

MANAGED CARE PERSPECTIVES: 2010 UPDATE*

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ABSTRACT

Multiple sclerosis (MS) is a chronic disease that requires ongoing drug therapy to delay disability progression. This article reviews various patient-specific factors (ie, lifestyle, financial status, and tolerance to adverse effects) that should be considered when individualizing drug therapy to best meet a patient's needs. This is followed by a discussion of recent issues pertaining to managed care pharmacy (ie, healthcare legislation, specialty pharmacies, blood testing for β -interferon efficacy, introduction of dalfampridine, and approval of biosimilar products and generic formulations), and how they impact MS management.

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CASE STUDY

RE is a 17-year-old white female who was recently diagnosed with multiple sclerosis (MS) based on a magnetic resonance imaging (MRI) evaluation. She is a high school student with a very busy schedule and is afraid that her drug therapy may slow her down. What treatment option(s) may be best for RE at this time?

Multiple sclerosis is an incurable, chronic demyelinating disease of the central nervous system (CNS). Natural history data suggest that 50% of patients diagnosed with relapsing-remitting disease develop disabling symptoms characteristic of progressive MS within 10 years of disease onset,¹ and that 43% to 65% develop cognitive impairment.² As such, delaying disease progression and the associated disability and cognitive dysfunction is a fundamental goal of MS therapy. To achieve this objective, an individualized, dynamic, long-term treatment plan must be implemented, along with ongoing management of medication-related adverse effects.³

LONG-TERM DISEASE MANAGEMENT AND TREATMENT CONSIDERATIONS

Three interferon (IFN) β products (ie, intramuscular [IM] IFN β -1a, subcutaneous [SC] IFN β -1b, and SC IFN β -1a) and SC glatiramer acetate are currently approved for first-line treatment of early stage MS. Although studies have shown that these disease-modifying therapies (DMTs) have similar efficacy profiles,⁴⁻⁷ it is important to individualize therapy based on administration and cost considerations, as well as a patient's ability to tolerate adverse effects. In terms of drug administration, it is important to note that each of these products is taken parenterally; if an individual is unable to self-inject, a friend or family member must be available to provide assistance. As such, many patients prefer treatment with IM IFN β -1a; this agent is dosed once weekly, as opposed to glatiramer acetate and the other IFN β products, which are dosed once daily and every other day/3 times per week, respectively.⁸⁻¹¹ Other patients, however, favor glatiramer acetate because they cannot tolerate the flu-like symptoms associated with IFN β products. Those who have very demanding schedules, for instance, may find these

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symptoms particularly bothersome and/or inconvenient. Additionally, patients who have difficulty affording treatment may be opposed to costly medications. Thus, it is important to consider all of these patient-specific issues when making therapeutic decisions.

In addition to administration and monitoring of drug therapy, comprehensive disease management also includes monitoring of disease progression via MRI and management of progression-related symptoms and breakthrough events. Pulse corticosteroids may be used to treat acute episodes,¹² whereas immunosuppressive medications (ie, natalizumab and mitoxantrone) are often used to manage treatment-resistant or progressive disease.^{12,13} It is important to note that these agents may have unfavorable toxicity profiles that necessitate considerable monitoring; specifically, natalizumab has been associated with progressive multifocal leukoencephalopathy,¹³ and mitoxantrone is known to cause myelosuppression and cardiotoxicity.¹⁴ Oral therapies (ie, cladribine, fingolimod, and laquinimod) are also on the horizon and may become available in the future.¹⁵

CASE STUDY (cont'd)

RE's pharmacist suggests that she be treated with glatiramer acetate, to avoid the flu-like symptoms commonly seen with the IFN β products. Although glatiramer acetate must be injected daily, RE lives at home with her parents and is confident that they can assist her with her therapy. What follow-up education should RE's pharmacist provide?

