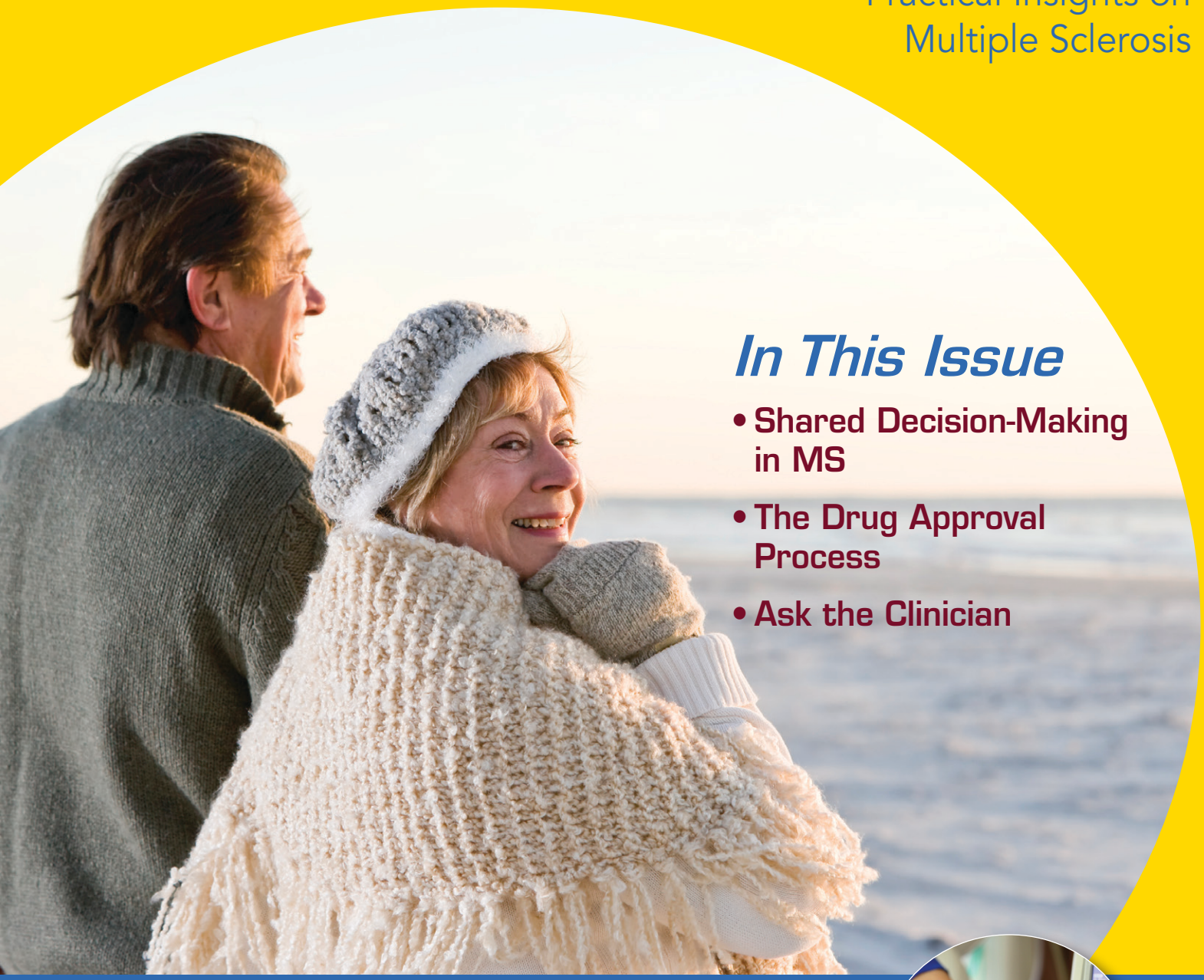
Winter 2014

MS Perspectives™

Volume 7, Issue 2

Practical Insights on Multiple Sclerosis



In This Issue

The Complexity of MS Treatment

Page 3

This publication is supported by Teva Neuroscience and Genentech.

