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# MSPerspectives™

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Practical Insights on  
Multiple Sclerosis



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- Wellness in the Time of COVID

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# MS Treatment Update

Over the past few years, several new drugs in multiple sclerosis (MS) have been introduced, swelling the ranks of treatments to 20-plus medications. These disease-modifying therapies (or DMTs) have broadened treatment options for many people by quieting the over-reactive immune system that is the hallmark of MS and changing the course of the disease.

Most of the new drugs fall into a few classes of medications and work in a similar way (what's known as their mechanism of action) to older drugs in the same category, but may have fewer side effects or more targeted or specific effects. It's important to have many drugs with similar mechanisms of action as well as drugs with different actions since MS is such an individualized disease and it's hard to predict who will respond to which drug.

To help you get a handle on the many DMTs now available, here's a run-down of the current classes of MS drugs.

## Interferons (for relapsing MS and active secondary-progressive MS)

*Interferon beta-1a (Avonex®)*  
*Interferon beta-1a (Rebif®)*  
*Interferon beta-1b (Betaseron®)*  
*Interferon beta-1b (Extavia®)*  
*Peginterferon beta-1a (Plegridy®)*

The interferon class of medications was revolutionary because it was the first type of DMT to be approved to treat relapsing-remitting MS (RRMS) back in the 1990s. These injectables are thought to work by stabilizing the blood-brain barrier, which in turn reduces the number of inflammatory T and B immune cells (or lymphocytes) that can enter the central nervous system. Interferons are also believed to affect T and B cells and immune-system proteins called cytokines by increasing production of anti-inflammatory cells and cytokines and decreasing production of inflammatory cells and cytokines that lead to the damage or loss of myelin (the protective coating around nerves) and axons (nerves) in the brain and spinal cord.

## Glatiramer Acetate (for relapsing MS and active secondary-progressive MS)

*Glatiramer acetate (Copaxone®)*  
*Glatiramer acetate (Glatopa®)*  
*Glatiramer acetate (generic)*

Glatiramer acetate, a synthetic protein drug, is the only drug in this class of injectable medications. Glatiramer acetate is believed to create a shift so the body produces fewer pro-inflammatory T cells and cytokines and more anti-inflammatory T cells and cytokines. There is also evidence that this drug may have a broader effect on both the immune system you were born with and the one that has developed over time in response to your environment.

**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: ©Ksuksa / iStock

## FDA-Approved MS Medications

Oral	Injections	Infusions
Aubagio®	Avonex®	Lemtrada®
Bafiertam®	Betaseron®	Ocrevus®
Gilenya®	Copaxone®	Tysabri®
Mavenclad®	Extavia®	
Mayzent®	Glatiramer Acetate Injection	
Ponvory™	Glatopa®	
Tecfidera®	Kesimpta®	
Vumerity®	Plegridy®	
Zeposia®	Rebif®	

**Enzyme Blocker** (for relapsing MS and active secondary-progressive MS)

*Teriflunomide (Aubagio®)*

Teriflunimide inhibits an enzyme called dihydroorotate dehydrogenase (DHODH), which is needed for T and B cells in the immune system to reproduce. This oral drug appears to work by decreasing the number of abnormal or dysfunctional T and B cells that cause nerve damage, while protecting the reproduction of normal T and B cells.

**Fumarates** (for relapsing MS and active secondary-progressive MS)

*Dimethyl fumarate (Tecfidera®)*  
*Dimethyl fumarate (generic)*  
*Diroximel fumarate (Vumerity®)*  
*Monomethyl fumarate (Bafiertam®)*

These oral drugs all break down to the same active metabolite, monomethyl fumarate. They are thought to stimulate the Nrf-2 pathway, which plays a role in reducing the byproducts of inflammation in the body. This effect may help prevent damage to cells in the central nervous system caused by MS. The newest agent in this class, diroximel fumarate, has fewer side effects than dimethyl fumarate.

**Purine Antimetabolite** (for relapsing MS and active secondary-progressive MS)

*Cladribine (Mavenclad®)*

Cladribine is a unique MS drug known as a purine antimetabolite that is taken as a tablet. It appears to work by decreasing the numbers of abnormal T and B cells in the immune system that cause damage associated with MS. These lymphocytes are then replaced by new

immune cells that do not attack the central nervous system.

