

TALKING TO YOUR MS PATIENTS:
**TALKING ABOUT PRIMARY
PROGRESSIVE MS**



**National
Multiple Sclerosis
Society**

This paper is designed to facilitate conversations with your patients about primary progressive MS (PPMS). Because there are fewer treatment options for PPMS than for relapsing forms of MS, and the prognosis is generally poorer, both you and your patients may find the diagnostic and management issues somewhat difficult to discuss. The information provided here can help pave the way.

Physicians, as well as nurses, rehabilitation specialists and mental health professionals, have a critical role to play in helping people learn how to manage this challenging disease course in ways that promote function, independence, quality of life and hope. The first step is to establish open, comfortable lines of communication.

1. When is it appropriate to talk about the diagnosis of PPMS?

As soon as you have confirmed that the person has multiple sclerosis, and determined that the course appears to be primary progressive, it's important to share that information with your patient so that treatment can be initiated. A clear and open conversation about the diagnosis sets the stage for an effective doctor-patient collaboration to manage the disease.

According to the 2017 Revised McDonald MS Diagnostic Criteria ([Thompson et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol.* 2018;72\(2\):162-173](#)), PPMS is defined by one year of disease progression (retrospective or prospective) AND at least two of the following: *dissemination in space* in the brain based on ≥ 1 T2 lesion in the periventricular, juxtacortical or infratentorial regions; *dissemination in space* in the spinal cord based on ≥ 2 T2 lesions; or abnormal cerebrospinal fluid findings consistent with MS.

In their revision of the MS clinical course definitions, Lublin and colleagues ([Lublin et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology.* 2014;15;83\(3\):278-86](#)) made significant changes that relate to PPMS. They eliminated the progressive relapsing course and added descriptors to the remaining courses, so that PPMS can now be described as either *active* or *not active* AND *worsening* or *not worsening* (a detailed graphic describing PPMS is available at www.nationalMSSociety.org/PPMS). With these changes, a patient who would previously have been diagnosed with progressive relapsing MS would now be considered to have PPMS with activity.

In order to arrive at a diagnosis of PPMS, a very careful medical history must be taken to identify any past symptoms or neurologic events that might suggest that the current course is secondary progressive rather than primary progressive MS. Engaging both the patient and close family members in this process is essential for obtaining the best possible historical information.

Once the diagnosis of PPMS has been made, it is important to be alert for any acute neurologic events—clinical or radiologic—that may impact your treatment recommendations.

2. What is the most important information to share with my patients about PPMS?

Patients need to know that approximately 15% of people with MS experience a primary progressive course, which is characterized initially by steady worsening of neurologic functioning without any distinct relapses (also called *attacks* or *exacerbations*) or periods of remission. It's important to emphasize that the rate of progression differs significantly from one person to another and each person's rate of progression may vary over time—with or without an occasional relapse, plateaus or apparent improvements along the way.

Although more than a dozen medications have been approved to treat relapsing forms of MS, only one medication—ocrelizumab ([Ocrevus®](#))—is also approved to treat primary progressive MS. Ocrelizumab is a monoclonal antibody that depletes B lymphocytes, thereby reducing inflammation in the central nervous system (CNS). Some experts infer from the findings of the pivotal clinical trial ([ORATORIO](#)) that the medication may be most effective in people with PPMS who are younger and have abnormal spinal fluid findings and clinical or MRI evidence of inflammatory activity as defined by Lublin and colleagues (2014). In other words, ocrelizumab may be most effective in patients with at least some degree of inflammatory activity.

In addition to immunomodulatory therapy, there are a range of [symptomatic management](#) and rehabilitation strategies available to enhance mobility, safety and independence and promote [wellness](#), emotional well-being and quality of life.

3. How can I explain the differences between PPMS and the other disease courses without causing undue alarm and anxiety?

Although there is a lot of variability among people with PPMS, we know that as a group, they differ in several ways from people with relapsing forms of MS:

- Relapsing MS is defined by inflammatory attacks on myelin in the CNS, during which activated immune cells cause small, localized areas of damage that cause symptoms to abruptly appear or worsen. PPMS involves much less inflammation of the type seen in relapsing MS and more of a gradual progression of symptoms related to degeneration of nerve cells. People with PPMS tend to have fewer brain lesions (also called plaques) than people with relapsing MS. People with PPMS also tend to have more lesions in the spinal cord than in the brain. Together, these differences make PPMS more challenging to diagnose and treat than relapsing forms of MS.
- In the relapsing forms of MS, women are affected 2–3 times more often as men; in PPMS, the sex ratio is 1:1.
- The average age of onset is approximately 10 years later in PPMS than in relapsing MS.
- People with PPMS tend to experience more problems with walking than other people with MS, but less difficulty with other symptoms such as cognitive impairment or visual problems.

