

The MS Disease-Modifying Drugs

GENERAL INFORMATION



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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 drug. The Society's National Clinical Advisory Board agrees that disease-modifying drugs 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 sudden worsening of an MS symptom or symptoms, 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 drugs, 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 make a person feel better, they can be looked upon as an investment in the future.

Options

There are currently seven 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). They may work differently for everyone,

and none of them are a cure for MS. None will prevent recurring symptoms, such as fatigue or numbness, which typically come and go. All of them have proven records of partial to substantial success. Unfortunately, none of the currently available disease-modifying drugs are approved for treating primary progressive MS — the type of MS that shows steady progression at onset.

Decisions about taking a disease-modifying drug are best made by carefully considering and weighing factors including individual lifestyles, known side effects, and the potential risks and benefits of the different therapies. A full discussion with a knowledgeable healthcare 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 sort out and present some of the relevant facts. Rebif®, Copaxone®, Betaseron®, Extavia® and Avonex® are self-injectable drugs for long-term use; they modulate the immune system, which means they adjust or modify how the immune system functions. Tysabri®, which is also an immune-modulating drug, is delivered by IV infusion (into the vein) at a registered infusion facility. Novantrone® is a powerful immune system suppressor, delivered by IV infusion in a medical setting.

Brand & Generic Name

Immunomodulating drugs

Avonex®	interferon beta-1a
Betaseron®	interferon beta-1b
Copaxone®	glatiramer acetate
Extavia®	interferon beta-1b
Rebif®	interferon beta-1a
Tysabri®	natalizumab

Immunosuppressant drug

Novantrone®	Mitoxantrone; as of 2006, available as a generic drug
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Manufacturer/Distributor & Year of FDA Approval

Immunomodulating drugs

Avonex®	Biogen Idec — 1996
Betaseron®	Bayer HealthCare Pharmaceuticals, Inc. — 1993
Copaxone®	Teva Neuroscience — 1996
Extavia®	Novartis Pharmaceuticals Corp. — 2009
Rebif®	EMD Serono, Inc./Pfizer, Inc. — 2002
Tysabri®	Biogen Idec/Elan Pharmaceuticals, Inc. — 2006

Immunosuppressant drug

Novantrone®	EMD Serono, Inc./Immunex Corporation — 2000
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Indication (FDA-approved Use)

Immunomodulating drugs

Avonex®

For the treatment of relapsing forms of MS, and for a first clinical episode if MRI features consistent with MS are also present.

Betaseron®

For the treatment of relapsing forms of MS and secondary-progressive MS with relapses; 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; 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 and secondary-progressive MS with relapses; and for patients who have experienced a first clinical episode and have MRI features consistent with MS.

Rebif®

For the treatment of relapsing forms of MS.

Tysabri®

For the treatment of relapsing forms of MS as a monotherapy (not used in combination with any other disease-modifying medication). Generally recommended for patients who have had inadequate response to, or are unable to tolerate, another disease modifying medication.

Immunosuppressant drug

Novantrone®

For treatment of worsening relapsing-remitting MS and for progressive-relapsing or secondary-progressive MS.

Frequency/Route of Delivery/Usual Dose

Immunomodulating drugs

Avonex®

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

Betaseron®

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

Copaxone®

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

Extavia®

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

Rebif®

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

Tysabri®

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

Immunosuppressant drug

Novantrone®

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).

Common Side Effects (Always inform your healthcare professional of side effects)

Immunomodulating drugs

Avonex®

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

Betaseron®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects on page 9.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities*, low white blood cell counts.

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, passes without treatment, and has no known long-term effects.

Extavia®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” on page 9.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities*, low white blood cell counts.

Rebif®

Flu-like symptoms following injection, which lessen over time for many. (See “Managing side effects” on page 9.) Injection site reactions. Less common: Liver abnormalities*, depression, allergic reactions, and low red or white blood cell counts.

Immunomodulating drugs

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 10.)

Immunosuppressant drug

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 10.)

* It is recommended that people taking Avonex, Betaseron, Extavia, Rebif, or Tysabri receive baseline liver function testing at the start of treatment and periodic testing thereafter.