### Monoclonal Antibodies

*Alemtuzumab (Lemtrada®)* (for relapsing MS and active secondary-progressive MS)  
*Natalizumab (Tysabri®)* (for relapsing MS and active secondary-progressive MS)  
*Ocrelizumab (Ocrevus®)* (for relapsing MS, active secondary-progressive MS, and primary-progressive MS)  
*Ofatumumab (Kesimpta®)* (for relapsing MS and active secondary-progressive MS)

Monoclonal antibodies target either T or B cells or both in the immune system. Ocrelizumab is the only drug approved to treat both relapsing forms of MS and primary-progressive MS (PPMS). Ofatumumab is delivered via injection, but the others are administered by infusion.

**S1P Modulators** (for relapsing MS and active secondary-progressive MS)

*Fingolimod (Gilenya®)*  
*Ozanimod (Zeposia®)*  
*Ponesidmod (Ponvory™)*  
*Siponimod (Mayzent®)*

Sphingosine 1-phosphate (S1P) receptor modulators are oral drugs that trap lymphocytes in the lymph nodes and other tissue reservoirs, thereby reducing the number in the circulation that can then enter the central nervous system and cause damage. S1P receptors are found on the outside of lymphocytes.

### What's Next?

BTK inhibitors are the next focus of interest as DMTs for MS and are showing promise in early trials. BTK stands for Bruton tyrosine kinase, an enzyme that is essential for the development of the immune system's B cells and cytokines. These drugs are being designed to tamp down the inflammatory actions of B cells, but it's hoped they will be able to do so without entirely depleting the B-cell population and leading to an immunosuppressed state. Three BTK inhibitors—evobrutinib, PRN2246, and BILB091—are being studied.

A different medication for relapsing MS that is under application to the FDA is the monoclonal antibody ublituximab, which targets B cells in the immune system. It would be given via a short infusion if approved.

**For More Information on DMTs:** Download the National MS Society's brochure Disease-Modifying Therapies for MS from its website at [https://www.nationalmssociety.org/Programs-and-Services/Resources/The-MS-Disease-Modifying-Medications-\(-pdf\)](https://www.nationalmssociety.org/Programs-and-Services/Resources/The-MS-Disease-Modifying-Medications-(-pdf)).

# Making Sense of CANNABIS

**M**any people with multiple sclerosis (MS) are interested in using cannabis as an alternative treatment for difficult symptoms like pain, spasticity, and sleeping problems. In fact, a recent survey of over 1,200 people with MS found that close to half were already using cannabis for both medical and recreational purposes.

Although the federal government still classifies cannabis as an illegal controlled substance, 36 states and four territories allow patients to purchase medical marijuana with a prescription, and 18 states, two territories, and Washington, DC allow consumers over the age of 21 to purchase recreational cannabis without a prescription. The cannabis business in the United States has exploded with these approvals, but it's important to approach the use of these products under the guidance of your healthcare provider, says Aliza Bitton Ben-Zacharia, PhD, DNP, ANP-BC, FAAN, Assistant Professor at Hunter Bellevue School of Nursing in New York City and an *MS Perspectives*' advisor.

## ***What is Cannabis?***

Cannabis (the marijuana plant) is one of the world's oldest cultivated plants and has been grown for thousands of years. It contains a variety of chemically active compounds, the best known of which is tetrahydrocannabinol or THC, which produces the high sought by recreational users.

There is a good amount of medical research to show that THC-rich cannabis can help to manage spasticity, muscle spasms, pain, and bladder frequency and urgency in people with MS, reports Ben Thrower, MD, Medical Director of the Andrew C. Carlos Multiple Sclerosis Institute at Shepherd Center in Atlanta, GA. On the downside, cannabis can also carry health risks for these patients. It can be addictive, and it can cause dizziness, dry mouth, increased appetite, nausea, fatigue, sleepiness, confusion, impaired balance, visual disturbances, cognitive impairment, and even hallucinations. "A 2015 survey of medical marijuana use found that half of users experience side effects, which are mostly mild," he says. "Only 2% of the survey respondents had severe side effects." In addition, THC-

rich cannabis can interact with other drugs, and chronic use can actually cause nausea and vomiting. "That's paradoxical, though," he notes, "since medical marijuana is often taken to relieve nausea."

Another compound found in cannabis is cannabidiol (CBD). Unlike THC-rich cannabis, it does not make users "high." CBD typically comes from hemp, a plant similar to the THC-containing marijuana plant but one that contains less than a 0.3% concentration of THC. CBD is legal in all 50 states, according to Dr. Thrower, and is so mainstream today that "we even sell hemp-based CBD products in our gift shop at Shepherd Center," he reports, adding that they may be helpful for relieving sleeping difficulties and anxiety. However, they don't usually help with spasticity, pain, and bladder issues related to MS.

