs of urinary tract infection), back pain and high blood pressure (see warnings, page 22)

Intravenous infusion treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Lemtrada® (alemtuzumab)</p> <p>Sanofi Genzyme</p>	<p>12 mg per day for five consecutive days, followed by 12 mg per day on three consecutive days one year later</p>	<p>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.</p> <p>Approval: 2014 US; 2014 CAN</p> <p>Pregnancy: May cause fetal harm</p>	<p>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, page 24)</p>
<p>Novantrone® (mitoxantrone)</p> <p>Available only as a generic medication</p>	<p>12 mg/m² every 3 months. Lifetime cumulative dose limit of approximately 8–12 doses over 2–3 years (140 mg/m²).</p>	<p>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.</p> <p>Approval: 2000 US</p> <p>Pregnancy: May cause fetal harm when administered to a pregnant woman</p>	<p>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, page 26)</p>

Intravenous infusion treatments

Treatment (chemical name) Manufacturer	Dose/ Administration	FDA approval	Most common side effects
<p>Ocrevus® (ocrelizumab)</p> <p>Genentech (a member of the Roche Group)</p>	<p>600 mg every 6 months (first dose: 300 mg IV on day one and 300 mg IV 2 weeks later)</p>	<p>For the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.</p> <p>Approval: 2017 US; 2013 CAN</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>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, page 26)</p>
<p>Tysabri® (natalizumab)</p> <p>Biogen</p>	<p>300 mg once every 28 days. Must take place in an approved infusion facility</p>	<p>Used as a monotherapy (not in combination with any other MS disease-modifying treatment or other immune suppressant drugs) for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri increases the risk of PML, a rare and potentially fatal brain infection.</p> <p>Approval: 2006 US; 2006 CAN</p> <p>Pregnancy: May cause fetal harm based on animal data</p>	<p>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, page 27)</p>

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 2–5% of participants in clinical trials and were more frequent in treatment groups than in 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 31**) 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.
- It is not known if interferon beta-1a medications can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

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.
- It is not known if interferon beta-1b medications can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

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.
- It is not known if glatiramer acetate medications can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

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 six months before you start taking Aubagio and once a month for six months after you start taking Aubagio. Continued blood tests after six 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. Females should be given a pregnancy test prior to starting the medication. After stopping Aubagio, continue using effective birth control until you have blood tests to make sure your blood levels of Aubagio are low enough. If you become pregnant while taking Aubagio or during the two years after you stop taking it, tell your healthcare provider right away. For men taking Aubagio, if your female partner does not plan to become pregnant, you and your female partner should use effective birth control during your treatment with Aubagio. If you plan to father a child, you should stop taking Aubagio and ask your healthcare provider how to quickly lower the levels of Aubagio in your blood.

The prescribing information also contains the following additional warnings:

- Aubagio may stay in your blood for up to two 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 for more information.
- Upon discontinuing Aubagio, it is recommended that all females of reproductive potential undergo an accelerated drug elimination procedure.
- 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 six 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.
- It is not known if Aubagio passes into your breast milk. You and your doctor should decide if you will take Aubagio or breastfeed.

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 six hours after taking your first dose of Gilenya and have another ECG at the end of that six-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 one 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 one 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 two 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 three to four months after you start taking Gilenya. Your healthcare provider should test your vision before you start taking Gilenya, three to four 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.
- Consult your doctor before getting pregnant. You should avoid becoming pregnant while taking Gilenya or in the two months after you stop taking it because of the risk of harm to the baby. If you are a female who can become pregnant, you should use effective birth control during your treatment with Gilenya and for at least 2 months after you stop taking Gilenya. It is not known if Gilenya passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take Gilenya.
- Children need to have completed their vaccination schedule before starting treatment with Gilenya.

