

The MS Disease- Modifying Medications

GENERAL INFORMATION



National
Multiple Sclerosis
Society



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For some people, a diagnosis of MS is a relief, giving a name and a reason for a parade of strange symptoms. For others, a diagnosis of MS brings images of the worst possible future. Both reactions will likely change somewhat over time, but for many with MS, diagnosis is a day when life changes.

Even before the news can be fully absorbed, people with MS face a decision about taking a disease-modifying medication. The Society's National Clinical Advisory Board agrees that disease-modifying medications are most effective when started early, before the disease has the opportunity to progress further.

Disease-modifying medications:

- Reduce the frequency and severity of clinical attacks (also called relapses or exacerbations), which are defined as the worsening of an MS symptom or symptoms, and/or the appearance of new symptoms, which lasts at least 24 hours and is separated from a previous exacerbation by at least one month.

- Reduce the accumulation of lesions (damaged or active disease areas) within the brain and spinal cord as seen on MRI (magnetic resonance imaging).
- Appear to slow down the accumulation of disability.

These medications, which are generally taken on a long-term basis, are the best defense currently available to slow the natural course of MS. Even though the disease-modifying medications don't generally make a person feel better, they can be looked upon as an investment in the future.

Options

There are currently eight disease-modifying medications approved by the U.S. Food and Drug Administration (FDA) for use in relapsing forms of MS (including secondary-progressive MS for those people who are still experiencing relapses).

Of these, one is also approved specifically for secondary-progressive MS. None of these medications is a cure, and none will prevent recurring symptoms, such as fatigue or numbness. However each of them has a proven record of effectiveness. Unfortunately, no disease-modifying medication has yet been approved to treat primary progressive MS — the type of MS that shows steady progression at onset.

Decisions about taking a disease-modifying medication are best made by carefully considering and weighing factors including individual lifestyle, disease course, known side effects, and the potential risks and benefits of the different therapies. A full discussion with a knowledgeable health care professional is the best guide for your decision. Each person's body or disease can respond to these medications in different ways.

The following charts present important information about each of the medications, which are listed in alphabetical order.

Brand (Generic Name) & Frequency/Route of Delivery/Usual Dose

Avonex® (*interferon beta-1a*)

Once a week; intramuscular (into the muscle) injection; 30 mcg.

Betaseron® (*interferon beta-1b*)

Every other day; subcutaneous (under the skin) injection; 250 mcg.

Copaxone® (*glatiramer acetate*)

Every day; subcutaneous (under the skin) injection; 20 mg (20,000 mcg).

Extavia® (*interferon beta-1b*)

Every other day; subcutaneous (under the skin) injection; 250 mcg.

Gilenya™ (*fingolimod*)

Every day; capsule taken orally.

Novantrone®

(*mitoxantrone*; as of 2006, available as a generic drug)

Four times a year by IV infusion in a medical facility. Lifetime cumulative dose limit of approximately 8–12 doses over 2–3 years (140 mg/m²).

Rebif® (*interferon beta-1a*)

Three times a week; subcutaneous (under the skin) injection; 44 mcg.

Tysabri® (*natalizumab*)

Every four weeks by IV infusion in a registered infusion facility; 300 mg.

Manufacturer/Distributor & Year of FDA Approval

Avonex®	Biogen Idec — 1996
Betaseron®	Bayer HealthCare Pharmaceuticals, Inc. — 1993
Copaxone®	Teva Pharmaceuticals Industries, Ltd. — 1996
Extavia®	Novartis Pharmaceuticals Corp. — 2009
Gilenya™	Novartis Pharmaceuticals Corp. — 2010
Novantrone®	EMD Serono, Inc./Immunex Corporation — 2000
Rebif®	EMD Serono, Inc./Pfizer, Inc. — 2002
Tysabri®	Biogen Idec/Elan Pharmaceuticals, Inc. — 2006

Indication (FDA-approved Use)

Avonex®

For the treatment of relapsing forms of MS to slow the accumulation of physical disability and reduce the frequency of clinical exacerbations, and for patients who have experienced a first clinical episode and have MRI features consistent with MS.

Betaseron®

For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; and for patients who have experienced a first clinical episode and have MRI features consistent with MS.