TREATMENT ALGORITHMS

Treatment algorithms can help clinicians make evidence-based therapeutic decisions and optimize patient outcomes. As illustrated in the Figure, patients who meet diagnostic criteria for MS should be given platform therapy with a first-line DMT. Patients who stop responding to treatment should be questioned regarding compliance, and testing for neutralizing antibodies should be considered. Alternative medications (ie, other first-line or second-line agents) should be considered in patients with recurrent exacerbations or disease progression.³

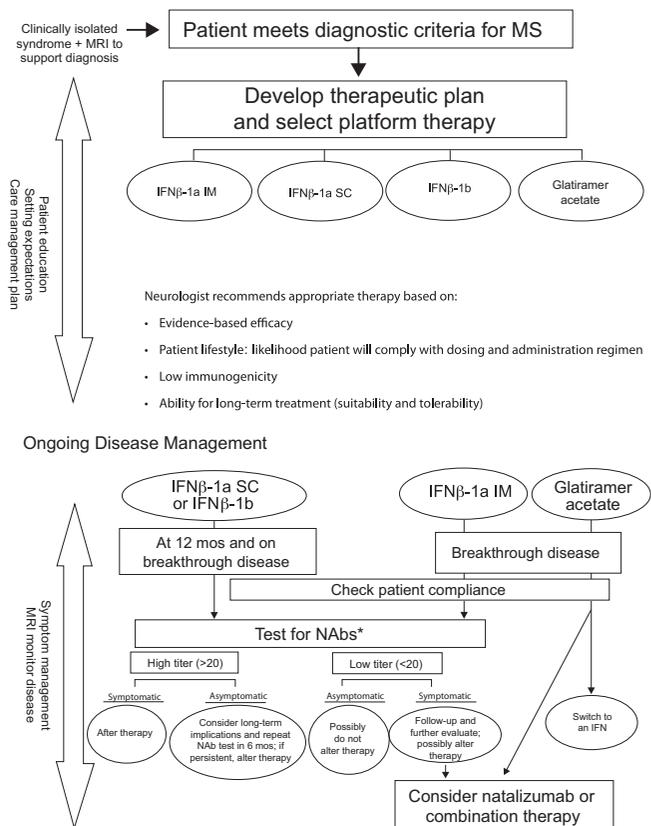
Dr Lipsy: Although treatment algorithms will continue to be used, the emergence of new therapies, and the potential for combination therapy, will introduce a wide range of treatment options; thus, these guidelines

may need to be individualized, based on patient-specific characteristics and presentation.

IMPORTANCE OF PATIENT EDUCATION

Many patients have a poor understanding of their disease state and may not realize that MS is a lifelong condition. Education is therefore crucial, and should focus on realistic expectations regarding drug therapy; specifically, patients must be made aware that their condition is incurable, but that treatment can help to reduce relapses and slow progression. Moreover, they must understand that DMT does not entirely eliminate MS symptoms or future disease activity, nor does it reverse existing damage to the CNS. Drug therapy is designed to delay disability progression, but is only

Figure. Treatment Algorithm for MS



*Wait at least 30 days after last steroid treatment if patient is being treated with steroids. IFN = interferon; IM = intramuscular; MRI = magnetic resonance imaging; MS = multiple sclerosis; NAb = neutralizing antibody; SC = subcutaneous. Adapted with permission from Rich et al. *J Manag Care Pharm.* 2004;10(3, suppl B): S26-S32.³

effective when taken appropriately. Unfortunately, data indicate that adherence rates are low, with 17% to 40% of patients discontinuing treatment within 1 year of initiation; this may be due to a perceived lack of efficacy, adverse effects, and/or depression.¹⁶⁻¹⁹ Education can help to improve adherence rates, thereby increasing therapeutic efficacy.

Dr Miravalle: Counting lesions is another powerful tool that may be used to improve patient compliance; if patients recognize that their lesions have accumulated over time, they may be more willing to take their medications. In addition, clinicians may use a bank account analogy to help patients understand the value of drug therapy. Just as people put money in the bank to improve their future economic status, they should adhere to medication therapy to improve their future health. Although the immediate results of drug therapy may not be evident, the long-term benefits are unmistakable.