Published in partnership with:

IOMSN
The International Organization of Multiple Sclerosis Nurses

www.MSperspectives.com

Publishing Information

Publishers
Joseph J. D'Onofrio
Frank M. Marino
Delaware Media Group
66 South Maple Avenue
Ridgewood, NJ 07450
Tel: 201-612-7676, Fax: 201-612-8282
Website: www.delmedgroup.com

Writer/Editor
Nancy Monson

Art Director
James Ticchio

MS Perspectives™

Winter 2014 Volume 7, Issue 2

Scan this code to visit
www.msperspectives.com

Disclaimer: The goal of this publication is to provide patients with multiple sclerosis with the latest information about the disease and its treatment. The information provided in *MS Perspectives™* is not a substitute for the advice of your healthcare nurse or doctor. Please consult a qualified healthcare provider for individualized care and information.

Cover photo credit: ©goldenKB / Veer

THE COMPLEXITY OF MS TREATMENT

We are now in an exciting new era of multiple injectable, infusible, and oral disease-modifying therapies (DMTs) to treat relapsing forms of multiple sclerosis (MS). And it's only going to become more challenging to choose the right drug for each individual person as additional medications become available, including generic formulations of brand-name drugs.

All of the currently available DMTs are effective and have research to show they have a positive impact on relapse rates, disease activity as seen on magnetic resonance imaging (MRI) scans, and the progression of disability. However, they differ in the way they attack MS (what's called the mechanism of action), dosing schedules, route of delivery, and side effects. An added layer of complexity comes in with the recognition that MS is not just one disease process—there are actually multiple types of MS. Patients also have genetic differences that influence how and if they respond to different DMTs.

"I like to think of treatment options as a ladder," say Aliza Ben-Zacharia, DrNP, nurse practitioner at The Corinne Goldsmith Dickinson Center for Multiple Sclerosis at New York City's Mount Sinai Medical Center and an *MS Perspectives*' advisor. "It's a science and an art to find the right drug for each person."

FYI

Did you know that...

- ***Relapsing MS is a highly complex disease to treat.***
- ***The disease varies widely and unpredictably from patient to patient.***
- ***There are 11 injectable, infusible, and oral medications for relapsing MS today, with more on the way, adding to the complexity of finding the best treatment for each person.***

Patients must rely on their MS clinicians to help them in finding their way through the therapeutic maze and getting the most from the DMT they choose. Pharmaceutical company support services and call centers can also be a big help in helping them stay on DMTs and other pharmacologic treatments (see the box below for information on these programs). Research shows that the free support of MS nurses at pharmaceutical companies can help people stick with (or adhere to) a DMT regimen, and better adherence has been shown to lead to better outcomes over time for people with relapsing MS.

Support Programs for MS Disease-modifying Therapies (DMTs)

Aubagio®, Genzyme Corporation:
www.aubagio.com, 855-MSONE2ONE (855-676-6326)

Avonex®, Biogen Idec:
http://www.avonex.com/multiple-sclerosis-support.xml, 800-456-2255

Betaseron®, Bayer HealthCare:
http://www.betaseron.com, 800-788-1467

Copaxone®, Teva Neuroscience:
http://copaxone.com/AboutSharedSolutions.aspx, 800-887-8100

Extavia®, Novartis:
http://www.extavia.com/info/PatientSupport/Patient-support-program.jsp, 888-NOW-NOVA (888-669-6682)

Gilenya®, Novartis:
http://www.gilenya.com/c/go-program, 800-GILENYA (800-445-3692)

Plegridy™, Biogen Idec:
http://www.plegridy.com, 800-456-2255

Rebif®, EMD Serono/Pfizer Inc:
www.mslifelines.com, 877-447-3243

Tecfidera®, Biogen Idec:
http://www.tecfidera.com/support/ms-support-services.html, 800-456-2255

Tysabri®, Biogen Idec:
http://www.tysabri.com/ms-support-services.xml, 800-456-2255

MS News, Support, and Self-Help Groups

MS Views & News
www.msviewsandnews.org

MS World
www.msworld.org

Multiple Sclerosis Association of America
www.msassociation.org, 800-532-7667

Multiple Sclerosis International Federation
www.msif.org

Multiple Sclerosis Foundation
www.msfocus.org, 888-MSFOCUS

National Multiple Sclerosis Society
www.nationalmssociety.org, 800-344-4867

Currently Available Medications

Eleven drugs are used to treat relapsing MS today (see the **Table** on page 6 for more information):

Injectable drugs. Injectables have long-term safety records, which newer preparations do not. Although they work in different ways from one another, both glatiramer acetate (Copaxone®) and the interferons (Avonex®, Betaseron®, Extavia®, and Rebif®) have similar benefits. They all reduce the number and severity of relapses, reduce the brain and spinal cord damage that can be seen on MRI scans, and delay the progression of MS and cognitive problems.

