



Medications to Slow Multiple Sclerosis Progression

Multiple sclerosis disease-modifying medications

There are several medications for patients with MS that help slow the course of the disease.

Fortunately, we now have several medications to slow the course of multiple sclerosis (MS). The medications described in this section have all been proven to benefit MS patients in well-designed large studies. Based on the results of these studies, the National Multiple Sclerosis Society states: “Initiation of therapy is advised as soon as possible following a definite diagnosis of MS and determination of a relapsing course.” Patients must decide for themselves, with the help of their doctor, whether they wish to use one of these medications.

Some of the reasons that patients choose to use these medications include:

- They are the only ones that have been proven to slow the disease. We believe that use of these drugs may lead to less disability. After 20 years, 15 to 20% of **untreated** patients are in wheelchairs and 50% need aids to walk.
- Some patients believe they do not have enough attacks to warrant their use. However, patients are not aware of many MS attacks. A very conservative estimate is that for every attack the patient is aware of, there are approximately 10 silent attacks. These "silent" attacks can affect memory, cognition, and other important areas of brain function.

- We now know that one of the effects of MS can be in thinking or memory loss. This can be a serious symptom and decreasing this loss should be a high priority.
- Some patients wait to see if they will become more disabled before using them. However, these drugs do not reverse damage; they decrease future damage. Our advice is to start these drugs before more damage occurs.
- There is some evidence that patients using these drugs early in the disease respond better than those later in disease. There are even studies indicating benefit in patients using these drugs after their first attack and before the diagnosis of MS could be technically made (the firm diagnosis of MS requires at least two attacks).
- Although there are drug side effects, when used appropriately, none of the side effects is medically serious, and these drugs are very safe (Avonex[®], Betaseron[®], Copaxone[®], and Rebif[®] can be safely used indefinitely; Novantrone[®] [mitoxantrone] can be used for two and a half years).

Some of the reasons that patients hesitate or wait to use these medications include:

- On the average, they decrease disease activity by about one third. Each patient must balance the one-third slowing of disease with the inconvenience of using these drugs.
- Though the majority of patients develop some impairment with time, about 15% have very little or no disability even after 20 years. Some patients do not use these medications, hoping they will be one of the fortunate ones. However, there is no way to predict the future and which patients will remain without disability.

Consider the reasons patients choose to:

- ***use medications;***
- ***to not use medications; or***
- ***to wait.***

If you decide to use medications, you and your doctor must decide which is best for you.

- The medications are expensive. They are generally covered by insurance, but some insurance plans have high medication co-payments. Also, they are not FDA-approved for all types of MS and insurance plans may refuse to cover the cost in these cases.
- These drugs are given by injection (needles). The needles are small and usually cause little pain. The greatest barrier to using them is the inconvenience of injections rather than the pain.
- Though the side effects are not medically serious, they can be uncomfortable.

Once patients choose to use a disease-modifying medication, they must then decide with their physician which one is best for them. Only two studies directly comparing these medications to each other have been completed. In one study, 25% of patients treated with Rebif[®] had attacks while 37% of those on Avonex[®] had attacks. Patients were only on this study for 6 months, so the results from longer treatment periods are not known. In a different study, 11% of those treated with Betaseron[®] had attacks while 20% of those on Avonex[®] had attacks. Both studies showed a difference in MRI activity. These modest differences in effectiveness must be balanced against the greater convenience of Avonex[®].

Avonex[®] (Interferon beta-1a)

- Available since 1995.
- Given by injection once a week (with a 1-1/4 inch needle, in a muscle).
- Needs refrigeration.
- Costs about \$10,000/year.



