

# Managed Care Aspects of Managing Multiple Sclerosis

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**M**ultiple sclerosis (MS) is a disease of the central nervous system that is diagnosed in 2 to 3 times as many women as men, most of whom are between the ages of 20 and 50 years.<sup>1,2</sup> Because MS is characterized by inflammation and breakdown of the protective insulation surrounding nerve fibers (myelin), signals from within the brain and between the brain and body are disrupted, resulting in a variety of debilitating symptoms.<sup>3</sup> Not only does MS degrade patient health-related quality of life (HRQoL),<sup>4-6</sup> but the condition is also associated with a high economic burden for individuals, healthcare systems, and society.<sup>7-10</sup> The overall burden of MS is substantial due to its early age of onset and its incurable, generally non-terminal nature, which necessitates lifelong treatment.

Payers have witnessed a rapid evolution of therapeutic treatment options for MS in recent years, as well as an increase in treatment costs over that time.<sup>5</sup> Their clients, such as employers, have also experienced a significant rise in costs for patients with MS, and are asking payers to “justify” these growing expenses.<sup>8</sup> Therefore, the treatment of MS is closely evaluated by payers, and as such, their needs for appropriately treating this illness include strategies that are population based, such as guidelines for the optimal management of patients that can be used in clinical and formulary management decision making, and methodologies to determine which agents will work effectively on individual patients from both the clinical and cost standpoints.

## The Burden of Multiple Sclerosis

Managed care professionals and organizations must take into account that MS and its symptoms are associated with substantial personal, professional, and economic burdens. There are 4 subtypes of MS: (1) relapse-remitting (RRMS), (2) primary-progressive, (3) secondary-progressive (SPMS), and (4) progressive-relapsing (PRMS).<sup>11</sup> The relapsing form of MS is the most commonly diagnosed form of MS and is marked by flare-ups, referred to as relapses or exacerbations, which are characterized by episodes of acute worsening of neurologic function.<sup>2,11</sup> These flare-ups are followed by partial or complete recovery periods, referred to as remissions, that occur between attacks and are free of disease progression.<sup>11</sup> Of the remaining subtypes of MS, SPMS and PRMS have unpredictable relapses and can result in a steady worsening and progression of the disease course, with approximately 50% and 90% of patients

## Abstract

Multiple sclerosis (MS) is a chronic disease of the central nervous system usually diagnosed in the second or third decade of life; MS is more common among women than men by a ratio of 3 to 1. With its relatively early age of onset and symptoms that impair patients' quality of life, MS requires lifelong, dynamic treatment, and places a substantial economic burden on individuals, healthcare systems, and society. The costs associated with providing benefits for MS therapy are growing rapidly and the increasing complexity of the MS market is impacting disease management for payers. Employers are also increasingly aware of the costs associated with MS and are asking health plans to advise on the most appropriate and cost-effective ways to manage both pharmacologic and non-pharmacologic therapies for MS. Health plans, by necessity, must therefore balance appropriate access to treatments for MS with the need to manage rising treatment costs. To meet this goal, payers require population-based solutions, guidelines, and treatment algorithms for the management of MS that can be used in clinical and formulary management decision making in the context of an evolving therapeutic landscape. Further, comparative studies are necessary for payers to determine which agents may work best on a population basis. Due to the current lack of appropriate clinical guidance and insufficient head-to-head data on disease-modifying drugs, strategies for health plans and clinical management have been designed using the best available evidence. Undoubtedly, management of this class will continue to evolve with the launch of newer agents.

*(Am J Manag Care. 2013;19(16):S307-S312)*

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afflicted by RRMS progressing to SPMS after 10 years and 25 years, respectively.<sup>11</sup> The very nature of MS makes the disease not only quite costly but also detrimental to patient HRQoL due to significant negative impact on physical functioning, vitality, and general health.<sup>4,7-10</sup> Therefore, it is incumbent upon both managed care and healthcare authorities to develop effective strategies that increase patient HRQoL as well as reduce costs.

A decade ago, the average cost per patient in the United States who required hospitalization to manage the characteristic relapses of MS was \$12,870 (in 2002 dollars).<sup>7</sup> Subsequent US-based studies have reported similar if not greater total average annual costs for patients with MS, which were largely attributable to the high cost of prescription medications.<sup>8-10</sup> Additionally, the results of the recently published MS Benchmarks Analysis revealed that the cost burden of MS varied according to the types of comorbidities and complications associated with MS such that costs (in 2009 dollars) were highest for those patients with ataxia (\$31,483), followed by abnormality of gait (\$31,175), muscle weakness (\$29,104), spasms (\$28,843), urinary incontinence (\$28,561), and optic neuritis (\$28,353).<sup>10</sup> It should be noted that disease-modifying drugs (DMDs) accounted for 95% of the total annual pharmacy costs per patient, and 69% of the total costs for managing MS.<sup>10</sup> Furthermore, 2 studies have reported a relationship between disease severity, impairments in HRQoL, and economic burden such that reductions in quality-adjusted life-years translated to estimated intangible costs that ranged from \$7000 to \$15,315 per patient, respectively.<sup>5,6</sup>