Cladribine (Mavenclad®) warnings

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

- Treatment with Mavenclad may increase your risk of developing cancer. Talk to your healthcare provider about your risk of developing cancer if you receive Mavenclad. You should follow your healthcare provider's instructions about screening for cancer.
- Mavenclad may cause birth defects if used during pregnancy. Females must not be pregnant when they start treatment with Mavenclad or become pregnant during Mavenclad dosing and within six months after the last dose of each yearly treatment course. Stop your treatment with Mavenclad and call your healthcare provider right away if you become pregnant during treatment with Mavenclad.
 - » For females who are able to become pregnant:
 - Your healthcare provider should order a pregnancy test for you before you begin your first and second yearly treatment course of Mavenclad to make sure that you are not pregnant. Your healthcare provider will decide when to do the test.
 - » Use effective birth control (contraception) on the days on which you take Mavenclad and for at least six months after the last dose of each yearly treatment course.
 - Talk to your healthcare provider if you use oral contraceptives (the "pill").
 - You should use a second method of birth control on the days on which you take Mavenclad and for at least four weeks after your last dose of each yearly treatment course.
 - » For males with female partners who are able to become pregnant:
 - Use effective birth control (contraception) during the days on which you take Mavenclad and for at least six months after the last dose of each yearly treatment course.

The prescribing information also contains the following additional warnings:

- Mavenclad may cause low blood cell counts. Low blood cell counts can increase your risk of infections during your treatment with Mavenclad. Your healthcare provider will do blood tests before you start treatment with Mavenclad, during your treatment with Mavenclad, and afterward, as needed.
- Mavenclad may cause serious infections such as TB, hepatitis B or C, and shingles (herpes zoster). Fatal cases of TB and hepatitis happened with cladribine during clinical studies.
- PML is a rare brain infection that usually leads to death or severe disability. Although PML has not been seen in MS patients taking Mavenclad, it may happen in people with weakened immune systems.
- Mavenclad may cause liver problems. Your healthcare provider should do blood tests to check your liver before you start taking Mavenclad.

- Mavenclad can cause serious allergic reactions. Stop your treatment with Mavenclad and go to the closest emergency room for medical help right away if you have any signs or symptoms of allergic reactions.
- Mavenclad may cause heart failure, which means your heart may not pump as well as it should.
- You should not receive live or live-attenuated vaccines within the four to six weeks preceding your treatment with Mavenclad. You should not receive these types of vaccines during your treatment with Mavenclad and until your healthcare provider tells you that your immune system is no longer weakened.
- Talk to your healthcare provider before receiving a blood transfusion after receiving treatment with Mavenclad.
- Do not take Mavenclad if you:
 - » Have cancer (malignancy).
 - » Are human immunodeficiency virus (HIV) positive.
 - » Have active infections, including tuberculosis (TB), hepatitis B or C.
 - » Are allergic to cladribine.
 - » Are breastfeeding.
- Before you take Mavenclad, tell your healthcare provider about all of your medical conditions, including if you:
 - » Think you have an infection.
 - » Have heart failure.
 - » Have liver or kidney problems.
 - » Have taken, take, or plan to take medicines that affect your immune system or your blood cells, or other treatments for MS. Certain medicines can increase your risk of getting an infection.
 - » Have had a recent vaccination or are scheduled to receive any vaccinations.
 - » Have or have had cancer.
 - » Are breastfeeding or plan to breastfeed. It is not known if Mavenclad passes into your breast milk. Do not breastfeed on the days, on which you take Mavenclad and for 10 days after the last dose.

Siponimod (Mayzent®) warnings

The FDA prescribing information for Mayzent (siponimod) includes the following warnings and precautions:

- Mayzent can cause your heart rate to slow down (bradycardia or bradyarrhythmia), especially after you take your first dose. You should have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose of Mayzent. During the initial up dosing period (four days for the 1 mg daily dose or five days for the 2 mg daily dose), if you miss one or more doses of Mayzent, you need to restart the up dosing. Call your healthcare provider if you miss a dose of Mayzent.