Now, new injectable options are available, such as a three-times-a-week Copaxone® injection (at a dose of 40 mg/mL versus the daily dose of 20 mg/mL) and a pegylated form of interferon beta-1a called Plegridy™, which is administered twice a month. (Pegylation of interferon increases the size of the drug molecule and thus extends the length of time it circulates in the body.) These less-frequent dosing options offer the safety and efficacy track record of the traditional injectable DMTs but more convenient dosing schedules. This can be attractive for people who are tired of daily injections or who have had bruising, swelling, or scarring from injections.

Infusible drugs. Natalizumab (Tysabri®), which is delivered monthly by infusion for relapsing forms of MS, is very effective in reducing the rate of relapse and the progression of disability, but over time it can suppress the immune system. In some rare cases, it can lead to the serious infection known as progressive multifocal leukoencephalopathy (PML). Therefore, additional monitoring such as more frequent blood tests and MRIs may be used to help determine an individual patient's risk. MS clinicians now know that people who have been exposed to the John Cunningham (JC) virus and are making antibodies to the virus are at greater risk for developing PML than people who test negative for the JC virus. Use of other immune-

suppressing drugs and taking Tysabri® for more than 2 years have also been shown to increase the risk of PML. People on Tysabri® should be re-tested for the JC virus every few months, since they can switch from negative to positive status, and they should be monitored for signs of PML. The earlier PML is treated, the better it can be managed. Mitoxantrone (Novantrone®) is another infusible, but it is not often used today.

Oral drugs. Three oral DMTs have been approved for relapsing forms of MS to date: Dimethyl fumarate (Tecfidera®), fingolimod (Gilenya®), and teriflunomide (Aubagio®). The three drugs work in different ways from one another and from the injectable and infusible DMTs. Many patients like the convenience of an oral MS drug, but some of the drugs may require more monitoring than the injectables due to potential safety issues.

Disease-modifying Therapies (DMTs) for Relapsing MS

Brand Name	Generic Name	Dosing Route	Frequency
Injectables			
Avonex®	Interferon beta-1a	Into the muscle	Once a week
Betaseron®/Extavia®	Interferon beta-1b	Under the skin	Every other day
Copaxone®	Glatiramer acetate	Under the skin	Daily (20 mg/mL) or three times a week (40 mg/mL)
Plegridy™	Peginterferon beta-1a	Under the skin	Twice a month
Rebif®	Interferon beta-1a	Under the skin	Three times a week
Infusibles			
Novantrone®	Mitoxantrone	Intravenous; given at an infusion clinic	Every 3 months
Tysabri®	Natalizumab	Intravenous; given at an infusion clinic	Every 28 days
Oral			
Aubagio®	Teriflunomide	By mouth	Daily
Gilenya®	Fingolimod	By mouth	Daily
Tecfidera®	Dimethyl fumarate	By mouth	Twice a day

Dictionary: Under the skin=subcutaneous; into the muscle=intramuscular; into a vein=intravenous.

Shared Decision-Making in MS

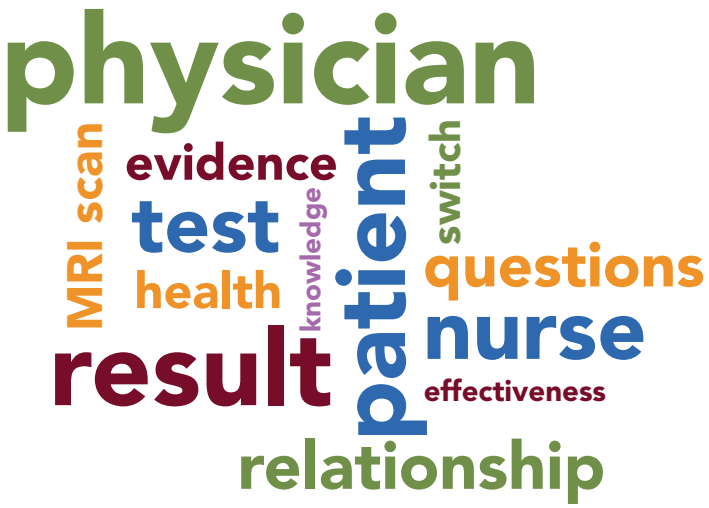
Making the right medical decision can significantly affect your life—but the truth is, in multiple sclerosis (MS) and other areas of medicine, there may not be one clear right way to go. That means you need to make the right decision *for you*, which requires that you examine your tolerance for risk, anxiety, and the unknown.