## ***Regulated Cannabis Categories***

THC-rich cannabis products can be divided into two categories:

**Pharmaceutical cannabis.** There are two synthetic cannabis products on the US market that have been approved by the Food and Drug Administration (FDA) and can be prescribed by healthcare providers: Both dronabinol (brand names Marinol® and Syndros®) and nabilone (Cesamet®) come in capsule form. These synthetics are approved by the FDA to manage



nausea and vomiting associated with cancer treatment; dronabinol is also approved to stimulate the appetite in people with AIDS. The drugs can be prescribed off-label for MS-related pain, and may even be covered by insurance companies with prior authorization.

"We do prescribe these synthetics, although we've found that patients may experience more euphoria and paranoia with them than with natural THC-containing cannabis," says Dr. Thrower. "Taking CBD with the synthetics can tone these side effects down a bit, however."

A third FDA-approved drug that is actually derived from the cannabis plant rather than a synthetic called cannabidiol (Epidiolex®) was approved in 2020 to treat rare forms of epilepsy in children.

Another natural cannabis extract called nabiximols (Sativex®) that is administered as a mouth spray may be on the verge of US approval. It has been well-studied in Europe and has been available in 25 other countries for the past decade. Trials have shown that nabiximols is useful for improving spasticity related to MS and can be administered twice daily up to a maximum of 12 sprays a day when symptoms emerge. "These spasms can be uncomfortable and painful, and can affect a person's quality of life," says Dr. Ben-Zacharia. "Nabiximols acts quickly to relieve spasms and it is well-tolerated." Side effects can include dizziness, sleepiness, fatigue, and dry mouth. Unlike other anti-spasticity medications like baclofen (brand names Gablofen® and Lioresal®), nabiximols does not cause muscle weakness as a side effect. This is important since balance issues and falling related to muscle weakness may be a problem for people with MS. A trial is ongoing in the US, including at Shepherd Center, and it is hoped that nabiximols will be approved by the FDA in 2022. "It will be important to have this sanctioned option for spasticity," Dr. Thrower says.

**Medical cannabis.** Products that you can buy in a commercial dispensary with a healthcare provider's signature fall into this category. Regulation of this industry is governed by individual states and not the FDA, so it's difficult to know if you are getting the product you think you are buying. Cannabis products can contain varying quantities of THC and CBD, and are available in many different formulations, too, ranging from liquids and gels that can be inhaled using vaping devices; oils, creams, balms, salves, and lotions that can be rubbed on the body and absorbed through the skin; and a large number of edible products, such as gummies, baked goods,

### **American Academy of Neurology (AAN) Medical Marijuana in Certain Neurological Disorders Patient Information Sheet**

<https://www.aan.com/Guidelines/home/GetGuidelineContent/650>

### **Americans for Safe Access**

<https://www.safeaccessnow.org>

### **Dr. Ben Thrower Presentation for the MS Foundation on "Cannabinoids and MS"**

<https://www.youtube.com/watch?v=AJeIVf1pKk>

### **FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers**

<https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#othercbdapproved>

### **Marijuana Information from Allen C. Bowling, MD, an MS and Cannabis Expert**

<http://neurologycare.net/mj.html>

### **MS Society: Medical Marijuana (Cannabis) FAQs**

<https://www.nationalmssociety.org/Treating-MS/Complementary-Alternative-Medicines/Marijuana/Marijuana-FAQs#question-What-is-cannabis>

### **National Institute on Drug Abuse. National Institutes of Health Research on Marijuana and Cannabinoids**

<https://www.drugabuse.gov/drug-topics/marijuana/nih-research-marijuana-cannabinoids>

chewing gum, meat jerky, beverages, tinctures, powders, and sprays.

## **Summing Up**

"Social opinions about medical cannabis have changed in recent years with its legalization in more and more states," says Dr. Ben-Zacharia. "Patients ask me about it a lot, and there are some data that it is beneficial. We even have guidelines from the American Academy of Neurology to refer to on cannabis in regard to spasticity and pain in people with MS. But we need more research on it."

Ultimately, though, she says that while cannabis is a plant, "it is also a medication, so you need to talk to your healthcare provider about the pros and cons of it for you, and you need to educate yourself about what these products can do for you. Information is empowering."

# WELLNESS IN THE AGE OF COVID

**W**ellness is an important topic that we have explored in *MS Perspectives*<sup>TM</sup> several times. The pursuit of wellness can be very challenging—some might even say impossible—for someone with a chronic illness like multiple sclerosis (MS).