Side Effects

- A red spot occurs only rarely at the site of the injections (4%) because the injection is into the muscle rather than just under the skin. Breakdown of these spots into sores has not been seen.
- Many patients (61%) feel like they have the flu after taking the medicine. This includes fever, chills, sweating, muscle aches and fatigue. Nausea and stomach upset are not usually seen. The flu-like symptoms last for 24 to 36 hours or more. Most patients tolerate these symptoms very well by using aspirin, acetaminophen (Tylenol), or ibuprofen (Motrin). The first injection has the most side effects with subsequent injections having less. It may take a few months for the reactions to reach their lowest amount. These side effects can be reduced by starting with a low dose and gradually increasing to a full dose. Most patients have very few flu-like side effects after 6 months.
- Blood tests need to be done every three months to check the white blood cell count and liver function. After one year, blood tests can be decreased to every four months.
- There is some concern that this drug and other interferons may cause depression. This has never been shown in research studies with Avonex[®].

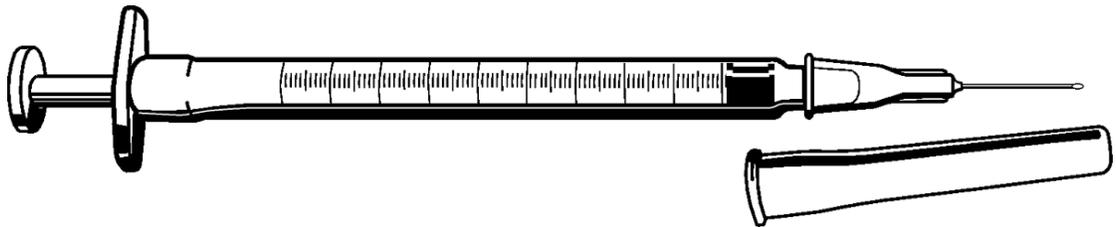
Results for Avonex[®]

Avonex[®] was studied in mild relapsing-remitting MS. The Avonex[®] study showed the time that it took for patients to become more impaired decreased 37%. Attacks were decreased 18% to 38% depending on which types of patients were treated and for what length of time they were treated. There was not a statistically significant change in MRI lesions, primarily because the placebo group did so well. There was a positive effect on active MRI lesions and newer studies have found an effect on MRI lesions. It may take a

few months for the drug to start working. Avonex[®] has been studied in primary progressive disease.

Betaseron[®] (Interferon beta-1b)

- Available since 1993.
- Given by injection every other day (with a 5/8 inch needle in the tissues between the skin and the muscle).
- Costs about \$10,000/year.
- Does not need refrigeration.



Side Effects

- A red spot may occur at the site of the injections (85%). Each red spot may last for several weeks. Rarely (5% or less) the spot may break down, forming a sore.
- Many patients (76%) feel like they have the flu after taking the medicine. This includes fever, chills, sweating, muscle aches and fatigue. Nausea and stomach upset are not usually seen. The flu-like symptoms may last for 8 hours or more. Most patients tolerate these symptoms very well using aspirin, acetaminophen (Tylenol) or ibuprofen (Motrin). The first injection has the most side effects with subsequent injections having less. It may take a few months for the reactions to reach their lowest amount. Most patients have very few flu-like side effects after 6 months. These side effects can be diminished by starting with a low dose, and gradually increasing to full dose.

- Blood tests need to be done every three months to check the white blood cell count and liver function. After one year, blood tests can be decreased to every four months.
- During the first major study of the drug, it was questioned whether depression was a side effect. However, additional studies found no evidence of depression.

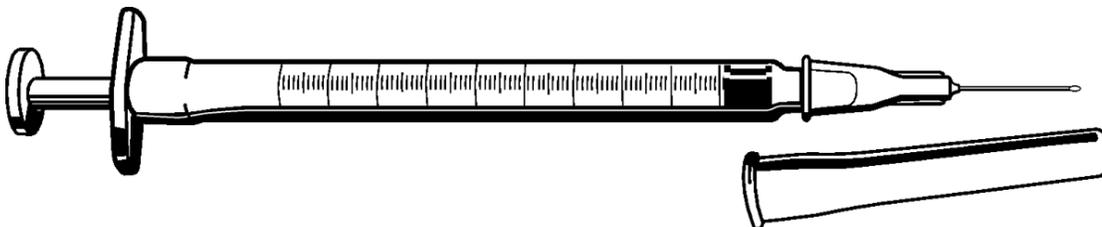
Results for Betaseron[®]

Betaseron[®] was studied in mild to moderately severe relapsing-remitting MS. The primary outcome measure in the study was the number of MS attacks, which decreased by 34%. The number of moderate or severe attacks decreased 49%. The effect on disability was less clear. Those treated with Betaseron[®] had significantly less abnormality visible on MRI and had fewer active lesions on MRI. Betaseron[®] may take a few months to start working.