- Mayzent can increase your risk of serious infections that can be life-threatening and cause death. Mayzent lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within three to four weeks of stopping treatment. Your healthcare provider should review a recent blood test of your white blood cells before you start taking Mayzent.
- Mayzent may cause a problem with your vision called macular edema. Macular edema can cause some of the same vision symptoms as a multiple sclerosis (MS) attack (optic neuritis). You may not notice any symptoms with macular edema. If macular edema happens, it usually starts in the first one to four months after you start taking Mayzent. Your healthcare provider should test your vision before you start taking Mayzent and any time you notice vision changes during treatment with Mayzent. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis.
- Mayzent may cause increased blood pressure. Your healthcare provider should check your blood pressure during treatment with Mayzent.
- Mayzent may cause liver problems. Your healthcare provider should do blood tests to check your liver before you start taking Mayzent.
- Mayzent may cause breathing problems. Some people who take Mayzent have shortness of breath.
- Mayzent may cause swelling and narrowing of the blood vessels in your brain. This condition is called PRES (Posterior Reversible Encephalopathy Syndrome) and has happened with drugs in the same class. Symptoms of PRES usually get better when you stop taking Mayzent.
- Mayzent may cause severe worsening of MS after stopping it. When Mayzent is stopped, symptoms of MS may return and become worse compared to before or during treatment. Always talk to your healthcare provider before you stop taking Mayzent for any reason. Tell your healthcare provider if you have worsening symptoms of MS after stopping Mayzent.
- Mayzent may harm your unborn baby. Talk to your healthcare provider right away if you become pregnant while taking Mayzent or if you become pregnant within 10 days after you stop taking Mayzent. If you are a woman who can become pregnant, you should use effective birth control during your treatment with Mayzent and for at least 10 days after you stop taking Mayzent.
- Tell your healthcare provider if you are breastfeeding or plan to breastfeed. It is not known if Mayzent passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Mayzent.
- You should avoid receiving live vaccines during treatment with Mayzent. Mayzent should be stopped one week before and for four weeks after receiving a live vaccine. If you receive a live vaccine, you may get the infection the vaccine was meant to prevent. Vaccines may not work as well when given during treatment with Mayzent.
- PML is a rare brain infection that usually leads to death or severe disability. Although PML has not been seen in MS patients taking Mayzent, it has been seen with drugs in the same class and it may happen in people with weakened immune systems.

- Do not take Mayzent if you:
 - » Have a CYP2C9*3/*3 genotype. Before starting treatment with Mayzent, your CYP2C9 genotype should be determined by your healthcare provider. Ask your healthcare provider if you are not sure.
 - » Have had a heart attack, chest pain called unstable angina, stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last six months.
 - » Have certain types of heart block or irregular or abnormal heartbeat (arrhythmia), unless you have a pacemaker.
 - » Are pregnant or plan to become pregnant.
- Before taking Mayzent, tell your healthcare provider about all of your medical conditions, including if you:
 - » Had chicken pox or have received the vaccine for chicken pox. Your healthcare provider may do a blood test for chicken pox virus. You may need to get the full course of vaccine for chicken pox and then wait one month before you start taking Mayzent.
 - » Take medicines that affect your immune system, such as beta-interferon or glatiramer acetate, or any MS medicines that you took in the past.

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 may cause herpes zoster infections (shingles) and other serious opportunistic infections. Your healthcare provider should monitor you for serious infections while you are taking Tecfidera. If you have an infection, your healthcare provider may stop Tecfidera until the infection resolves.
- 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.
- It is not known if Tecfidera can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

Diroximel fumarate (Vumerity®) warnings

The FDA prescribing information for Vumerity (diroximel fumarate) includes the following warnings and precautions:

- Vumerity 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 (which has the same active metabolite as Vumerity).
- Vumerity can cause decreases in your white blood cell count. Your healthcare provider should do a blood test to check your white blood cell count before you start treatment with Vumerity and while you are on therapy. You should have blood tests after six months of treatment and every six to twelve months after that.
- Vumerity may cause herpes zoster infections (shingles) and other serious opportunistic infections. Your healthcare provider should monitor you for serious infections while you are taking Vumerity. If you have an infection, your healthcare provider may stop Vumerity until the infection resolves.
- Vumerity can cause liver problems. Your healthcare provider should do blood tests to check your liver function before you start taking Vumerity and during treatment if needed.
- It is not known if Vumerity can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

Ozanimod (Zeposia®) warnings

The FDA prescribing information for Zeposia (ozanimod) includes the following warnings and precautions:

- Zeposia may cause your heart rate to temporarily slow down (bradycardia or bradyarrhythmia), especially during the first 8 days of treatment. You will have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose of Zeposia. During the initial up dosing period (2 weeks), if you miss one or more doses of Zeposia, you may need to restart the up dosing. Call your healthcare provider if you miss a dose of Zeposia.
- Zeposia can increase your risk of serious infections that can be life-threatening and cause death. Zeposia lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 3 months of stopping treatment. Your healthcare provider may do a blood test of your white blood cells before you start taking Zeposia.
- Zeposia may cause a problem with your vision called macular edema. Your risk for macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis. Your healthcare provider should test your vision before you start taking Zeposia if you are at higher risk for macular edema or at any time you notice vision changes during treatment.