Enter 2020 and a pandemic and wow: It turns out we didn't know what challenging was! COVID has brought many changes to our day-to-day lives and offered new perspectives. Many of the busy daily activities we used to be distracted by came to an abrupt halt, leaving us time to re-evaluate priorities in our lives and hopefully bringing us a new appreciation for the benefits of pursuing wellness.

So how can you navigate these new challenges in pursuing wellness during a pandemic when you need it more than ever? Read on!

## **Wellness Defined**

The National Wellness Institute defines wellness as “an active process through which people become aware of, and make choices toward, a more successful existence.” The National MS Society defines wellness as a “dynamic state of physical, emotional, spiritual, and social wellbeing that can be achieved even in the presence of a chronic illness or disability.” Understanding and embracing this broad view of wellness can restore hope, which is a powerful motivator for change. Wellness is a way of living and being that involves action—like moving your body, connecting with other people, and taking the time to be mindful. The icing on the cake is that all of these actions have been shown to have specific benefits for the immune system, too!

To achieve wellness, people need to figure out how to balance their physical and emotional health with their employment or volunteer work, family life, social activities, and spirituality.

## **Physical Wellness**

Although wellness encompasses much more than physical health, the body is an important place to start. When COVID first hit, the recommendation was to postpone wellness checks and yearly exams until it was considered safe to resume. Now medical facilities and providers have learned how to sanitize their offices and keep their



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patients safe so you can feel comfortable resuming these visits. These visits are very important to screen for and prevent common issues that can affect your general health as well as have significant negative impacts on your MS. These include tests and bloodwork for cardiovascular disease, cancer, diabetes, liver and kidney function, and nutrition status. Catching and treating health problems early can prevent bigger problems from developing. So if you haven't scheduled your annual exam yet, call your provider today!

The pandemic has also put the spotlight on immunity, so now is the time to discuss your immune system and how you can help it function at its best with your healthcare provider. We have recently learned more about supplements like vitamins C and D3 and zinc, which can boost the functioning of the immune system. Some studies suggest that low vitamin D levels could be a risk factor for a COVID infection, and possibly even a factor in predicting who will have a more severe disease course among those who do get infected. Vitamin D3 has also been shown to affect the risk of MS, so be sure you have your vitamin D level tested and start taking supplements if you need to. We also know that some MS therapies affect the immune system and that can further complicate things, so maintaining a healthy immune response is critical right now.

Physical activity and exercise are key to achieving and maintaining wellness. Many people have told me that they have not maintained the regular exercise habits that they had established prior to the pandemic for a variety of reasons. For example, COVID restrictions have limited access to many gyms, pools, group activities, and public parks. For others, their usual routines have been changed, and the healthy habits they had established were disrupted. On the other hand, working from home has given some people the extra time to finally establish an exercise program—plus there are many new online options for group and supervised activities.

## **Emotional Health**

In the age of COVID-19, the process of adapting to the “new normal” and dealing with the unknowns in our future have led to significantly increased stress levels.

If it's not managed, this stress can cause depression, anxiety, and even increased MS symptoms. Suicide rates have increased during the pandemic, as well. It's important to make stress-management techniques like mindfulness, meditation, and regular exercise a priority in your daily life. Laughter is also a great tool for stress relief and relaxation. Take time to read a funny book, watch a comedy, or spend time with an upbeat friend. Laughter really is the best medicine!

Also make sure you are connecting with friends and family on a regular basis to reduce feelings of isolation and loneliness. If you find yourself having more symptoms of depression or hopelessness than before, reach out to a professional for help.

### ***Occupational and Cognitive Health***

The pandemic has definitely changed the way we work. Many offices and places of work have incorporated technology to enable people to work remotely—if not every day, then at least part of the week. For some people, working from home can be a positive thing. They find it gives them more flexibility and saves time usually spent in the car for long commutes that can now be used for exercise or leisure time. They may find working from home helps them be more productive with fewer interruptions from coworkers. People can also find their home environment more relaxing than being in a formal work setting, allowing them to be more creative.

But for other people, working from home can actually mean extra work. Not everything can be done as easily or as effectively at home as it can in person or at the office.

If spouses or children are working or attending school from home, there may be distractions and it may be hard to focus. People with MS who have cognitive challenges may find this to be a real problem. Others may miss the social life that work provided. If these things are an issue for you, see if there are creative solutions or options that allow you to be in the office part time. Or explore working at a quiet public space like a library or a friend's house.