Betaseron[®] was also studied in secondary progressive MS, and in one study showed a statistically significant slowing in progression of disability in patients in the early stages of secondary progressive disease.

Copaxone[®] (Glatiramer acetate)

- Available since 1996.
- Given by injection every day (with a 5/8 inch needle in the tissues between the skin and the muscle).
- Needs refrigeration, though may be at room temperature for 7 days.
- Costs about \$10,000/year.
- Pre-filled syringes provided.



Side Effects

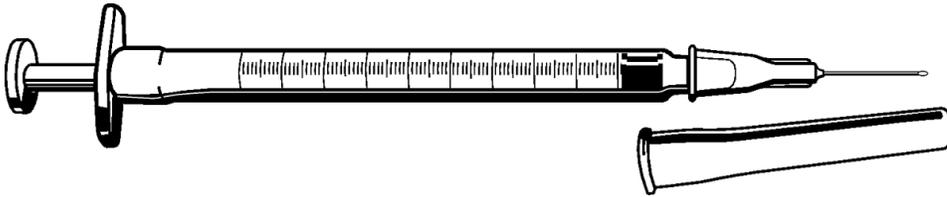
- A red spot may occur at the site of the injections (90%). Each red spot may last for several days. There is often a lump under the skin at the site of the injection and the injection site may sting for a brief period.
- A reaction (called a systemic reaction) may occur on rare occasion. This is not medically dangerous, but may be frightening. Within minutes of the injection, patients who have a systemic reaction may feel chest pain, flushing, shortness of breath, awareness of a strong heartbeat and anxiety. The reaction does not require medical treatment and resolves within 15 to 20 minutes. A few cases last up to 45 minutes. In one 2-year long study, these reactions occurred in 15% of patients. Most of these had only one reaction in the 2 years. The worse case had 7 episodes in 2 years.

Results for Copaxone[®]

Copaxone[®] was studied in mild to moderately severe relapsing-remitting MS. The Copaxone[®] study showed the number of attacks decreased by 29%. There was an effect on disability and a 31% increase in the time it took for more disability to occur. Another study found less MRI lesions and fewer active lesions in those treated with Copaxone[®]. It may take a number of months for the drug to start working.

Rebif[®] (Interferon beta 1-a)

- Available since 2002.
- Given by injection three times a week (with a 5/8 inch needle in the tissue between the skin and muscle).
- Needs refrigeration.
- Cost: About \$15,600 per year.
- Provided in prefilled syringes.
- pH is 3.8.



Side Effects

- A red spot may occur at the sight of the injection (71%).
- Many patients (69%) feel like they have the flu after taking the medicine. This includes fever, chills, sweating, muscle aches and fatigue. Nausea and stomach upset are not usually seen. The flu-like symptoms may last 8 hours or more. Most patients tolerate these symptoms very well using aspirin, acetaminophen (Tylenol) or ibuprofen (Motrin). The first injection has the most side effects with subsequent injections having less. It may take a few months for the reactions to reach their lowest amount. These side effects can be diminished by starting with a low dose, and gradually increasing to full dose.
- Blood tests need to be done every three months to check the white blood count and liver function. After one year, blood tests can be decreased to every four months.
- Depression in those given Rebif[®] was no higher than in those given placebo.

Results for Rebif[®]

Rebif[®] was studied in mild to moderately severe relapsing/remitting MS. The primary outcome measure in the study was the number of relapses, which decreased by 33%.

Novantrone[®] (Mitoxantrone)

- Available since 2000.
- Given through a vein (intravenous/IV) over one hour once every three months for up to two to three years only.
- Intravenous infusion given by trained nursing staff.
- Costs about \$3,000/year.

