

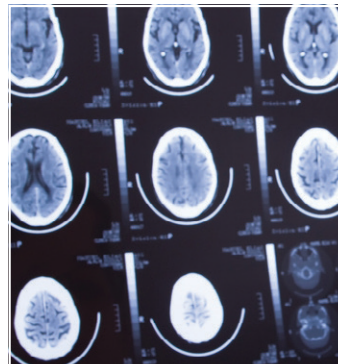
Offering  
Complimentary Continuing  
Education Credit for Nurses

Spring 2015  
Volume 10, Number 4

# Counseling Points™

Enhancing Patient Communication for the MS Nurse

## Encouraging Monitoring and Follow-up in MS Care



**Series Editor**  
Amy Perrin Ross, APN, MSN, CNRN, MSCN

**Faculty Panel**  
Beverly A. Layton RN, CCRC, MSCN  
Marie Moore, FNP  
Valerie Stickel-Diehl, RN, MS, MSCN

This continuing education publication is supported by an educational grant from Teva Pharmaceuticals.

## FACULTY:

### Series Editor

**Amy Perrin Ross, APN, MSN, CNRN, MSCN**  
Neuroscience Program Coordinator  
Loyola University Medical Center  
Maywood, IL

### Faculty Panel

**Beverly A. Layton RN, CCRC, MSCN**  
Multiple Sclerosis Nurse Consultant  
Birmingham, AL

### Marie Moore, FNP

Nurse Practitioner  
CMC-Multiple Sclerosis Center  
Charlotte, NC

### Valerie Stickel-Diehl, RN, MS, MSCN

Nurse Case Manager  
Mercy Ruan Neuroscience Center  
Des Moines, IA

### Faculty Disclosure Statements

Amy Perrin Ross has received honoraria for participating on the Speakers' Bureaus for Acorda, Bayer HealthCare, Inc., Biogen Idec, EMD Serono, Genzyme, Mallinckrodt, Novartis, Pfizer, and Teva Pharmaceuticals, and as a consultant for Acorda, Bayer HealthCare, Inc., EMD Serono, Genzyme, Mallinckrodt, Novartis, and Teva Pharmaceuticals.

Marie Moore has received honoraria for participating on the Speakers' Bureaus for Biogen Idec, Genzyme, Novartis, and Pfizer.

Beverly Layton has received honoraria for participating on the Speaker's Bureaus for Biogen Idec, Genzyme, and Pfizer; consulting for Bayer, Genzyme, Novartis, and Questcor; and from Biogen Idec for research support.

Valerie Stickel-Diehl has received honoraria for participating on the Speakers' Bureaus for Acorda Therapeutics, Biogen Idec, Genzyme, Novartis, and Pfizer.

### Planners and Managers

The following planners and managers have declared no relevant financial relationships: Joseph J. D'Onofrio, Frank Marino, Katherine Wandersee.

## 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  
Websites: [www.delmedgroup.com](http://www.delmedgroup.com)  
[www.counselingpoints.com](http://www.counselingpoints.com)

### Medical Writer

Katherine Wandersee

### Art Director

James Ticchio

Cover photo credits: © StockPhotosArt.com / Veer; Thomas Pajot / Veer; PicsFive / Veer; cienpies / Veer; Alloy Photography / Veer

Copyright © 2015, Delaware Media Group, Inc. All rights reserved. None of the contents may be reproduced in any form without prior written permission from the publisher. The opinions expressed in this publication are those of the faculty and do not necessarily reflect the opinions or recommendations of their affiliated institutions, the publisher, or Teva Pharmaceuticals.

# Counseling Points™

## Encouraging Monitoring and Follow-up in MS Care

## Continuing Education Information

### Target Audience

This educational activity is designed to meet the needs of nurses who treat or who have an interest in patients with multiple sclerosis (MS).

### Purpose

To provide nurses who treat patients with MS with information and practice advice related to safety monitoring and follow-up associated with MS disease-modifying therapies.

### Learning Objectives

*Upon completion of this educational activity, the participant should be able to:*

- Discuss current challenges associated with pre-treatment monitoring for MS disease-modifying therapies (DMTs)
- Assess methods for recommending and encouraging regular follow-up while on MS DMT
- Review how appropriate monitoring can prevent complications of MS DMTs

### Continuing Education Credit

This continuing nursing education activity is developed under the joint providership of Delaware Media Group and NP Alternatives.

NP Alternatives is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Laurie Scudder, DNP, NP, served as nurse planner and reviewer for this activity. She has declared no relevant financial relationships.

This activity has been awarded 1.0 contact hours (1.0 contact hours are in the area of pharmacology). Code: MSCP04015.

In order to earn credit, please read the entire activity and complete the post-test and evaluation at the end. Approximate time to complete this activity is 60 minutes.

This program expires April 1, 2017.

### Disclosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not approved by the FDA. Teva Pharmaceuticals and Delaware Media Group do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of Teva Pharmaceuticals and Delaware Media Group.

### Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any medications, diagnostic procedures, or treatments discussed in this publication should not be used by clinicians or other health care professionals without first evaluating their patients' conditions, considering possible contraindications or risks, reviewing any applicable manufacturer's product information, and comparing any therapeutic approach with the recommendations of other authorities.

# welcome

Dear Colleague,

Discussing safety risks and monitoring patients for potential adverse effects of treatment are increasingly important parts of management of MS. We want each patient with MS to receive the most efficacious therapy that is appropriate for that individual. But we also need to balance the potential for efficacy with safety, tolerability, and willingness to adhere to therapy.