### ***Spiritual Health***

Spiritual health is often overlooked or minimized when thinking about our overall wellness. But in times like these, spiritual health is more important than ever to help us deal with the changes and stress we are experiencing. Spiritual health means different things to different people, but regardless of our beliefs, having faith in something greater than ourselves helps keep things in perspective and reduces fear. Fear is a negative force that can lead to destructive life patterns that prevent us from experiencing joy and peace. Having a spiritual connection also helps us forgive ourselves and others who have harmed us. We all need an extra dose of grace and forgiveness during especially stressful times like these. We have to remember, though, that spiritual wellness is an active process that we need to practice or do. Whether it includes daily prayers, meditations, listening to or making music, or communing with nature, we have to make doing it a priority.

### ***Give Yourself and Others a Break!***

Finally, if you are struggling right now, give yourself a break! This is uncharted territory and a very challenging time for all of us. Don't expect too much from yourself or others. Remind yourself to be flexible and kind. If you are frustrated or depressed, try practicing a random act of kindness—pay for coffee for the person in line behind you or take a neighbor the flowers you picked on your walk. Let someone you care about know you are thinking about him or her. You will be amazed at how much these small acts of kindness will lift your spirits, too!



## Support Programs for MS Disease-Modifying Therapies (DMTs)

### **Aubagio<sup>®</sup>, Genzyme Corporation:**

www.aubagio.com, 855-MSONE2ONE (855-676-6326)

### **Avonex<sup>®</sup>, Biogen:**

www.avonex.com/en\_us/home/above-ms-program/join-biogen-support.html, 800-456-2255

### **Bafiertam<sup>®</sup>, Banner Life Sciences:**

www.bafiertam.com/#patient\_support, 1-855-3BANNER (855-322-6637)

### **Betaseron<sup>®</sup>, Bayer HealthCare:**

https://www.betaseron.com/why-betaseron, 844-788-1470

### **Copaxone<sup>®</sup>, Teva Neuroscience:**

http://copaxone.com/AboutSharedSolutions.aspx, 800-887-8100

### **Extavia<sup>®</sup>, Novartis:**

www.extavia.com, 888-NOW-NOVA (888-669-6682)

### **Gilenya<sup>®</sup>, Novartis:**

www.gilenya.com, 800-GILENYA (800-445-3692)

### **Glatiramer Acetate Injection, Mylan:**

www.glatiramercetate.com/en/patient-support, 844-695-2667

### **Glatopa<sup>®</sup>, Sandoz:**

www.glatopa.com, 855-452-8672

### **Kesimpta<sup>®</sup>, Novartis:**

www.kesimpta.com, 855-KESIMPTA (855-537-4678)

### **Lemtrada<sup>®</sup>, Genzyme:**

www.lemtrada.com, 855-MSONE2ONE (855-676-6326)

### **Mavenclad<sup>®</sup>, EMD Serono:**

www.ms lifelines.com, 877-447-3243

### **Mayzent<sup>®</sup>, Novartis:**

www.mayzent.com, 877-MAYZENT (877-629-9368)

### **Ocrevus<sup>®</sup>, Genentech:**

www.ocrevus.com, 844-OCREVUS (844-627-3887)

### **Plegridy<sup>®</sup>, Biogen:**

www.plegridy.com, 800-456-2255

### **Ponvory<sup>™</sup>, Janssen:**

www.ponvory.com, 877-MyCarePath (877-227-3728)

### **Rebif<sup>®</sup>, EMD Serono:**

www.ms lifelines.com, 877-447-3243

### **Tecfidera<sup>®</sup>, Biogen:**

www.tecfidera.com, 800-456-2255

### **Tysabri<sup>®</sup>, Biogen:**

www.tysabri.com/en\_us/home/join-biogen-support/join-biogen-support.html, 800-456-2255

### **Vumerity<sup>®</sup>, Biogen:**

www.abovems.com, 800-456-2255

### **Zeposia<sup>®</sup>, Bristol Myers Squibb:**

www.zeposia.com/support-program-for-patients/, 833-ZEPOSIA (833-937-6742)

## MS News, Support, and Self-Help Groups

### **Can Do Multiple Sclerosis**

www.msando.org

### **MS Views & News**

http://www.msviews.org/msviewsandnews4

### **MS World**

www.ms world.org

### **Multiple Sclerosis Association of America**

http://mymsaa.org, 800-532-7667

### **Multiple Sclerosis International Federation**

www.msif.org

### **Multiple Sclerosis Foundation**

www.msfocus.org, 888-MSFOCUS (888-673-6287)

### **National Multiple Sclerosis Society**

www.nationalmssociety.org, 800-344-4867

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