Knowing how other people make medical decisions about which disease-modifying therapy (DMT) to use may help, so *MS Perspectives* posed that question to MS neurologists, nurse practitioners, and patients. Here's what they had to say.

MS Neurologists' Perspectives

Barbara J. Green, MD
Director
The MS Center of St. Louis
St. Louis, Missouri

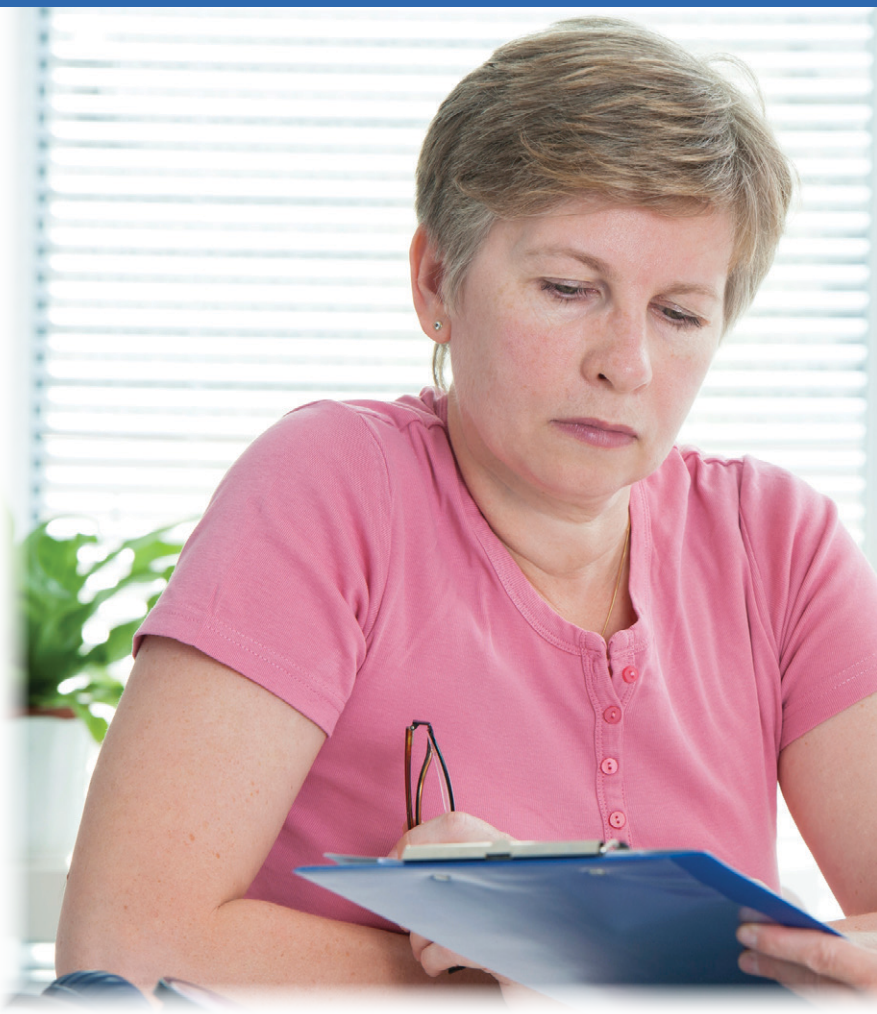
At every visit, I assess whether a patient's disease is stable, mild, or aggressive. Patients with aggressive disease may need stronger (and potentially more toxic) therapy at an earlier point in their disease. I carefully assess a patient's prior therapies when we are considering a change. I want to understand if prior drugs were effective, and how well he or she tolerated the drugs so we don't repeat a negative outcome. I also consider whether a



patient will be adherent to the regimen. Will he or she be faithful with taking an injectable medication? Or a twice-a-day oral drug? Will the patient be good about coming in to see care providers for the needed follow-up, and getting laboratory tests and magnetic resonance imaging (MRI) scans? Negative answers to these questions will rule out some drugs.