Fortunately, there are many strategies available to help people manage their symptoms so that they can remain active and productive.

4. What about the treatment of PPMS?

The approval of Ocrevus in 2017 was a major step forward in the treatment PPMS. The positive result of the [ORATORIO trial](#) shed light on the mechanism of progression in PPMS, suggesting that it involves some degree of inflammation. The hope is that this will lead to additional ways to treat inflammation generated in the adaptive immune system. However, the innate immune system also plays a role in disease progression in PPMS, and major efforts are underway worldwide to find strategies to treat the aspect of inflammation within the CNS that likely contributes to the neurodegenerative component of PPMS as well. The National MS Society spearheaded the [International Progressive MS Alliance](#), a collaborative global initiative that is working to end progressive MS in three ways: ensuring that research is focused on barriers to treatment development, integrated across the MS community and

systematically measured and refined; leveraging research already underway and stimulating new research through a significant grants program; driving worldwide resources to fund the best research.

While ocrelizumab represents a major step forward in the treatment of PPMS, it appears to be only partially effective. As already mentioned, some experts infer from the trial results that it works best to slow disease progression in younger individuals with evidence of clinical or MRI inflammation. However, it is clear that ocrelizumab does not reverse existing disability in PPMS.

Symptom management and rehabilitation continue to be essential elements in the ongoing treatment of people with PPMS. Exercise, medications (e.g., baclofen to manage spasticity, dalfampradine to improve walking speed, and others to manage bladder and bowel problems, sensory changes, mood and other symptoms), mobility aids and other assistive technology all contribute to a person's well-being and ability to function.

In talking about these essential treatment strategies, it will be important to provide information to your patients about the role of other clinicians in their care—nurses, rehabilitation professionals, speech/language pathologists and mental health specialists, among others—and help them access these clinicians in the community. The National MS Society can also help provide these referrals.

5. Why not give ocrelizumab to everyone with PPMS?

The risks may outweigh the benefits for older patients with no signs of active inflammation. The medication does not reverse disability that has been fixed over time. Most importantly, these patients may be more prone to the serious infections or possible malignancies that may occur with ocrelizumab.

6. Will insurance companies cover the cost of ocrelizumab?

It is too early to tell how insurance companies will deal with ocrelizumab. Because this medication had positive results in the pivotal trial for PPMS and the FDA has approved it for patients with PPMS, there is reason to hope that patients will receive some coverage for it from third party payers. For those without coverage, Genentech (866-422-2377) offers assistance for many people through their Genentech Access Solutions program.

7. When is it appropriate to start rehabilitation interventions?

Rehabilitation, including physical, occupational and speech/language therapy, is a key component of MS management. In an ideal world, every person living with MS would have ongoing guidance about exercise strategies, energy conservation, symptom management, assistive technology of all kinds, environmental adaptations, and strategies to deal with any cognitive changes they might experience. However, limitations on insurance coverage will likely make it necessary to save rehabilitation visits for specific time-limited interventions, including: early in the disease course to learn energy-management strategies or develop an at-home exercise program; as the disease progresses to maintain function or learn how to use mobility aids or other forms of assistive technology; as new symptoms develop, such as problems with speech or swallowing, or changes in cognitive abilities.

The key message to patients is that there are a variety of specialists available to help them manage the various kinds of symptoms and changes that can occur over the course of the disease.

8. When is the appropriate time to talk with family members?

With your patient's consent, it is important to engage family members as early as possible, particularly since their help will be crucial to the history-taking process. It often happens that a family member remembers a past symptom or event that the patient has forgotten or dismissed as being of no importance. If your patient is initially unwilling to involve family members, you may gradually be able to convince him or her of the value of having family participation and support, and of offering information and support to their loved ones who share the impact of this chronic, unpredictable disease.