CASE STUDY (cont'd)

RE's pharmacist informs her that the effects of drug therapy may not be seen immediately, but that adherence is necessary to delay disability progression. RE is satisfied, but would like to know if there is anyone else she could turn to for support, or to help her with medication access.

RECENT ISSUES OF CONCERN TO MANAGED CARE

Recent issues pertaining to managed care pharmacy and its impact on MS management include new healthcare legislation, the increasing use of specialty pharmacies, blood testing for β -interferon efficacy, the introduction of dalfampridine, and the approval of biosimilar products and generic formulations.

HEALTHCARE LEGISLATION

The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, along with the Health Care and Education Reconciliation Act, signed into law on March 30, 2010, are rulings that may significantly impact MS management. As of 2014, the recently enacted legislation will entitle everyone to health insurance, regardless of health or financial status. Thus, patients with high-cost disease states such as MS will be guaranteed coverage for MRI evaluations and drug therapy, which are often quite expensive. Moreover, insurers

will be prohibited from discriminating against or charging higher rates for individuals based on pre-existing medical conditions, thus patients with MS will be able to switch plans without difficulty. Additionally, the Medicare Part D coverage gap will be gradually reduced over the coming years; beginning with a 50% discount on all brand name drugs and biologics in 2011, the gap should be eliminated by 2020, making expensive drug therapy more affordable for patients.²⁰

The new legislation also includes more immediate components that may impact the MS population. Effective September 23, 2010, plans may no longer impose a lifetime cap on insurance coverage.²⁰ This largely affects patients with MS, whose disease management may cost up to \$30 000 to \$60 000 per year. In addition, dependents may remain on their parents' policy up until the age of 26,²⁰ which may be significant, given that many patients with MS develop the condition at a young age.²¹

SPECIALTY PHARMACIES

Specialty pharmacies, or pharmacies that help patients manage chronic conditions that require high-cost therapy or complex care/drug delivery, are designed to ensure that patients adhere to their prescribed regimens, to achieve an overall cost savings. Targeted disease states include cancer, hepatitis C, hemophilia, Crohn's disease, and MS, all of which require the ongoing administration of expensive, injectable drug therapy, as well as clinical support to ensure that the medications are used appropriately.²²

From the perspective of the patient with MS, specialty pharmacies can help to improve medication access, ease drug administration, assist with insurance coverage, and optimize therapeutic outcomes. By reaching out to patients, these pharmacies also can monitor and improve medication compliance. From the health plan's standpoint, specialty pharmacies can lower drug costs through negotiations, assure product access, and improve utilization management through the use of just-in-time delivery systems (ie, inventory systems that replenish and deliver products to the retailer just as the current supply is depleted), which reduce medication wastage. In addition, these pharmacies can increase physician and patient satisfaction, and optimize overall outcomes (Author communication, Medmark Specialty Pharmacy Solutions).

Dr Lipsy: Many newly emerging products require a REMS (Risk Evaluation Mitigation Strategy) to improve patient safety, and specialty pharmacies can help to ensure that these criteria are fulfilled. In addi-

tion, pharmacists should inform patients with MS who do not have access to specialty pharmacies that patient assistance programs also are available to help those in need (Table).²³

CASE STUDY (cont'd)

RE is told that she can visit a specialty pharmacy or contact the glatiramer acetate patient assistance program for more information and support.