Next, I consider if a change in therapy is really warranted. This requires an honest analysis of whether a patient has stable or active disease and whether a drug has failed or if a patient has actually moved from a relapsing form of MS to a progressive form. If that's the case, a change in disease-modifying therapy probably is not going to help.

Finally, I consider whether the patient has other chronic diseases. Other autoimmune diseases may be worsened or bettered by certain treatment selections. The age and fertility status of patients will also influence the decision-making process for treatments, particularly if adequate birth control is not used.



Douglas Jeffery, MD, PhD
Director
The MS Center
Lake Norman Neurology
Piedmont Health Care
Mooresville, North Carolina

Making the choice of which MS drug to use is more complicated than ever. Most newly diagnosed patients prefer oral or infusible treatment. But even that choice is difficult. The oral agents are pretty equal in terms of effectiveness, so we have to look at other factors. If patients want to have children soon, I don't suggest they use teriflunomide (Aubagio®) or fingolimod (Gilenya®). If they have diabetes, they may not be a good candidate for Gilenya® because it increases the risk of macular edema, a serious eye problem. Gilenya® should also not be used by people who have recently had a heart attack or stroke. People who test positive for antibodies to the JC virus are at a greater risk for progressive multifocal

leukoencephalopathy (PML), but they may still be candidates for infusible natalizumab (Tysabri®) depending on how active their disease is.

For patients who have been on Tysabri® or one of the oral drugs and need to have the drug cleared from their system before safely starting a new drug, the biggest risk is leaving them untreated for longer than 4 to 6 weeks. That can lead to relapses and disease progression. It's always best to switch MS patients to a new therapy as quickly as possible.

MS Nurse Practitioner Perspectives

Aliza Ben-Zacharia, DrNP
Nurse Practitioner
The Corinne Goldsmith Dickinson Center for Multiple Sclerosis
The Mount Sinai Medical Center
New York, New York

It is a challenge to make treatment decisions today since there are so many options. I usually connect all of the dots, which include the patient's exam and history, MRI reports, the patient's goals, and his/her tolerance for risk. In patients who have a high burden of disease—meaning they have a lot of relapses and active disease on their MRI scan—I highly recommend starting with a robust medication such as natalizumab (Tysabri®) or oral therapies to suppress the activity of the disease. For patients who are conservative in their approach to treatment, I suggest the injectables, which have a long safety record. And for women who are considering pregnancy, I usually recommend glatiramer acetate (Copaxone®), because data supports its safe use during pregnancy.

The main point is to treat early and continuously, and decide upon a treatment as soon as the diagnosis is made.

Barbara S. Bishop, MS, ANP-C, MSCN, CNRN
Nurse Practitioner
Virginia Beach Neurology
Virginia Beach, Virginia

Choosing a DMT for patients with MS is not just a simple choice of choosing an interferon versus a non-interferon anymore, or choosing the frequency of an injection versus the depth of that injection. Factors that influence choices include the severity of the disease state: more aggressive disease may need more aggressive treatment. Plans for pregnancy for both male and female patients need to be considered as some of our DMTs can affect men as well as women. The existence of other chronic medical problems can impact the decision because some of the DMTs can make certain conditions worse or interact with their treatments. If patients have a history of adherence issues, certain DMTs are not an option due to potentially serious side effects that can occur if they abruptly start or stop their drug. The flip side to that is the value of choosing a DMT that offers good support structures—close nursing interaction with the patient, continued follow-up over time via phone calls, and financial support—to help patients stick to the drug regimen. Patients with unreliable transportation may not be a candidate for infusion treatments due to the importance of timing between infusions. In addition, a patient's functional and cognitive levels can influence the choice of DMT.