The growing number of therapeutic options for MS has broadened this decision-making process greatly. In most respects, this is a positive step forward. At the same time, MS nurses need to apply a more comprehensive approach to preparing patients for treatment and following patients on treatment. We need to be aware of how a DMT affects other aspects of a patient's health. We need to educate and inform our patients about the potential risks involved with some treatment approaches. And, we need to make sure that patients are evaluated to determine whether the therapy is achieving its goals for suppression of MS disease activity.

Most MS nurses face the challenges of increased time constraints, paperwork burden, and frustration when a therapeutic plan does not go forward as intended. Our nurse panelists discuss the challenges they are facing now, and those anticipated for the future as more new DMT categories are introduced. I hope you are able to benefit from these insights.



Amy Perrin Ross, APN, MSN, CNRN, MSCN (series editor)  
Neuroscience Program Coordinator  
Loyola University Medical Center  
Maywood, IL

# Encouraging Monitoring and Follow-up in MS Care

In a neurology clinic that manages approximately 200 patients with multiple sclerosis (MS), a newly hired neurology nurse practitioner (NP) is asked to review the charts of all active patients with a diagnosis of MS, to determine if they are up-to-date with the monitoring requirements needed to ensure safe and effective use of their disease-modifying therapies (DMTs). This sounds like a fairly straightforward task, so the NP begins with the practice's electronic medical record system to see if there is a system in place for keeping track of patients' blood test results, necessary eye exams, MRI data, etc. Unfortunately, the amount of information entered into this system seems to differ for each patient, and is incomplete for many of them. The NP starts making a list of the common problem areas where more information or follow-up appears to be needed:

- Some patients with MS have not had a follow-up appointment at the clinic for at least a year.
- In some cases, it's not clear whether patients are actually taking the most recent MS DMT prescribed, if they ever filled the initial prescription, or if they have returned to obtain appropriate refills.
- There is no single place to look to review current results of safety monitoring. Patients appear to be "on their own" to obtain most lab tests, eye exams, and follow-up MRI stud-

ies. Only a few patients regularly report back or bring copies of their lab results to the clinic.

- Notes in the charts indicate that many patients have encountered significant delays in obtaining their DMT due to difficulties getting through the prior authorization system.
- When some patients have tried to refill their medications, they are sometimes told by the pharmacy they need a particular test first. It's not clear from the chart whether the person completed these steps and was able to refill the medication.

This practice may sound particularly disorganized, but in fact it may be closer to the norm than the exception. Rapid changes in the MS therapeutic environment have demanded a much more personalized system for initiating and following patients on their therapies.<sup>1-3</sup> However, increasing complexity in both reimbursement and patient monitoring and follow-up have made it difficult for MS care providers in most practice settings to keep up with the demand for more hands-on care. This is true not only in MS, but also in other disease states such as cancer and rheumatoid arthritis, where personalized medicine goals are coupled with higher-cost specialty pharmaceuticals.<sup>4</sup> In these settings, nurses face increasing challenges for communication, support, and advocacy for patients.<sup>5</sup>

Balancing the best possible treatment outcomes with the need to minimize complications, maximize adherence to therapy, and control costs often

presents a set of conflicting goals. How to help patients accomplish these goals in a day-to-day MS care setting is the focus of this discussion.

## Need for Safety Monitoring in MS Therapies

At one time, a complete blood count (CBC), a complete metabolic panel (CMP), and regular magnetic resonance imaging (MRI) studies made up the mainstay of lab and radiologic tests for most patients with MS. Today, depending upon which DMT is prescribed, many other types of monitoring could be part of the required protocols, including pulmonary function tests, tuberculin skin tests, negative pregnancy test, serum JC virus (JCV) and varicella antibodies, ECG and heart rate monitoring, and ophthalmic screening for macular edema.<sup>2</sup> Regardless of which DMT

---

*Increasing complexity in reimbursement and patient monitoring and follow-up have made it difficult for MS care providers in most practice settings to keep up with the demand for more hands-on care.*

---

is selected, safety monitoring is a necessary step that cannot be overlooked by people with MS or those involved in their care. Increasingly, payers and health care organizations require that patients remain current on blood monitoring and other necessary evaluations before they will approve prescription refills for MS drugs or authorize reimbursement. All MS therapies require follow-up and monitoring to ensure safety and toler-

ability. However, many of the more newly introduced therapies have prompted different types of monitoring that were not previously needed in MS care practices. As more new agents are introduced (including the newly approved drug, alemtuzumab, and other biologic therapies in the pipeline), a greater variety of tests will be needed to detect early signs of potential serious adverse effects in patients receiving these treatments.<sup>6-9</sup>

The specific monitoring requirements and/or “risk evaluation and mitigation strategy” (REMS) for each of the approved MS agents have been subject to frequent changes and updates. Thus it is advisable for practitioners who treat patients with MS to keep track of the most current labeling information for each drug and to check for updates regularly. REMS systems for some of the higher-risk agents (such as alemtuzumab or natalizumab) include careful monitoring and record keeping among the requirements for prescribing the drug. For example, according to the Lemtrada (alemtuzumab) REMS program, “prescribers are required to keep track of laboratory monitoring status of all patients who have been infused with Lemtrada from the first infusion until 48 months after the last infusion.”<sup>10</sup> Monitoring of CBC, serum creatinine, and urinalysis with urine cell counts must be completed monthly for 4 years after the last infusion of alemtuzumab, and tests of thyroid function status are required every 3 months. Patient status forms must be completed by prescribers every 6 months.<sup>10</sup> For other MS DMTs, the individual clinic or practice may need to create its own systems to better track patient monitoring information. Some of the monitoring steps for each of the agents are listed in **Table 1**.