Copaxone®

For the treatment of relapsing-remitting MS to reduce the number of clinical exacerbations; and for patients who have experienced a first clinical episode and have MRI features consistent with MS.

Extavia®

For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; and for patients who have experienced a first clinical episode and have MRI features consistent with MS.

Gilenya™

For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

Novantrone®

For the treatment of worsening relapsing-remitting MS, progressive-relapsing MS or secondary-progressive MS to reduce neurologic disability and/or the frequency of clinical exacerbations.

Rebif®

For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations and delay the accumulation of physical disability.

Tysabri®

To be used as a monotherapy (not in combination with any other disease-modifying medications) for the treatment of relapsing forms of MS to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations; generally recommended for patients who have had inadequate response to, or are unable to tolerate, another disease modifying medication.

NOTE: Patients taking interferon beta-1a (Avonex or Rebif) or interferon beta-1b (Betaseron or Extavia) medications may develop immunity to the treatment demonstrated by the presence of “neutralizing antibodies” detected in their blood. Some neurologists believe that this is an important factor in managing patients receiving interferon.

Side Effects (always inform your health care professional of side effects)

Avonex®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” on page 8.) Less common: depression, mild anemia, liver abnormalities, allergic reactions, heart problems. (See “Avonex Warnings” on page 9.)

Betaseron®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” below.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities, low white blood cell counts. (See “Betaseron Warnings” on page 10.)

Copaxone®

Injection site reactions. Less common: vasodilation (dilation of blood vessels); chest pain; a reaction immediately after injection, which includes anxiety, chest pain, palpitations, shortness of breath, and flushing. This lasts 15-30 minutes, typically passes without treatment, and has no known long-term effects. (See “Copaxone Warnings” on page 10.)

Extavia®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” below.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities, low white blood cell counts. (See “Extavia Warnings” on page 11.)

Gilenya™

Headache, flu, diarrhea, back pain, liver enzyme elevations and cough. Less common: slowed heart rate following first dose, infections, swelling in the eye. (See “Gilenya Warnings” on page 11.)

Rebif®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” below.) Injection site reactions. Less common: liver abnormalities, depression, allergic reactions, and low red or white blood cell counts. (See “Rebif Warnings” on page 12.)

Novantrone®

Blue-green urine 24 hours after administration; infections, bone marrow suppression (fatigue, bruising, low blood cell counts), nausea, hair thinning, bladder infections, mouth sores. Patients must be monitored for serious liver and heart damage. (See “Novantrone Warnings” on page 13.)

Tysabri®

Headache, fatigue, urinary tract infections, depression, lower respiratory tract infections, joint pain, and chest discomfort. Less common: allergic or hypersensitivity reactions within two hours of infusion (dizziness, fever, rash, itching, nausea, flushing, low blood pressure, difficulty breathing, chest pain), liver abnormalities. Patients must be monitored for PML. (See “Tysabri Warnings” on page 13.)

Managing side effects of disease-modifying medications

Not everyone will experience every one of these side effects. Some adverse effects are common, and others are very infrequent but may be serious. Your health care provider can give you a better sense of how frequently problems occur with the specific agent he or she recommends for you. The industry-sponsored websites may also give you an idea of how frequently these effects occur.

The flu-like side effects of the interferon products — Avonex[®], Betaseron[®], Extavia[®], and Rebif[®] — can usually be managed successfully. Discuss this with your physician or other health care provider, and the patient support program of the pharmaceutical company (available through a toll-free number — see chart entitled “Industry-Sponsored Sites” on page 16). Should unacceptable side effects continue, discuss possible change to another medication with your health care professional.

The medications that are injected subcutaneously including Betaseron, Copaxone[®], Extavia, and Rebif, may cause injection site reactions, including bumps, bruises, pain, and infections. Good injection techniques can minimize problems. Auto-injecting devices may be helpful. The pharmaceutical company patient support programs offer injection training and helpful tips for avoiding or limiting site reactions (see chart entitled “Industry-Sponsored Sites” on page 16).