- Zeposia can cause increased blood pressure. Your healthcare provider should check your blood pressure during treatment with Zeposia. A sudden, severe increase in blood pressure (hypertensive crisis) can happen when you eat certain foods that contain high levels of tyramine while taking Zeposia.
- Zeposia may cause liver problems.
- Zeposia may cause new or worsening breathing problems, including shortness of breath and breathing problems during sleep (sleep apnea). Do not take Zeposia if you have untreated, severe sleep apnea.
- Zeposia may cause a rare condition called PRES (Posterior Reversible Encephalopathy Syndrome). PRES has happened with Zeposia and with drugs in the same class. Symptoms of PRES usually get better when you stop taking Zeposia. If left untreated, it may lead to a stroke. Your healthcare provider will do a test if you have any symptoms of PRES.
- Zeposia may cause severe worsening of MS after stopping it. Always talk to your healthcare provider before you stop taking Zeposia for any reason.
- Zeposia may harm your unborn baby. Talk with your healthcare provider if you are pregnant or plan to become pregnant. If you are a female who can become pregnant, you should use effective birth control during your treatment with Zeposia and for 3 months after you stop taking Zeposia.
- It is not known if Zeposia passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Zeposia.
- PML is a rare brain infection that usually leads to death or severe disability. Although PML has not been seen in MS patients taking Zeposia, it has been seen with drugs in the same class and it may happen in people with weakened immune systems.
- Do not take Zeposia if you:
 - » Have had a heart attack, chest pain (unstable angina), stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last 6 months.
 - » Have or have had a history of certain types of an irregular or abnormal heartbeat (arrhythmia) that is not corrected by a pacemaker.
 - » Take certain medicines called monoamine oxidase (MAO) inhibitors such as selegiline, phenelzine and linezolid.
- Before taking Zeposia, tell your healthcare provider about all of your medical conditions, including if you:
 - » Received a vaccine in the past 30 days or are scheduled to receive a vaccine. Zeposia may cause vaccines to be less effective.
 - » Tell your provider if you have had chickenpox or have received the vaccine for chickenpox. Your healthcare provider may do a blood test for the chickenpox virus. You may need to get the full course of the vaccine for chickenpox and then wait 1 month before you start taking Zeposia.
- You should not receive live vaccines during treatment with Zeposia, for at least 1 month before taking Zeposia and for 3 months after you stop taking Zeposia.

- Tell your healthcare provider about all the medicines you take or have recently taken, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you take or have taken medications that affect your immune system such as alemtuzumab, medications to control your heart rhythm or heartbeat, strong CYP2C8 inhibitors, CYP2C8 inducers, or medications for breast cancer.
- It is not recommended that a person take certain other medications along with Zeposia, since this may cause high blood pressure. These include opioid pain killers, medicines to treat depression, certain medicines to treat MS-related pain, medicines to treat Parkinson's disease, and certain over-the-counter decongestants (pseudoephedrine). Blood pressure should be monitored for individuals taking these types of medications along with Zeposia.

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. Tell your healthcare provider immediately if you have an infusion reaction.
- Lemtrada may increase your chance of getting certain cancers, including thyroid cancer, skin cancer (melanoma), blood cancers and lymphoma.
- Serious and life-threatening stroke, heart attack and tears in arteries that supply blood to the brain have been reported within three 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.
- Progressive multifocal leukoencephalopathy (PML), a rare brain infection that usually leads to death or severe disability has been reported with Lemtrada.
- Lemtrada can cause pneumonitis, the swelling of lung tissue.
- Lemtrada may increase the risk of a type of overactivity of the immune system (hemophagocytic lymphohistiocytosis) that can be fatal, especially if not diagnosed and treated early. This has happened about 13 months to 33 months after starting Lemtrada.