## Table 1. Key Monitoring Steps for MS Disease-Modifying Therapies

Partial listing; consult current prescribing information for each agent.

### Fingolimod (Gilenya)<sup>11</sup>

- Electrocardiogram (ECG) and monitoring for bradycardia on initial dosing
- Ophthalmic examinations to rule out macular edema, at baseline and 3 to 4 months after initial dosing
- Complete blood count and liver enzymes (also required for interferons, teriflunomide, and some other agents)

### Teriflunomide (Aubagio)<sup>12</sup>

- Pregnancy test and counseling of patients about risk of pregnancy
- Monthly liver function tests for first 6 months
- Tuberculosis skin testing
- Antibody testing for varicella zoster virus

### Glatiramer acetate (Copaxone)<sup>13</sup>

- Skin examination for signs of skin breakdown

### Interferon beta-1a and interferon beta-1b (Avonex, Betaseron, Rebif, Extavia, Plegridy)<sup>14,15</sup>

- Monitor CBC and liver enzymes
- Skin examination for signs of skin breakdown
- Thyroid hormone levels in patients with history of thyroid dysfunction or as clinically indicated

### Dimethyl fumarate (Tecfidera)<sup>16</sup>

- CBC with lymphocyte count prior to initiating therapy
- CBC with differential every 6 months and as clinically indicated

(Contains a partial listing; consult full prescribing information for each agent.)

In many practices, keeping up with this information will warrant a need for new in-office protocols for testing and surveillance of patients with MS to ensure that they are tolerating therapy and receiving the recommended tests to monitor for potential adverse events. Some practices also ask patients to document in writing that they have

received education about the risks of MS therapies and that they are aware of their own responsibilities for monitoring and follow-up while receiving the drug. Determining the patient's level of health literacy is an important aspect of this process. The Agency for Healthcare Research and Quality (AHRQ) offers an online Health Literacy Toolkit that includes a number of useful resources toward this goal, including:<sup>17</sup>

- Health Literacy Assessment Tool and User's Guide
- Training Program for Healthcare Staff on Communication
- Telephone Reminder Tool to Help Refill Medicines on Time

## Infectious Complications of MS Therapies

The development of newer immunomodulating therapies for MS has introduced new infectious risks and immune-mediated effects that are not normally encountered in patients with MS. These include opportunistic infections, which are defined as "illnesses caused by organisms that would not usually cause disease in a person with a normally functioning immune system."<sup>18</sup> Immunomodulation in MS may also lead to unexpected presentations of more typical infections (such as herpesvirus), development of malignancies, and risk of autoimmune conditions such as thyroid disease.

Natalizumab increases the risk of opportunistic infections because it prevents inflammatory cells from performing immunosurveillance of the central nervous system.<sup>19</sup> This risk appears to be largely confined to one serious CNS infectious

disorder, progressive multifocal leukoencephalopathy (PML). PML is a demyelinating white matter disease caused when the JC polyomavirus (JCV) proliferates in the CNS. The virus infects the oligodendrocytes and causes their death by necrosis and demyelination.<sup>20</sup> PML may develop in patients with underlying immunosuppressive conditions (e.g., Hodgkin's lymphoma, AIDS), but its incidence has been steadily increasing in people with MS treated with monoclonal antibodies such as natalizumab.<sup>21</sup> PML risk stratification has been discussed extensively in other literature, including a comprehensive Supplement to the *International Journal of MS Care*.<sup>22</sup>

Infectious complications associated with MS therapies are summarized in **Table 2**. For some drugs, the reported infectious complications have been observed mainly in other disease states such as rheumatoid arthritis or leukemia.

Use of interferons or glatiramer acetate are not associated with increased risk of infections, as demonstrated through more than 20 years of use.<sup>23,37</sup> Treatment with interferon may result in mild leukopenia, but there are no reports of opportunistic infections in patients with MS treated with these agents.<sup>38,39</sup> A study by Miller and colleagues to determine whether treatment with any interferon or glatiramer acetate would decrease expression of JC virus did not show an

**Table 2. Risk of Infectious Complications from MS Therapies**

Therapy	Potential Infectious Complications in MS
Interferon beta-1a Interferon beta-1b	May cause neutropenia or lymphopenia. Rarely of clinical significance in MS. <sup>23</sup>
Glatiramer acetate	None <sup>1</sup>
Mitoxantrone	Risk of opportunistic infection from severe leukopenia. <sup>24</sup> Urinary tract infection, pneumonia, varicella zoster, herpes simplex (0.6% of treated patients)
Fingolimod	Varicella zoster encephalitis and vasculopathy, herpes simplex encephalitis, PML (rare; cases may be associated with prior natalizumab use) <sup>25-27</sup>
Natalizumab	PML, herpes simplex, varicella zoster, CNS and ocular toxoplasmosis, human herpesvirus 6 (HHV6) reactivation <sup>22,28-31</sup>
Rituximab*	Hepatitis B reactivation, <i>Pneumocystis pneumonia</i> , about 80 cases of PML. Serious infections are rare among large populations treated for RA <sup>32,33</sup>
Teriflunomide	Similar to placebo <sup>34</sup>
Dimethyl fumarate	None noted in pivotal trials. Rare cases of PML in psoriasis patients treated with fumarate. One PML case in patient with MS taking drug for 4.5 years (lymphopenia 3.5 years) <sup>35,36</sup>
Alemtuzumab**	In organ transplant population, 50% greater risk of opportunistic infection; 2X risk of CMV reactivation; increased risk of fungal infections; 7 cases of PML in patients with immunosuppression (lung transplant, chronic lymphocytic leukemia). Prophylaxis is recommended to limit varicella zoster or herpes simplex activation or reactivation. <sup>7-9</sup>