BLOOD TESTING FOR EFFICACY

Research suggests that IFN β therapy, a \$6.1 billion annual expenditure, may not always be effective for the treatment of MS. Indeed, patients with high serum concentrations of interleukin (IL)-17 may not respond well to IFN β , whereas those whose disease is primarily driven by IL-1 tend to respond more favorably. Thus, a blood test measuring serum IL-1 and IL-17 may be used to determine the potential efficacy of IFN β , thereby enabling clinicians to individualize MS therapy. Pending further study, this test is likely to become a prerequisite for treatment.^{24,25}

INTRODUCTION OF DALFAMPRIDINE

Approved in January 2010, dalfampridine is the first medication designed to treat the symptoms of MS, as opposed to merely slowing disease progression. By blocking potassium channels and, consequently, enhancing neuronal conduction, this product improves walking speed and may improve walking distance in roughly 40% of patients with MS. Although dalfampridine costs approximately \$12 850 per year, a co-payment program limiting out-of-pocket expenses to \$40 per month has been instituted, where permitted by law. The medication is currently only available through a network of specialty pharmacy providers.^{26,27}

Dalfampridine is an oral agent, dosed at 10 mg twice daily. Associated with a risk of seizures, this product is contraindicated in patients with a prior history of seizures, as well as those with moderate-to-severe renal impairment.^{26,27} From a managed care perspective, a walking test should be conducted to determine which patients qualify for treatment, and a trial of drug therapy should then be provided. Additionally, it is important to ensure that the special-

Table. MS Patient Assistance Programs

Product	Company	Program	Description	More Information
IFN β -1b SC (Betaseron)	Bayer, Inc	Patient Assistance Program	Financial assistance program for those unable to gain access to therapy	www.needymeds.org
IFN β -1a IM (Avonex) Natalizumab (Tysabri)	Biogen Idec	Access Program	Financial assistance program for patients using IFN β -1a IM or natalizumab	www.AVONEX.com www.TYSABRI.com
IFN β -1a SC (Rebif)	EMD Serono, Inc and Pfizer Inc	MS Lifelines Access Made Simple Patient Assistance Program	For those newly prescribed IFN β -1a SC or who have restarted IFN β -1a SC therapy For those covered under Medicare Part D or with private or no insurance	www.msllifelines.com or 1-877-44-REBIF
IFN β -1b SC (Extavia)	Novartis Pharmaceuticals Corporation	Patient Support Program	Financial assistance for patients who cannot afford the cost of IFN β -1b SC treatment and have no private or public insurance coverage	1-866-925-2333
Glatiramer acetate (Copaxone)	Teva Neuroscience	Patient Assistance Program	A co-pay assistance program; also assistance for Medicare Part D and free product	1-800-887-8100

IFN = interferon; IM = intramuscular; MS = multiple sclerosis; SC = subcutaneous.

Adapted with permission from National Multiple Sclerosis Society. Patient assistance programs. Available at: <http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/adherence/patient-assistance-programs/index.aspx>. Accessed May 27, 2010.²³

ty pharmacy the patient chooses falls within the managed care organization's network. Finally, the cost of using this medication should be justified by its potential benefits.

Dr Guthrie: It is also important to make sure the medication is being used to improve walking, rather than for off-label uses such as heat intolerance or spinal cord disease.

APPROVAL OF BIOSIMILARS/GENERIC

When considering biosimilar products (ie, products with the same formulation, marketed by different pharmaceutical companies) or generic drug equivalents, it is essential that patients with MS be educated about the clinical implications associated with switching medications. Additionally, the potential for cost savings should always be evaluated when making therapeutic interchanges.

CONCLUSIONS

Multiple sclerosis is a chronic disease that requires ongoing drug therapy to delay disability progression. When making treatment decisions, it is important to consider patient-specific factors such as lifestyle, financial status, degree of support from friends and family, and tolerance to adverse effects. Although algorithms have been designed to guide treatment, management should be individualized to meet patients' needs, and patients should be educated on the importance of adhering to drug therapy. From a managed care perspective, new healthcare legislation and specialty pharmacies have improved access to medications, and are expected to optimize patient outcomes. Blood testing for β -interferon efficacy may help to improve and guide treatment in patients with MS, and the introduction of dalfampridine may lessen symptoms in qualifying individuals, allowing them to lead a more active lifestyle.

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