Avonex[®] Warnings

In response to events reported by patients and clinicians following approval of this medication, the FDA has added the following warnings about Avonex[®] (interferon beta-1a): Individuals with a history of depression, a seizure disorder, or cardiac problems should be closely monitored while on this medication; All patients on this medication should have baseline liver function testing and periodic testing thereafter;

Periodic blood testing is recommended to check for a possible reduction in infection-fighting blood cells, red blood cells, and cells that help blood to clots; Rare but significant allergic reactions have been reported to this medication.

Betaseron[®] Warnings

In response to events reported by patients and clinicians following approval of this medication, the FDA has added the following warning Betaseron[®] (interferon beta-1b): Individuals with a history of depression or a seizure disorder should be closely monitored while on this medication; This medication should be used with caution in people with depression; Rare but significant allergic reactions have been reported with this medication; Because skin infections or areas of severe skin damage can occur, injection sites should be rotated on a regular basis.

Copaxone[®] Warnings

The FDA labeling for Copaxone[®] (glatiramer acetate) contains the following warnings: Approximately 16% of people will experience an immediate post-injection reaction that includes at least two of the following: flushing, chest pain, palpitations, anxiety, shortness of breath, constriction of the throat, and transient skin eruptions. These symptoms generally disappear

spontaneously after about 15 minutes and have no long-term effects. This post-injection reaction generally occurs after the first few months of treatment and may occur more than once in a given individual. Transient chest pain — without any long-term effects — may also occur one or more times, either as part of the post-injection reaction or separately. Permanent depressions under the skin at injection sites can occur because of destruction of the fatty tissue. In addition, areas of severe skin damage can occur. For these reasons, careful rotation of injection sites is recommended so that no single area is injected more than one time per week.

Extavia® Warnings

Because Extavia® (interferon beta-1b) is identical to Betaseron® (interferon beta-1b), the FDA labeling includes the same warnings.

Gilenya™ warnings

Gilenya™ (fingolimod) has the following warnings included in its FDA label: If a person has not had chicken pox (varicella), his or her doctor may recommend the varicella vaccine prior to starting this medication; Because Gilenya can cause

a person's heart rate to drop after the first dose, patients will be monitored for six hours in the doctor's office after taking the first dose of medication; Because this medication reduces the number of white blood cells, leading to an increased risk of infection, a blood test to measure white blood cell count is recommended prior to starting treatment; A vision test is recommended prior to starting treatment and 2–3 months later to look for evidence of macular swelling in the eye; Because Gilenya can cause liver problems, a liver function test is recommended prior to starting treatment.

Rebif® Warnings

In response to events reported by patients and clinicians following approval of this medication, the FDA has added the following warnings about Rebif® (interferon beta-1a): Individuals with a history of depression or a seizure disorder should be closely monitored while on this medication; All patients on this medication should have baseline liver function testing and periodic testing thereafter; Periodic blood testing is recommended to check for a possible reduction in infection-fighting blood cells, red blood cells, and cells that help blood to clots; Rare but significant allergic reactions have been reported to this medication.

Novantrone® Warnings

Novantrone® (mitoxantrone) is a chemotherapeutic treatment originally developed to treat certain forms of cancer. The total lifetime dose is limited in order to avoid possible heart damage. People taking Novantrone should have tests of their heart function before each dose. It cannot be used in people with pre-existing heart problems, liver disease, and certain blood disorders. In addition to cardiac toxicity, acute myelogenous leukemia (AML), a type of cancer, has been reported in MS patients and cancer patients treated with Novantrone. AML can be fatal.

Tysabri® Warnings

Tysabri® (natalizumab) is a laboratory-produced monoclonal antibody that is given by intravenous (IV) infusion every four weeks. Tysabri cannot be infused at home, so your doctor will help you find an infusion center that is convenient to your home.

When talking with your health care professional about starting treatment with Tysabri, it is important to consider the following information: Individuals taking Tysabri are at increased risk for a rare, generally fatal brain disease called PML (progressive multifocal leukoencephalopathy), which is caused by the common JC virus.

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

In January, 2012, the FDA approved a change to the prescription label for Tysabri to show that a laboratory test that detects antibodies to the JC virus can help determine a person's risk of developing PML. Testing positive for the presence of antibodies indicates that a person has at some point been infected by or exposed to the virus, which puts that person at higher risk of developing PML. Previous findings have also shown that prior use of immune-suppressing drugs and taking Tysabri for more than two years each increase a person's risk for developing PML.