CMV=cytomegalovirus; PML= progressive multifocal leukoencephalopathy; RA=rheumatoid arthritis

\*Not approved for use in MS; data based on use in rheumatoid arthritis

\*\*Infectious complications based on use in organ transplant population

## How Well Do People With MS Understand Risk of Therapies?

### Survey Results from the NARCOMS Registry<sup>47</sup>

**Goal of Study:** To determine how well MS patients understand risks of serious complications related to therapies.

**Methods:** 10,259 people with MS in the NARCOMS Registry were invited to complete a web-based questionnaire on treatment decision-making. Several standard “gambling paradigms” were used to identify maximal risk tolerance, with risk described numerically (i.e. 1:1000) and graphically. Two scenarios presented to patients were “completely cure MS” and “prevent a one-step progression of disability on the Patient Defined Disease Steps (PDDS) scale.” The researchers used logistic regression analysis to study inconsistency among the responses.

**Results:** 5,446 people with MS completed the survey. Demographics included:

- Mean age: 52.7 years
- % female: 78
- Mean disease duration: 13.9 years
- Mean PDDS score: 3.2
- % on MS DMT: 74%

Female sex and higher education were, to the investigators’ surprise, associated with “illogical pairings,” which suggested a disconnect between the level of risk presented and the hypothetical decision made by the patient. In another analysis of the same data, increased risk tolerance was associated with higher levels of disability, male sex, and among patients not currently on an MS DMT.

**Conclusion:** “These observations suggest that additional attention is needed by clinicians in explaining risk of serious complications to MS therapies.”

Source: Fox R, Salter A, Alster JM, et al. Risk tolerance in MS patients: Survey results from the NARCOMS Registry. *Neurology* 2011;76(Suppl 4):A478; Abstract P06.057.<sup>47</sup> NARCOMS=North American Research Committee on Multiple Sclerosis

effect of treatment on blood or urinary viral prevalence or viral copy numbers.<sup>40</sup>

### How Prepared are Patients to Take Risks?

As the therapeutic options for MS have expanded, we have begun to learn more about acceptance of risk as it relates to the disease. For patients, this means knowingly accepting potential health risks that could be permanent (e.g., thyroid dysfunction) or even fatal (e.g., PML) as part of achieving control over the disease process. This concept may be akin to patients with cancer who accept the risks and potential long-term health effects associated with aggressive chemotherapy regimens in exchange for a chance at remission. These are difficult decisions to make for a person who may

still be trying to grapple with the shock of an MS diagnosis and what it means for one’s future. In addition, many people experience changes in their belief sets and risk acceptance as they age and enter different life stages.<sup>41</sup>

For patients who experience worsening disease or a particularly aggressive MS disease course, a greater degree of risk may be needed to gain control over the disease and may override other factors.<sup>42,43</sup> A 2010 survey by Heesen and colleagues of 69 natalizumab-treated patients treated and 66 neurologists suggested that patients with MS were willing to accept higher risks related to potential development of PML than were the physicians surveyed. Only 17% of patients said they would stop treatment with natalizumab when the risk of



PML reached 2 in 10,000 persons (compared with 49% of physicians who would stop the therapy).<sup>44</sup> The authors also concluded that “patients had a significantly worse perception of MS as a malignant disease,” than did the neurologists surveyed. Patients also indicated being open to information about treatment-related risk and the shared decision-making process.<sup>44</sup>

To what degree can people with MS—or even health professionals—understand the complex balance of risk and benefit associated with medical treatment? People watching consumer drug advertisements on television are often overwhelmed (or even bemused) by the long array of potential adverse effects that seem to overshadow any possible benefit of the drug. Research shows that these ads often lack the basic contextual information that could help a consumer to make an informed decision. Thus, most people “tune out” the information without being able to consider what it may mean for them.<sup>45,46</sup>

The North American Research Committee on Multiple Sclerosis (NARCOMS) Registry allows researchers to tap into real-world views and experiences of a large population of people with MS. Using NARCOMS data, Robert Fox and colleagues recently explored how people with MS who are using a variety of therapies view the concept of risk. As described in the Sidebar, these authors found a wide spectrum of risk tolerance, with some variation based on gender, patient age, and severity of disease.<sup>47</sup>

## Expanding Patient Communication and Counseling Skills

Communicating risk and risk assessment is crucial to enable shared decision making with patients.