Managing side effects of the self-injectable drugs

The flu-like side effects of the interferon products — Avonex[®], Betaseron[®], Extavia[®], and Rebif[®] — can usually be minimized. Discuss this with your physician or other healthcare provider, and the patient support program of the drug company (available through a toll-free number — see chart entitled “Industry-Sponsored Sites” on page 13). Should unacceptable side effects continue, discuss possible change to another drug with your health care professional.

The drugs 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 drug company patient support programs offer injection training and helpful tips for avoiding or limiting site reactions (see chart entitled “Industry-Sponsored Sites” on page 13).

Novantrone[®] warnings

Novantrone[®] (mitoxantrone) is a chemotherapeutic drug 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 attaches to a specific surface structure of immune T cells. Tysabri slows or stops T cells from moving out of the bloodstream and into the brain and spinal cord where they may stimulate the inflammation that is believed to result in MS attacks.

It is important to consider the following information in discussions with your health care professional about starting on treatment with Tysabri. 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.

Although the three cases of PML that occurred in the clinical trials were in patients who were also taking another immunomodulating or immunosuppressing medication, additional cases of PML in people who were not taking another immunomodulating or immunosuppressing medication at the same time have been reported in the post-marketing phase.

The absolute risk for PML in patients treated with Tysabri® cannot be precisely estimated. However, the drug's sponsor has released data suggesting that the risk increases with increasing time on therapy, starting out lower than the one-in-one thousand level that was estimated at the time of Tysabri's re-approval in 2006, and rising after two years of infusions to about one in one thousand. At this time, there is insufficient information to determine the risk of PML in those who have been on therapy for three years or more.

Because of the risk of PML, Tysabri is only available under a restricted distribution program referred to as the TOUCH™ program. Prescribing physicians and patients must enroll in this mandatory registry program. Infusion centers must also be enrolled in the TOUCH™ program. Tysabri cannot be infused at home. 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 drugs 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 drugs 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

Immunomodulating drugs

Avonex®

MS Active Source®

avonex.com | msactivesource.com

800-456-2255

Betaseron®

BETAPLUS™

betaseron.com | betaplusonline.com

800-788-1467

Copaxone®

Shared Solutions®

copaxone.com | sharedsolutions.com | mswatch.com

800-887-8100

Extavia®

Patient Support Program

866-925-2333

Rebif®

MS LifeLines®

mslifelines.com

877-447-3243

Tysabri®

biogenidec.com | tysabri.com

800-456-2255

Immunosuppressant drug

Novantrone®

novantrone.com

877-447-3243

Benefits of the Disease-Modifying Drugs

Reducing the frequency and severity of attacks

Most people using a disease-modifying drug have fewer and less severe MS attacks (relapses or exacerbations). In individual clinical trials comparing a drug versus an inactive placebo treatment, MS attacks were reduced by 28–68 percent by different agents. In addition, most people were 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 drug 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 drugs 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 Drug: Some Help is Available

Disease-modifying drugs 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 drugs, although they may cover procedures such as IV infusions in a medical facility. Plans that do cover prescription drugs often have a list of specific drugs covered by the plan (known as a formulary). It is possible that some disease-modifying drugs are covered by a plan and some are not. In addition, many drug 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.

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 drugs covered may vary from state to state. Call your state Medicaid office for more information.

Each of the drug 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 underinsured 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 Drugs for Symptom Management

In addition to the disease-modifying drugs discussed above, there are many other drugs, treatments, and strategies to help manage specific MS symptoms such as bowel and bladder function, spasticity and pain. Symptom management drugs 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 needyeds.org.

Avonex® is a registered trademark of Biogen Idec.

Betaplust® 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.

Novantrone® is a registered trademark of Immunex Corp.

MS Active Source® is a registered trademark Biogen, IDEC MA Inc.

MS Lifelines™ is a trademark of Ares Trading S.A.

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

Shared SolutionsSM is a service mark 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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**For Information:
1 800 FIGHT MS (1 800 344 4867)**