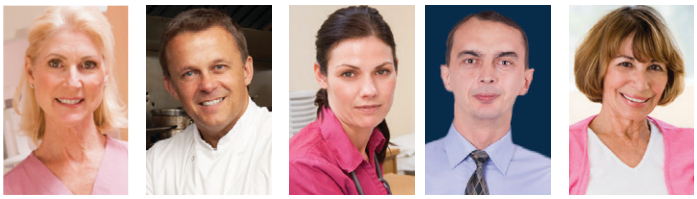
Tracy Walker, FNP-C
Nurse Practitioner
MS Institute at
Shepherd Center
Atlanta, Georgia

Research tells us that people do not take medications or follow through with treatment recommendations if they don't understand why they were recommended. Research also tells us that as healthcare providers the first thing we need to do is listen to our patients so we understand their goals. So in making treatment decisions with patients:

- I consider the patients' history. Are they new to treatment? If not, what

have they tried before? Do they have other medical issues limiting their treatment options? Why are they considering a new therapy—are they continuing to have disease activity on their current therapy? Can we see a lot of inflammation on their MRI scan?

- I ask patients what their concerns and preferences are for treatment. I quickly review the pros and cons of each treatment option to get an idea of what is most important to them. Do they prefer less frequent dosing even if it means more lab work and a clinic visit for an infusion? Or are they willing to take something more frequently if it requires less safety monitoring and fewer clinic visits? Do they want an oral treatment, even if that means more potential side effects? Or are they okay with an injection if there is less potential for side effects?
- Once patients and I have narrowed down the options together, we agree on a therapy and proceed. I review the goals, potential side effects they may experience, signs and symptoms to report to me, and follow-up monitoring requirements.



Patient Perspectives

JESSICA

Age and onset: 41, diagnosed with relapsing-remitting MS in her late-30s

When I was first diagnosed after an episode of optic neuritis, I was in shock, so I went with my general neurologist's suggestion to start on interferon beta-1a (Rebif®). I did a little research on my own and it seemed like a good choice. I had 11 MS lesions on my first MRI scan, and no active lesions after I went on Rebif®, so the drug quieted the MS down.

I was fortunate and my vision came back fully after my first episode. I occasionally experience numbness in my legs and arms, but nothing more than that.

I eventually went to see an MS neurologist. I think that's a good idea because these specialists are up to date with all of the new medications. They treat MS patients all day and they have a bigger bank of knowledge than general neurologists. That's important because MS is such a variable disease from one person to the next.

Six months ago, I switched to the oral drug fingolimod (Gilenya®) because I was having some issues with the injections. I had red spots on my stomach and they hurt. It was a scary decision to switch because my disease was under control, but I thought the improvement in my quality of life would be worth it. My neurologist agreed, and so far, I've had a good outcome with Gilenya®.

ROBERTA

Age and onset: 53, onset of relapsing-remitting MS in her mid-30s

I've been on a number of drugs, such as glatiramer acetate (Copaxone®), interferon beta 1-a (Rebif®), and natalizumab (Tysabri®). They have all worked for a while and then either stopped working or, in the case of Tysabri®, I was told to stop taking it after 2 years due to safety concerns. I'm now taking fingolimod (Gilenya®), and doing well on it so far. I know I have to take a pill every day, so I do.

I follow my doctors' and nurses' advice to the letter. I trust them because all of their suggestions have worked for me. My body has been fairly receptive to the disease-modifying drugs and I haven't had a lot of side effects. I don't try to self-diagnose or do research since I didn't go to medical school. I have healthcare experts to do that for me.

JAMIE

Age and onset: 52, diagnosed with relapsing-remitting MS in her mid-30s

I have been on glatiramer acetate (Copaxone®) since I was diagnosed, and I recently switched to the new three-times-a-week formulation because I've been doing injections for 16 years and my body is developing lumps. I'm running out of places to inject.

I talked with my MS neurologist about the different treatment options. It's wonderful that there are so many more drugs available now than when I was first diagnosed. Then, there were just three injectables.

I didn't want to change to an oral drug because I know there is more safety data with the injectables. I'm worried about the side effects of the oral drugs and the blood tests you need before and while you're on them. Cost is also an issue; I'm not sure my health insurance covers all of the drugs. And I've done well on Copaxone®—I've had no relapses or progression of my disease on my MRI scans.