Shared decision making is a concept that focuses on patient–provider communication in the medical decision-making process. In the exchange of information between the provider and the patient, the patient is encouraged to communicate values, risk attitudes, and treatment goals.<sup>44,48</sup> Research about medication-taking risks in general indi-

---

*“Individual patients do not experience ‘likelihood,’ or population-level rates of events. They experience single outcomes (something happens or does not).”*

---

cates that patients tend to *underestimate* common risks, but *overestimate* the rarer risks. Furthermore, patients may respond to risks primarily on the basis of emotion rather than facts.<sup>41</sup> “Individual patients do not experience ‘likelihood,’ or population-level rates of events,” authors Moore and colleagues observe. “They experience single outcomes (something happens or does not). People making decisions may be frightened or too ill to process complex information and make appropriate decisions.”<sup>41</sup> Statistical representations are often used to describe the risks of certain treatments, but patients’ have a limited ability to understand concepts such as relative risk reduction (RRR). It is also important to consider that each patient will have different priorities and risk tolerance and may change his or her perception and tolerance of risk over time.<sup>49</sup> Key issues related to discussion of treatment risks with patients are summarized in **Table 3**.<sup>49</sup>

Patients often answer “No” when asked if they

### Table 3. Recommendations for Managing Treatment Safety in MS

- Selection and timing of treatment should be a shared decision between the healthcare provider and the person with MS, based on individual assessment of disease risk, likelihood of treatment efficacy (benefit) and short- and long-term adverse effects (risk).
- Communication of known or possible risks/benefits should be objective, understandable for the patient, and comprehensively documented.
- The safety profile should take into account risk minimization plans proposed by regulatory agencies.
- Only pivotal clinical trials and several years of prescription use can determine the safety profile of a treatment. Documents used to inform patients must be periodically reviewed in this view of new perceptions or evidence of risk and benefits.
- Healthcare professionals and patients should be involved in the spontaneous reporting process of adverse events to regulators in the course of prescription use of treatments.
- Implementation of international long-term follow-up, cohort databases or registries should be required for all new treatments.
- Risk minimization over time should be based on transparent information provided by regulators and manufacturers that is provided on a timely basis to health care professionals and patients.

Adapted with permission from: Clanet MC, Wolinsky JS, Ashton RJ, et al. Risk evaluation and monitoring in multiple sclerosis therapeutics. *Mult Scler.* 2014;20(10):1306-1311.<sup>49</sup>

have any questions about their medications. This is usually not because they understand everything about the treatment—they simply don't know enough about the medication to ask the right

---

*Patients often answer “No” when asked if they have any questions about their medications. They may not know enough about the medication to be able to ask the right kinds questions.*

---

kinds of questions.<sup>50</sup> In addition, patients may sense that the nurse or other healthcare provider doesn't have time to answer all of their questions.

#### Effect of Reimbursement and Prior Authorization on Monitoring Needs

As most healthcare providers know, prior authorization systems do not necessarily promote quick

turnarounds. An analysis by Cohen and colleagues from Tufts University Medical School describes barriers related to reimbursement and diagnostic tests as “bottlenecks” that keep patients from getting the treatments prescribed for them.<sup>51</sup> Many MS nurses have made a 3-month follow-up appointment and/or MRI appointment for a patient who was started on a new therapy, only to find that the person had not yet begun using the new agent within that time period. Is a 6-month follow-up time period more realistic? Some nurses recommend that the patient return in 6 months, regardless of whether a therapy has been started, to determine whether and why a delay has occurred. Some practices use automated software systems such as Covermymeds.com to help streamline prior authorization paperwork.<sup>52</sup>

#### Conclusion

New and emerging therapies will continue to have a major impact on the treatment of MS.

Even as safety concerns increase, it is important to keep in mind that control of the disease is also a crucial issue, and the standards for what constitutes successful therapy are on the rise. Further data are required on long-term safety profiles of new therapies to establish their exact role in treating different stages and forms of MS (early vs. established, mild vs. severe) and their placement in relation to the established treatments. Appropriate programs for monitoring adverse events for specific therapies will continue to be enhanced with increased knowledge of the specific dangers that each may present, and thus help to minimize potentially serious and life-threatening consequences while creating a higher standard of efficacy and improved outcomes for MS patients.