The revised label suggests that the risks and benefits of starting or continuing Tysabri should be carefully considered in patients who test positive for antibodies to the JC virus and have one or more additional risk factors. Those found to be antibody positive, have used Tysabri for less than two years, and have no prior use of immune suppressing drugs are estimated to have a risk of PML of less than 1/1000; those with all three known risk factors have an estimated risk of PML of 11/1000.

A person who tests negative for anti-JCV antibodies is still at risk for the development of PML for two very important reasons. First, she or he can be infected by the JC virus at any time without knowing it. Second, the laboratory test to detect antibodies to the JC virus will produce a false negative result about three percent of the time. Therefore, testing should be considered prior to starting treatment with Tysabri, as well as periodic re-testing while a person is on treatment. The availability of the laboratory test will help people with MS and their physicians to weigh risks and benefits of this therapy.

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

Based on post-marketing experience with Tysabri®, the FDA added an additional warning to the product's labeling information in February, 2008. Tysabri has been found to increase the risk of liver damage, even after a single dose.

Any person experiencing symptoms of liver injury, including yellowing of the skin and eyes (jaundice) unusual darkening of the urine, nausea, feeling tired or weak, and vomiting, should contact his or her physician immediately. Blood tests can be done to check for liver damage.

Tysabri is **not** recommended for use by any person whose immune system is weakened by disease or by the use of medications that alter the immune system, including other disease-modifying therapies.

Currently, nothing is known about the safety of long-term use of Tysabri or whether additional side effects will emerge in time.

Warnings about IV infusions

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

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

Avonex®
MS ActiveSource®
avonex.com | msactivesource.com
800-456-2255

Betaseron®
BETAPLUS®
betaseron.com
800-788-1467

Copaxone®
Shared Solutions®
sharedsolutions.com
800-887-8100

Extavia®
extavia.com
Extavia Go Program
866-398-2842

Gilenya™
gilenya.com
Gilenya Go Program
800-445-3692

Novantrone®
888-275-7376

Rebif®
MS LifeLines™
rebif.com | mslifelines.com
877-447-3243

Tysabri®
tysabri.com
800-456-2255

Benefits of the Disease-Modifying Medications

Reducing the frequency of attacks and new lesions as seen on MRI

All of these medications have been shown to reduce the frequency of MS relapses and the development of new lesions. In individual clinical trials comparing a drug versus an inactive placebo treatment, MS attacks were reduced by 28–68 percent by different agents. In the clinical trials, most people were also found to have fewer, smaller, or no new lesions developing within their central nervous system as visible in MRI scans.

Preventing permanent damage

Permanent damage to nerve fibers (called axons) occurs early in MS in association with the destruction of myelin. Overall brain shrinkage (or atrophy), can occur early in the disease, and damage can be ongoing even when the person has no symptoms of an attack and feels well. Therefore, MS specialists advise the early use of a medication that effectively limits lesion formation and brain atrophy, or shrinkage. In the opinion of the National MS Society's Clinical Advisory Board, limiting lesions may be a key to reducing future permanent disability for many people with MS.

None of these medications is recommended for women who are pregnant or plan to become pregnant. Physicians should be consulted. Most women will be advised to avoid using these medications during pregnancy.

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 your options.

Paying for a Disease-Modifying Medication: Some Help is Available

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

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

Because Novantrone® and Tysabri® 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 Active Source® (800-456-2255).

Medicare Part D covers prescription drugs through private plans approved by Medicare. For more information on Medicare prescription drug coverage, go to: nationalMSsociety.org/medicare, or call 1-800-344-4867.

Medicaid includes prescription drug 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 the chart entitled “Industry-Sponsored Sites.” Ask for information on available assistance.

For additional information on specific industry assistance, visit: nationalMSsociety.org/AssistancePrograms.

Help with the Cost of Medications for Symptom Management

In addition to the disease-modifying medications discussed above, 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 our website at nationalMSsociety.org/insurance for more information.

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

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.

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MS Lifelines® is a registered trademark of EMD Serono, Inc.

Rebif® is a registered trademark of Ares Trading, S.A.

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

Tysabri® is a registered trademark of Elan Pharmaceuticals, Inc.

TOUCH™ is a trademark of Biogen Idec and Elan.

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