9. What is the best format for providing this type of information?

Information about the diagnosis of MS should always be given in person, in a manner that takes into account the patient's intellectual level and emotional state. Without that face-to-face interaction, you won't be able to gauge your patient's reactions or the degree to which he or she has understood what you are saying. Keeping in mind that people who are anxious and upset tend to miss much of what is being said to them, it's a good idea to avoid giving too much information at one time. Scheduling a follow-up appointment within the next few weeks will give the person an opportunity to absorb the news and return with questions and concerns. You might also want to encourage your patient to bring a family member or friend to take notes and act as a second pair of ears. And sending your patient home with print materials about PPMS can also be helpful. The National MS Society (1-800-344-4867) will be happy to provide you with brochures. Additional information about PPMS is available at nationalMSSociety.org/PPMS.

10. What kinds of emotional reactions might I expect from my patients and their families?

Receiving a diagnosis of MS is frightening enough; the diagnosis of PPMS is even more so. The word "progressive" is easily interpreted as disaster waiting to happen. The best way to support and reassure your patients is to provide information about the recently approved treatment option—Ocrevus—if appropriate, as well as the range of symptom management strategies that you will prescribe for them. It's also important to provide assurances that you will work with them to manage the disease and its challenges. This is an opportune time to refer them to the National MS Society for education and support. And, if needed, the Society can provide a referral to a mental health professional with expertise in chronic illness.

11. How can I best assist my patients and their families to deal with disease progression?

Patients tend to be more confident and less anxious when they feel they have a strong relationship with their doctor. You can facilitate that connection by:

- Seeing them on a regular basis (every six months or a year)
- Taking time to respond to their questions and concerns
- Assuring them that you will work with them over the long haul to manage problems that arise
- Prescribing immunodulatory therapy, if appropriate, and setting realistic expectations concerning the benefits and risks

- Focusing proactively on symptom management, including medication, rehabilitation and assistive technology
- Paying close attention to the patient’s mood and family issues, and providing referrals to mental health professionals for diagnosis and treatment
- Encouraging the development of an active support network, including connection with the National MS Society and other MS organizations
- Avoiding any message that suggests you have nothing more to offer. Your patient and the patient’s family need to know you will be there with them no matter what.

12. How can I best answer patients’ and family members’ questions about the prognosis of PPMS?

With a chronic, unpredictable illness, the message should always be honest but hopeful. Your willingness to be frank and open about potential challenges will lay the groundwork for an effective and trusting working relationship. You can promote hopefulness in your patients in several ways: by emphasizing that every person with MS is different and that only time will tell whether the progression will be gradual or more rapid; by assuring them that you will work with them to manage the disease and its challenges; and by reminding them that productivity and function are possible even if mobility is affected.

As the disease progresses, patients and family members can easily become overwhelmed by fears of the future. The best strategy is to listen to their concerns and help them connect with the professionals who can best support their efforts to plan and problem-solve effectively. The National MS Society can provide referrals to employment counselors, home care providers, care managers, financial planners, elder care attorneys, and other community resources—and offer information about long-term care options, as needed.

13. Why have there been fewer clinical trials in PPMS than in other MS disease courses?

People often ask why so few clinical trials have been done in PPMS compared to the large number in relapsing MS. In answering their questions, it’s helpful to say that MS clinicians and researchers share this frustration and are actively looking for new and better therapies for PPMS. Several obstacles have stood in the way:

- The immune-modulating drugs used to treat relapsing forms of MS are all primarily anti-inflammatory, and therefore possibly not as effective in PPMS, which involves much less inflammation than the relapsing forms.
- In PPMS, there is a lack of easily identifiable outcomes to measure in clinical trials. In the trials for the disease-modifying therapies for relapsing forms of MS, investigators looked at outcomes such as number of relapses and number of new lesions seen on MRI to determine whether people who received the treatment had lower numbers than those who received a placebo (non-active substance) or another medication (active treatment). In other words, the investigators looked at things they could easily count over the course of a two- or three-year trial. Because people with PPMS don’t experience relapses or the same degree of inflammation in the central nervous system, there are fewer events that can be counted.
- The disease progression that occurs in PPMS can be quite slow—which means that a trial has to go on long enough to determine whether a treatment slowed or halted that progression.

Researchers are working to identify other ways to measure the changes that occur in PPMS so that they can more easily test potential treatments.