## References

- Rommer PS, Zettl UK, Kieseier B, et al. Requirement for safety monitoring for approved multiple sclerosis therapies: an overview. *Clin Exp Immunol*. 2014;175(3):397-407.
- Wingerchuk DM, Carter JL. Multiple sclerosis: current and emerging disease-modifying therapies and treatment strategies. *Mayo Clin Proc*. 2014;89(2):225-240.
- Vargas WS, Perumal JS. Fingolimod and cardiac risk: latest findings and clinical implications. *Ther Adv Drug Saf*. 2013;4(3):119-124.
- Cohen JP. Overcoming regulatory and economic challenges facing pharmacogenomics. *N Biotechnol*. 2012;29(6):751-756.
- Vorderstrasse AA, Hammer MJ, Dungan JR. Nursing implications of personalized and precision medicine. *Semin Oncol Nurs*. 2014;30(2):130-136.
- Caon C, Meyer C, Mayer L, et al. Efficacy and safety of alemtuzumab in multiple sclerosis and impact on nursing role. *Int J MS Care*. 2013;15(4):159-168.
- Willis M, Robertson NP. Drug safety evaluation of alemtuzumab for multiple sclerosis. *Expert Opin Drug Saf*. 2014;13(8):1115-1124.
- Tuohy O, Costelloe L, Hill-Cawthorne G, et al. Alemtuzumab treatment of multiple sclerosis: long-term safety and efficacy. *J Neurol Neurosurg Psychiatry*. 2014.
- Havrdova E, Horakova D, Kovarova I. Alemtuzumab in the treatment of multiple sclerosis: key clinical trial results and considerations for use. *Ther Adv Neurol Disord*. 2015;8(1):31-45.
- LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program. Available at: <http://www.lemtradarems.com>.
- Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2008;57(RR-5):1-30; quiz CE32-34.
- Sibley WA, Bamford CR, Clark K. Clinical viral infections and multiple sclerosis. *Lancet*. 1985;1(8441):1313-1315.
- Copaxone (glatiramer acetate injection) [package insert]. Kansas City, MO: Teva Neuroscience; 2012.
- Edwards S, Zvartau M, Clarke H, et al. Clinical relapses and disease activity on magnetic resonance imaging associated with viral upper respiratory tract infections in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 1998;64(6):736-741.
- Metz LM, McGuinness SD, Harris C. Urinary tract infections may trigger relapse in multiple sclerosis. *Axone*. 1998;19(4):67-70.
- Harbecke R, Oxman MN, Arnold BA, et al. A real-time PCR assay to identify and discriminate among wild-type and vaccine strains of varicella-zoster virus and herpes simplex virus in clinical specimens, and comparison with the clinical diagnoses. *J Med Virol*. 2009;81(7):1310-1322.
- Agency for Healthcare Research and Quality. AHRQ Health Literacy Universal Precautions Toolkit. Available at: <http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/literacy-toolkit/>.
- Berger J. Mechanisms of immune suppression in MS therapy. In: Progressive Multifocal Leukoencephalopathy and Other Infectious Complications in the Care of Multiple Sclerosis. Report on a Consensus Development Conference. *Int J MS Care*. May 2014;16(Suppl 2):1-6. Available at: <http://ijmsc.org/toc/ijmc/16/S2>.
- Kure K, Llena JF, Lyman WD, et al. Human immunodeficiency virus-1 infection of the nervous system: an autopsy study of 268 adult, pediatric, and fetal brains. *Hum Pathol*. 1991;22(7):700-710.
- Saribas AS, Ozdemir A, Lam C, et al. JC virus-induced progressive multifocal leukoencephalopathy. *Future Virol*. 2010;5(3):313-323.
- Bloomgren G, Richman S, Hotermans C, et al. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. *N Engl J Med*. 2012;366(20):1870-1880.
- Progressive Multifocal Leukoencephalopathy and Other Infectious Complications in the Care of Multiple Sclerosis. Report on a Consensus Development Conference. *Int J MS Care*. May 2014;16(Suppl 2). Available at: <http://ijmsc.org/toc/ijmc/16/S2>.
- Lam S, Wang S, Gottesman M. Interferon-beta1b for the treatment of multiple sclerosis. *Expert Opin Drug Metab Toxicol*. 2008;4(8):1111-1117.
- Hofmann A, Stellmann JP, Kasper J, et al. Long-term treatment risks in multiple sclerosis: risk knowledge and risk perception in a large cohort of mitoxantrone-treated patients. *Mult Scler*. 2013;19(7):920-925.
- Uccelli A, Ginocchio F, Mancardi GL, et al. Primary varicella zoster infection associated with fingolimod treatment. *Neurology*. 2011;76(11):1023-1024.
- Gross CM, Baumgartner A, Rauer S, et al. Multiple sclerosis rebound following herpes zoster infection and suspension of fingolimod. *Neurology*. 2012;79(19):2006-2007.
- Berger JR. Varicella vaccination after fingolimod: a case report. *MSARD*. 2013;2(4):391-394.
- Yao K, Gagnon S, Akhyani N, et al. Reactivation of human herpesvirus-6 in natalizumab treated multiple sclerosis patients. *PLoS One*. 2008;3(4):e2028.
- Fine AJ, Sorbello A. Central nervous system infections due to herpes simplex and varicella-zoster viruses in natalizumab-treated patients: post-market data from the FDA adverse event reporting system. Presented at 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); Sept 9, 2012; San Francisco, CA. Abstract T-342.
- Fine AJ, Sorbello A, Kortepeter C, et al. Central nervous system herpes simplex and varicella zoster virus infections in natalizumab-treated patients. *Clin Infect Dis*. 2013;57(6):849-852.
- Berger JR, Aksamit AJ, Clifford DB, et al. PML diagnostic criteria: consensus statement from the AAN Neuroinfectious Disease Section. *Neurology*. 2013;80(15):1430-1438.
- He D, Guo R, Zhang F, et al. Rituximab for relapsing-remitting multiple sclerosis. *Cochrane Database Syst Rev*. 2013;12:CD009130.
- van Vollenhoven RF, Emery P, Bingham CO, 3rd, et al. Long-term safety of rituximab in rheumatoid arthritis: 9.5-year follow-up of the global