Side Effects

- The most worrisome side effect is irreversible damage to the heart. This does not usually occur until the total dose exceeds 140mg/m². This dosage usually takes two and a half years, or 10 doses. After this dosage is reached, monitoring of heart function will be needed before more doses are given. It is unlikely that a patient can be given more than 11 doses.
- Nausea may occur shortly after giving the medication and may last for several hours and sometimes days. Sometimes there is vomiting. The nausea and vomiting may be treated with medication.
- Irritation of the vein where the medication is given may occur. This may lead to pain, redness or swelling.
- Starting a few days after each dose, the white blood count may fall. This may lead to an increased risk of infection, especially lung and bladder infections. This may last a few weeks after each dose and then returns to normal.
- Sores may develop in the mouth. They may be painful or lead to difficulty swallowing. The sores heal completely with time.
- You may have an increased tendency to bleeding or bruising. This may last a few weeks after each dose. It then returns to normal.
- Allergic reactions may occur including rash, itching, hives, or difficulty breathing.
- Your urine or the whites of your eyes may turn blue or blue-green for a few days after each dose.
- There may be some hair loss.
- Blood tests need to be drawn before and after each dose.
- Virtually all women stop their periods while on the drug. Up to 29% of those completing a full course of treatment never regain their periods and are infertile.

Multiple Sclerosis Disease Modifying Drugs

Brand Name	Avonex [®]	Betaseron [®]	Copaxone [®]	Rebif [®]
Generic Name	Interferon beta 1-a	Interferon beta 1-b	Glatiramer acetate	Interferon beta-1a
Year Marketed	1996	1993	1996	2002
Administration	Intramuscular injection	Subcutaneous injection	Subcutaneous injection	Subcutaneous injection
Frequency of Injections	Once a week	Every other day	Daily	Three times a week at equal length intervals
Injection Site Reactions	Rare	Yes	Yes	Yes
Injection Site Necrosis (skin breakdown)	No	Possible	No	Possible
Flu-like Symptoms	Yes	Yes	No	Yes
Panic-like Reaction	No	No	Yes	No
Automatic Injection Device	No	Yes	Yes	Yes
Refrigeration	Yes	No	Yes	Yes
Lab Tests Required	Yes	Yes	No	Yes
Discontinue if Pregnant	Yes	Yes	Yes	Yes
Financial Assistance Program	Avonex Access Program 1-800-456-2255	Betaseron Foundation 1-800-998-5777	National Organization for Rare Disorders 1-203-746-6518	MS Lifelines 1-877-447-3243
Patient Support Programs	Avonex Alliance 1-800-456-2255	Pathways 1-800-788-1467	Shared Solution 1-800-887-8700	MS Lifelines 1-877-447-3243

Traveling with Your Multiple Sclerosis Disease Modifying Medications

When traveling away from home, it is important to bring your medications with you. Alterations in daily routines that occur while traveling can disrupt your injection schedule, so it is important to plan for this.

The injectable medications do not tolerate extreme heat or cold situations. Bring your medications with you and carry them with your carry-on luggage when you fly. The injectable medications can safely pass through an airport X-ray machine, but the heat or cold in the luggage compartment of a plane or the trunk of a car can reduce the stability of the drug. Don't put them in the trunk of your car or leave them in the car where heat or cold could affect them.

When flying with medications, an original printed pharmacy label is required for travel within the United States. The label is usually located outside of the box. The FAA recommends that passengers bring their medication in its original container. Prescriptions and letters from physicians cannot be accepted as proof, because they can be forged.

Each medication is different, so refrigeration needs vary:

Avonex[®] (Interferon B-1a) – Pre-filled syringes must be refrigerated for storage. The pre-filled syringes may be kept outside of a refrigerator at room temperature for up to 12 hours.

Betaseron[®] (Interferon B-1b) – The room temperature formulation of Betaseron requires no refrigeration.

Compaxone[®] (Glatiramer acetate) – The pre-filled syringes should be kept refrigerated, but may be stored at room temperature for up to 7 days.

Rebif[®] (Interferon B-1a) – The pre-filled syringes should be kept refrigerated, but may be stored at room temperature for up to 30 days.