14. What recommendations should I be giving about financial and life planning?

Have a frank discussion with your patients about the status of their disease and what may happen in the future. Refer your patients to their National MS Society for assistance with future planning. The Society will encourage and support their efforts to:

- Take a “financial inventory” early in the course of their disease (What are their assets and debts? What about expenses that might now need to be added to their budget, such as medications or physical therapy?)
- Explore and understand protections that exist for someone who has a pre-existing condition and may want or need to change employment
- Look at options for assistance, e.g., community services, benefits and entitlements that could help address their needs in the future. The best time to be an educated consumer is not when one is in crisis, but when one can take the time to learn about options and gather information for future reference.
- Refer them to financial planners and attorneys with expertise in chronic illness and disability

In your ongoing conversations with patients, encourage them to maintain open lines of communication within their families, thinking together about what would happen if MS imposed changes in the future. Questions to consider include:

- What if they require assistance with personal care in the future?
- How available are family members?
- What other life demands are competing with the needs of the family member with MS?
- Is the home accessible?

15. Why has it been so difficult to find an effective treatment for PPMS?

The disease-modifying medications we have available today are primarily anti-inflammatory, which means that they do not work as well for a disease course that is more degenerative than inflammatory. The good news is that we now have one medication that has shown benefit in primary progressive MS and researchers are working to identify new ways to measure the changes that occur in PPMS so that they can more easily test other potential treatments. People who are interested in learning about ongoing clinical trials in PPMS can visit [nationalMSSociety.org/researchparticipation](https://www.nationalmssociety.org/researchparticipation).

Alongside these efforts to identify more effective medications to slow the progression of PPMS, researchers are looking for ways to [protect and repair CNS tissue](#) that is damaged or lost in MS. Potential cell-based therapies and myelin-repair strategies are now in clinical trials and creative new rehabilitation strategies and symptom management techniques are being explored to maximize ability and treat debilitating symptoms.

16. What other resources are available?

Organizations

- National MS Society (1-800-344-4867; nationalMSSociety.org) The National MS Society has created educational materials on a wide range of topics. Your patients can obtain any of the following materials at no charge by calling the National MS Society's MS Navigator service at 1-800-344-4867 or in the multimedia section of the website at nationalMSSociety.org/brochures:
 - Momentum® magazine
 - Adapting: Financial Planning for a Life with Multiple Sclerosis
 - Managing Progressive MS
 - A Guide for Caregivers
 - At Home with MS: Adapting Your Environment
 - So You Have Progressive MS?

Online programming (webcasts, podcasts, online classes)

Connection opportunities: self-help groups and chatrooms

Financial planning consultations

Employment consultations

Clinical trial information

- Multiple Sclerosis Association of America (800-532-7667; mymsaa.org)
 - Reassurance call program
 - MRI Access Fund
 - Equipment distribution
 - Cooling equipment distribution
 - Barrier-free housing
 - Brochures and videos
 - Lending library
- Multiple Sclerosis Foundation (800-673-6287MSFOCUS; msfocus.org)
 - Support groups
 - Financial assistance
 - Computer program
 - Cooling Program
 - MS Cruise for a Cause
 - Publications
 - Online services
 - Internet helpline
 - Lending Library
- Can Do MS (800-367-3101; mscando.org) A nonprofit organization offering lifestyle empowerment programming for people with MS and their support partners, with an emphasis on exercise, nutrition and symptom management to help individuals and families thrive in spite of MS.

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Dr. Goodman's interests include clinical and experimental therapeutics research. He has been the lead investigator (or a member of the steering committee) for various national and international clinical trials of new therapies for multiple sclerosis including natalizumab and dalfampridine. Dr. Goodman is the Rochester co-PI (along with Steven Goldman, MD, PhD) of a project funded by New York State Stem Cell program (NYSTEM) that plans to perform a phase 1, first in man study testing the safety of transplanting oligodendrocyte progenitor cells into patients with secondary progressive multiple sclerosis.

Dr. Goodman is a past Chair of the Multiple Sclerosis Section of the American Academy of Neurology. He has served the National Multiple Sclerosis Society as Co-Chair of the Long-term Care Committee, member of the Client Education Committee, and member of the Executive Committee of the National Clinical Advisory Board. He is the current president of the New York State Neurological Society.