- clinical trial programme with a focus on adverse events of interest in RA patients. *Ann Rheum Dis*. 2013;72(9):1496-1502.
34. Warnke C, Stuve O, Kieseier BC. Teriflunomide for the treatment of multiple sclerosis. *Clin Neurol Neurosurg*. 2013;115 Suppl 1:S90-94.
  35. van Oosten BW, Killestein J, Barkhof F, et al. PML in a patient treated with dimethyl fumarate from a compounding pharmacy. *N Engl J Med*. 2013;368(17):1658-1659.
  36. Ermis U, Weis J, Schulz JB. PML in a patient treated with fumaric acid. *N Engl J Med*. 2013;368(17):1657-1658.
  37. Johnson KP. Glatiramer acetate for treatment of relapsing-remitting multiple sclerosis. *Expert Rev Neurother*. 2012;12(4):371-384.
  38. Garcia-Montojo M, De Las Heras V, Bartolome M, et al. Interferon beta treatment: bioavailability and antiviral activity in multiple sclerosis patients. *J Neurovirol*. 2007;13(6):504-512.
  39. Carr DJ, Al-khatib K, James CM, et al. Interferon-beta suppresses herpes simplex virus type 1 replication in trigeminal ganglion cells through an RNase L-dependent pathway. *J Neuroimmunol*. 2003;141(1-2):40-46.
  40. Miller CS, Houff SA, Hopper J, et al. Disease-modifying drugs for multiple sclerosis and JC virus expression. *J Neurovirol*. 2012;18(5):411-415.
  41. Moore RA, Derry S, McQuay HJ, et al. What do we know about communicating risk? A brief review and suggestion for contextualising serious, but rare, risk, and the example of cox-2 selective and non-selective NSAIDs. *Arthritis Res Ther*. 2008;10(1):R20.
  42. Menon S, Shirani A, Zhao Y, et al. Characterising aggressive multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2013.
  43. Edan G, Le Page E. Induction therapy for patients with multiple sclerosis: why? When? How? *CNS Drugs*. 2013;27(6):403-409.
  44. Heesen C, Kleiter I, Nguyen F, et al. Risk perception in natalizumab-treated multiple sclerosis patients and their neurologists. *Mult Scler*. 2010;16(12):1507-1512.
  45. Kaphingst KA, DeJong W. The educational potential of direct-to-consumer prescription drug advertising. *Health Aff (Millwood)*. 2004;23(4):143-150.
  46. Khanfar N, Loudon D, Sircar-Ramsewak F. FDA direct-to-consumer advertising for prescription drugs: what are consumer preferences and response tendencies? *Health Mark Q*. 2007;24(1-2):77-91.
  47. Fox R, Salter A, Alster JM, et al. Risk tolerance in MS patients: Survey results from the NARCOMS Registry. *Neurology*. 2011;76(Suppl 4):A478; Abstract P06.057.
  48. Heesen C, Kopke S, Richter T, et al. Shared decision making and self-management in multiple sclerosis—a consequence of evidence. *J Neurol*. 2007;254 Suppl 2:II116-121.
  49. Clanet MC, Wolinsky JS, Ashton RJ, et al. Risk evaluation and monitoring in multiple sclerosis therapeutics. *Mult Scler*. 2014;20(10):1306-1311.
  50. Bermel RA, Puli SR, Rudick RA, et al. Prediction of longitudinal brain atrophy in multiple sclerosis by gray matter magnetic resonance imaging T2 hypointensity. *Arch Neurol*. 2005;62(9):1371-1376.
  51. Cohen JP, Felix AE. Personalized Medicine's Bottleneck: Diagnostic Test Evidence and Reimbursement. *J Pers Med*. 2014;4(2):163-175.
  52. CoverMyMeds Prior Authorization Software. Available at: <http://www.covermymeds.com>.

# CP Counseling Points™

## Encouraging Monitoring and Follow-up in MS Care

- MS nurses need to apply a comprehensive approach to preparing patients for treatment and monitoring patients on treatment.
- Selection of the most efficacious therapy for each individual with MS must be balanced with issues relating to safety, tolerability, and willingness to adhere to therapy.
- While all MS therapies require monitoring to ensure safety and tolerability, some newer therapies may require monitoring practices not previously required for MS.
- Risk evaluation and mitigation strategies (REMS) for the approved MS agents are subject to frequent changes, so it is advisable to keep track of the most current labeling updates.
- Some practices may implement in-office protocols for testing and surveillance of patients with MS to ensure that they are tolerating therapy and receiving the recommended monitoring.
- Reimbursement procedures such as prior authorization may delay the start of new treatment or a switch in therapy, so monitoring procedures may need to be adjusted to account for possible delays.
- Communicating risk is crucial to enable shared decision-making with patients. Some practices may ask patients to document in writing that they have received education about the risks of MS therapies.
- Patients' acceptance of the complex balance of risk and benefit associated with medical treatment varies widely. Studies in MS show that patients are open to discussing risk and view MS as a serious enough disease to accept risk.

# Counseling Points™

## Encouraging Monitoring and Follow-up in MS Care

### Continuing Education Post-test

To receive contact hours, please read the program in its entirety, answer the following post-test questions, and complete the program evaluation. A certificate will be awarded for a score of 80% (8 correct) or better. A certificate will be mailed within 4 to 6 weeks. There is no charge for CNE credit.

**By Mail:** Delaware Media Group, 66 S. Maple Ave., Ridgewood, NJ 07450. **By Fax:** (201) 612-8282

**Via the Web:** Applicants can access this program at the International Organization of MS Nurses' website, [www.IOMSN.org](http://www.IOMSN.org). Click on Educational Materials > Publications > *Counseling Points* and follow the instructions to complete the online post-test and application forms.