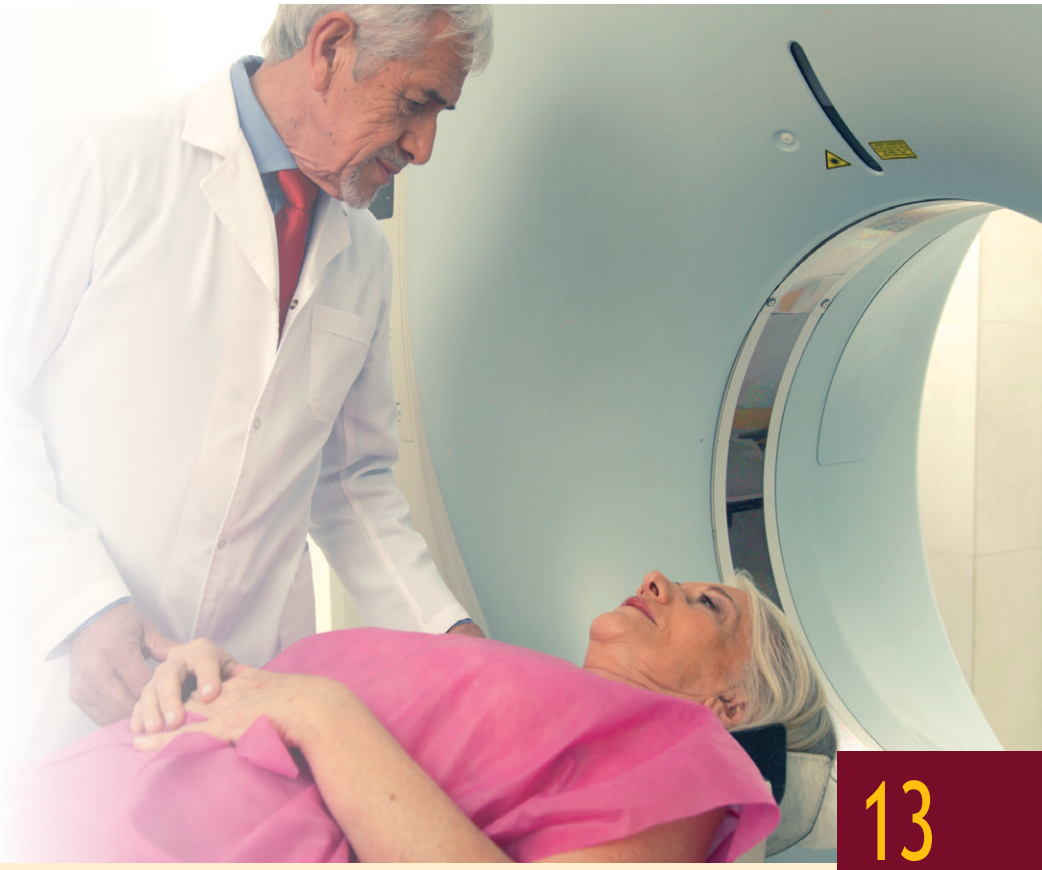
I like the three-times-a-week regimen better than the daily injectable. It hasn't been hard adjusting to it at all and it gives my body a rest while still treating my MS.

THE Drug Approval PROCESS

The path a multiple sclerosis (MS) medication takes from research to market is usually long and costly. First, a potential disease-modifying therapy (DMT) is tested in pre-clinical research (in the laboratory and in animals) and then in clinical trials (in humans), a process that may take 15 to 20 years. The drug is evaluated for safety and its effects on preventing relapses, slowing disability, and stabilizing the MS lesions that can be seen on magnetic resonance imaging (MRI) scans. At any point along the way, pitfalls such as unexpected side effects, toxicity, or a lack of the expected disease-modifying goals can stop a drug's development in its tracks. In fact, many more agents are developed and researched than actually make it to market.

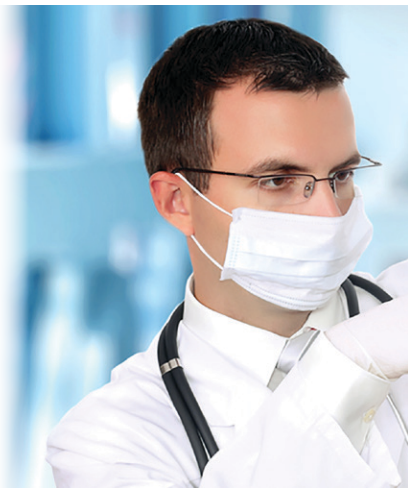
Once an MS drug has undergone successful clinical testing in humans, the pharmaceutical manufacturer can apply to the US Food and Drug Administration (FDA) to market the drug. The FDA requires evidence that the drug is effective and that the benefits of using it outweigh any risks before granting approval. The agency also insists that pharmaceutical companies demonstrate a reliable manufacturing process that ensures the quality of the drug.