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 six 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 three 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.
- It is not known if Lemtrada can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider. You should use birth control while receiving Lemtrada and for 4 months after your course of treatment.

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 [ntlms.org/mitoxantrone](https://www.natlms.org/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 one 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 four weeks before you start treatment with Ocrevus or 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 two 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.
- It is not known if Ocrevus can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider. You should use birth control while receiving Ocrevus and for 4 months after your course of treatment.

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 two 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 and 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 two 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.
- It is not known if Tysabri can harm your unborn baby or pass into your breastmilk. If you are pregnant or breastfeeding, or planning to become pregnant or breastfeed, talk to your healthcare provider.

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 [nationalmssociety.org/Treating-MS/Medications](https://www.nationalmssociety.org/Treating-MS/Medications), or from each manufacturer (see page 31). 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 an 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 associated with the medication you are taking, do not hesitate to ask your healthcare provider.

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: 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 healthcare provider'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. These pharmaceutical 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 31**). 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
aubagio.com/cost

AVONEX®

MS ActiveSource®
800-456-2255
avonex.com or aboveMS.com

BETASERON® and 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

GLATIRAMER ACETATE

Mylan Support Program
844-695-2667
glatirameracetate.com/en/patient-support

LEMTRADA®

MS One to One®
855-676-6326
lemtrada.com

MAVENCLAD®

MS LifeLines®
877-447-3243
ntlms.org/mavencladresources

MAYZENT®

Novartis Patient Assistance Foundation
800-277-2254
ntlms.org/novartisassistance

NOVANTRONE®

No patient support program at this time

OCREVUS®

Genentech Access Solutions®
844-627-3887 or 866-422-2377
Genentech-Access.com

PLEGRIDY®

MS ActiveSource®
800-456-2255
plegridy.com or aboveMS.com

REBIF®

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

TECFIDERA®

MS ActiveSource®
800-456-2255
tecfidera.com or aboveMS.com

TYSABRI®

MS ActiveSource®
800-456-2255
tysabri.com or aboveMS.com

VUMERITY®

800-456-2255
aboveMS.com

ZEPOSIA®

ZEPOSIA 360 SUPPORT™
1-833-937-6742
zeposia.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](https://www.nationalmssociety.org/insurance) for more information.

For detailed information on patient assistance programs from manufacturers, visit [needymeds.org](https://www.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](https://www.ms-coalition.org/EmergingTherapies).

Aubagio® is a registered trademark of Genzyme Corporation.
Avonex® is a registered trademark of Biogen Idec.
BETAPLUS® is a registered trademark of Bayer Schering Pharma.
Betaseron® is a registered trademark of Bayer Schering Pharma Aktiengesellschaft.
Copaxone® is a registered trademark of Teva Pharmaceutical Industries Ltd.
Extavia® is a registered trademark of Novartis AG Corporation.
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.
Glatopa® is a trademark of Novartis AG.
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.
Vumerity® is a trademark of Biogen.
Zeposia is a registered trademark of Bristol Myers Squibb.
ZEPOSIA 360 SUPPORT is a trademark of Bristol Myers Squibb.

The National Multiple Sclerosis Society is proud to be a source of information about multiple sclerosis. Our comments are based on professional advice, published experience and expert opinion, but do not represent individual therapeutic recommendations or prescriptions. For specific information and advice, consult your physician.

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 Society at **[nationalMSSociety.org](https://www.nationalmssociety.org)** or 1-800-344-4867.

The Society publishes many other resources about various aspects of MS. Visit **[nationalMSSociety.org/brochures](https://www.nationalmssociety.org/brochures)** or call 1-800-344-4867.

The Society mobilizes people and resources so that everyone affected by multiple sclerosis can live their best lives as we **stop MS in its tracks, restore what has been lost and end MS forever**. Last year, the Society invested \$35 million in MS research with more than 340 active projects around the world. Through its comprehensive nationwide network of services, the Society is focused on helping those affected by MS connect to the people, information and resources needed to live their best lives. We are united in our collective power to do something about MS now and end this disease forever. Learn more at **[nationalMSSociety.org](https://www.nationalmssociety.org)**.



**National
Multiple Sclerosis
Society**

[nationalMSSociety.org](https://www.nationalmssociety.org)

**For information:
1-800-344-4867**