#### PLEASE SELECT THE BEST ANSWER

- 1. Patients with multiple sclerosis (MS) who are on disease-modifying therapy (DMT) should be monitored for safety and adverse effects of therapy:**
  - a. at initiation of therapy and after 6 months
  - b. at initiation of therapy, after 3 months, and then every 6 months thereafter
  - c. only if the patient complains about adverse effects or if lab results are abnormal
  - d. this determination must be individualized for the specific DMT and the patient's circumstances
- 2. A patient with MS in your practice has been prescribed a DMT, but 3 months later has not yet filled the prescription. An appropriate course of action would be:**
  - a. call the pharmacy and ask them to contact the patient
  - b. wait another 3 months and then follow up to see if the patient has started on the drug
  - c. follow up to determine whether insurance limitations or prior authorization requirements may be causing a delay
  - d. assume that the patient is not yet ready to commit to regular use of a DMT
- 3. Electrocardiogram (ECG) and heart rate monitoring are part of the safety monitoring protocol for:**
  - a. fingolimod (Gilenya)
  - b. natalizumab (Tysabri)
  - c. alemtuzumab (Lemtrada)
  - d. teriflunomide (Aubagio)
- 4. Monthly liver function testing is recommended for patients receiving which of the following DMTs?**
  - a. glatiramer acetate (Copaxone)
  - b. interferon beta 1b (Betaseron)
  - c. dimethyl fumarate (Tecfidera)
  - d. teriflunomide (Aubagio)
- 5. Among patients receiving a DMT, complete blood count (CBC) is recommended:**
  - a. mainly for those on an immunosuppressive agent such as alemtuzumab
  - b. only for those receiving an interferon
  - c. for most patients, as a way to monitor immune cell response and infection risk
  - d. primarily for patients with low white blood cell counts at initiation of therapy
- 6. Progressive multifocal leukoencephalopathy (PML) is caused when:**
  - a. immunosurveillance of the central nervous system (CNS) is blocked or inhibited
  - b. JC virus proliferates in the CNS
  - c. JC virus invades oligodendrocytes in the CNS
  - d. all of the above
- 7. True or False? Leukopenia due to treatment with interferon-based DMTs has been associated with serious opportunistic infections among patients with MS.**
  - a. True
  - b. False
- 8. In discussing risk acceptance with a patient in regard to a new MS therapy, the MS nurse should always:**
  - a. recognize that younger people are more open to accepting risk
  - b. take into account the patient's level of health literacy
  - c. try to play down some of the least-likely, serious risks of DMTs
  - d. encourage the patient that it's worth taking on some greater health risks for better disease control
- 9. Research about medication use in general shows that patients:**
  - a. underestimate common risks
  - b. overestimate serious risks
  - c. have an accurate view of how adverse effects may impact their health
  - d. both (a) and (b) above
- 10. Potential adverse effects of MS DMTs:**
  - a. are well understood based on pre-approval clinical trial data
  - b. may not become apparent until after several years of postmarketing use
  - c. are usually outweighed by the efficacy potential of the drug
  - d. can always be detected early through monitoring

# Counseling Points™: Program Evaluation Form

## Encouraging Monitoring and Follow-up in MS Care

Using the scale provided (Strongly Agree = 5 and Strongly Disagree = 1) please complete the program evaluation so that we may continue to provide you with high-quality educational programming. Please fax this form to **(201) 612-8282** or complete it online as instructed below.

5 = Strongly Agree    4 = Agree    3 = Neutral    2 = Disagree    1 = Strongly Disagree

**At the end of this program, I was able to:** *(Please circle the appropriate number on the scale.)*

- 1) Discuss current challenges associated with pre-treatment monitoring for MS disease-modifying therapies (DMTs) ..... 5 4 3 2 1
- 2) Assess methods for recommending and encouraging regular follow-up while on MS DMT ..... 5 4 3 2 1
- 3) Review how appropriate monitoring can prevent complications of MS DMTs ..... 5 4 3 2 1

**To what extent was the content:**

- 4) Well-organized and clearly presented ..... 5 4 3 2 1
- 5) Current and relevant to your area of professional interest ..... 5 4 3 2 1
- 6) Free of commercial bias ..... 5 4 3 2 1
- 7) Clear in providing disclosure information..... 5 4 3 2 1

**General Comments**

- 8) As a result of this continuing education activity (check only one):
- I will modify my practice. (If you checked this box, how do you plan to modify your practice?) \_\_\_\_\_
  - I will wait for more information before modifying my practice.
  - The program reinforces my current practice.
- 9) Please indicate any barriers you perceive in implementing these changes (check all that apply):
- Cost
  - Lack of opportunity (patients)
  - Patient adherence issues
  - Other (please specify) \_\_\_\_\_
  - Lack of administrative support
  - Reimbursement/insurance
  - Lack of professional guidelines
  - Lack of experience
  - Lack of time to assess/counsel patients
  - No barriers
- 10) Will you attempt to address these barriers in order to implement changes in your knowledge, skills, and/or patients' outcomes?
- Yes. How? \_\_\_\_\_
  - Not applicable
  - No. Why not? \_\_\_\_\_
- Suggestions for future topics/additional comments: \_\_\_\_\_

**Follow-up**

As part of our continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please check one:

- Yes, I would be interested in participating in a follow-up survey.
- No, I would not be interested in participating in a follow-up survey.

There is no fee for this educational activity.

Post-test Answer Key	1	2	3	4	5	6	7	8	9	10

**Request for Credit** *(Please print clearly)*

Name \_\_\_\_\_ Degree \_\_\_\_\_

Organization \_\_\_\_\_ Specialty \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

Phone \_\_\_\_\_ Fax \_\_\_\_\_ E-mail \_\_\_\_\_

Signature \_\_\_\_\_ Date \_\_\_\_\_

**By Mail:** Delaware Media Group, 66 S. Maple Ave., Ridgewood, NJ 07450

**By Fax:** (201) 612-8282

**Via the Web:** Applicants can access this program at the International Organization of MS Nurses' website, [www.IOMSN.org](http://www.IOMSN.org). Click on Educational Materials > Publications > *Counseling Points* and follow the instructions to complete the online post-test and application forms.

# CP



[www.delmedgroup.com](http://www.delmedgroup.com)