In the future, generic DMTs for MS will likely be approved by the FDA (see



the box below for explanations of the terms "brand name" and "generic"). Many people with MS are already taking generic medications to manage symptoms. Since generic medications are traditionally less expensive, many health insurance companies require patients to take currently available generics and may continue to do so in the future for DMTs.

As informed consumers, when considering a generic versus a brand-name medication, there are questions you must ask. For example, will the manufacturing of the generic product be the same as for the branded medication? Will the delivery system be

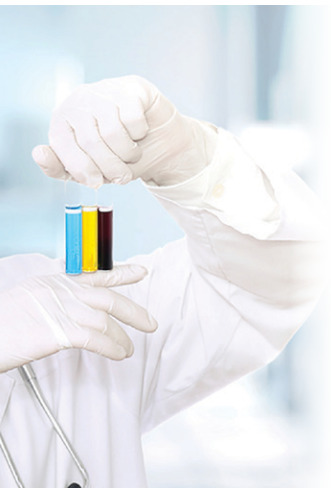


Understanding Drug Terms

Brand name: A brand-name drug is developed by a pharmaceutical company and must undergo years of testing before being approved for marketing by the Food and Drug Administration (FDA). When it is approved, it is protected by a patent that lasts 20 years so the drug company can make back its research and development costs. The patent prevents other companies from selling the drug for that time.

Generic: A generic drug costs less than a brand-name drug, but it must be bioequivalent to that drug, meaning it has the same strength, purity, and stability. Many generic drugs are even made in the same manufacturing plant as brand-name drugs. Repeat clinical trials are not required for the marketing of generic versions of brand-name drugs.

Biosimilar: Many of the disease-modifying therapies (DMTs) today are biologics, which means they require complex manufacturing processes. The generic equals of biologics are known as biosimilars. They, too, are complex to manufacture, and just small changes in the manufacturing process from how the brand-name drugs are made may result in significant changes in safety or effectiveness. Currently, there are no guidelines or requirements from the FDA that address that complexity.



the same? Will the generic be well tolerated? Unfortunately, generic medications are not always tested to the same standard as brand-name medications. These are some of the issues that need to be addressed by high-quality clinical trials comparing a generic to the brand-name formulation of a drug.

It should also be noted that branded products come with significant support resources such as access to nurses for training, education, and advocacy, which often leads to better adherence for a patient. There also are numerous financial support programs available for patients who have difficulty affording a brand-name drug.

Ask the Clinician

Q. What resources will help me make treatment decisions with my MS team?

A. It is important to get your information from reliable sources and experts who are involved in patient care. I suggest that patients who want to learn more about the disease, the treatments, and the decision-making process attend programs run by MS centers or well-established neurology practices that treat patients with MS. In addition, you can turn to reliable internet sources such as the National MS Society, the American Academy of Neurology, and the Multiple Sclerosis Society of America (MSAA)—see the box on page 4 for contact information. Magazines from trusted experts, such as *MS Perspectives*, *Momentum* (published by the National MS Society), and *The Motivator* from the MSAA, can be helpful, too.

Ask your healthcare team about educational resources and ways to become a more knowledgeable consumer and advocate for yourself!

—Aliza Ben-Zacharia, DrNP

Receive a free subscription to MS Perspectives™!

To subscribe to *MS Perspectives*™, visit www.MSperspectives.com or fill out the card below, cut it out, and fax it or mail it in an envelope to:

Delaware Media Group
66 South Maple Avenue
Ridgewood, NJ 07450
Fax: 201-612-8282

You can sign up to receive an electronic version, and we will email you a link to each new issue. Or you can subscribe to a print version that will be mailed to you in a plain white envelope.

Yes! I'd like to receive *MS Perspectives*™ ☐ by mail ☐ by email

Name _____

Address _____

City _____ State_____ Zip _____

Email_____

The publisher values your privacy and the confidentiality of your personal information. We will use your contact information only to provide you with a free subscription to *MS Perspectives*™. Please be assured that your name will not be sold or distributed for any commercial purposes or otherwise.

Delaware Media GROUP

www.delmedgroup.com