MS also places a high burden on occupational factors that affect patients, employers, and society as a whole. The results of several longitudinal studies have demonstrated that MS is tied to high unemployment rates, such that only 40% to 70% of persons with MS remain employed.<sup>6,12-15</sup> Even for those patients who maintain employment, the impact of absenteeism and its consequences has been found to be quite high. The results of one study published in 2009 determined that, depending on the agent used for treatment, the annual number of days of sick leave used by employees with MS ranged from 2.98 to 8.13 days, with combined sick leave and short-term disability times ranging from 7.33 to 20.67 days, and costs associated with sick leave ranging from \$523 to \$1431 (inflation-adjusted to 2007 dollars).<sup>16</sup> It is interesting to note that treatment may affect these outcomes. In a study of employees with untreated MS versus individuals who had at least 1 DMD claim, the risk-adjusted total annual medical and indirect costs were \$6187 versus \$4393 and \$3053 versus \$2252, respectively, with expenditures for treated employees found to be significantly lower ( $P < .0001$  for both compar-

isons).<sup>17</sup> Lastly, those responsible for providing care to patients with MS, such as parents, grandparents, spouses/partners, and other household members, may also experience a substantial negative impact on their own HRQoL due to spillover disutility and other collateral consequences.<sup>18</sup>

### Medical and Pharmacy Cost Trends and the Employer Perspective

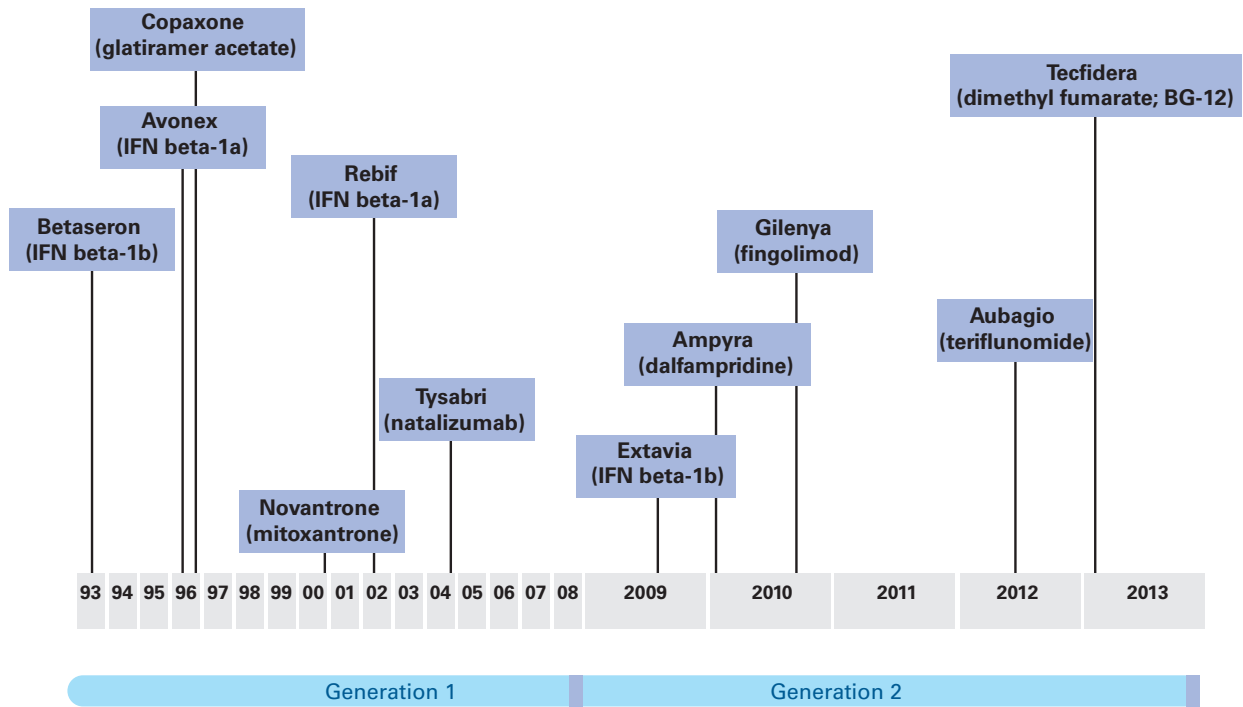
In 2012, 4 specialty classes accounted for over 75% of spend for specialty drugs: (1) inflammatory conditions, (2) MS, (3) cancer, and (4) human immunodeficiency virus.<sup>19</sup> Moreover, in recent years, the healthcare and managed care communities have witnessed a progressive shift in spend away from medical benefits and toward pharmacy benefits, especially for newer oral agents that treat cancer or manage MS. Specialty pharmacy is the largest driver of cost increases for pharmacy in 2013,<sup>19</sup> and based on pharmacy reports, employers are witnessing an undeniable growth of specialty pharmaceutical costs.

According to a report prepared by Express Scripts, Inc, the average cost per prescription for an MS agent for an employer is \$3583.<sup>19</sup> Further, drugs for the treatment of MS accounted for almost \$38 in per member per year (PMPY) drug spend during 2012.<sup>19</sup> In a plan of 1 million members, that equates to an increased drug spend of approximately \$38 million for the management of MS alone. In 2012, PMPY spend for MS grew 17.9% to \$8.09, and with the introduction of 2 new oral agents for MS into the therapeutic market in 2012 and 2013, as well as an ever-growing drug pipeline, this figure is expected to increase further.<sup>19</sup> Unfortunately, despite the detrimental clinical consequences of inappropriately managed MS and the high costs associated with the disease, an estimated 26.3% of patients with MS remain nonadherent to their therapies,<sup>19</sup> which highlights the irrefutable need to address educational gaps and to improve current strategies in the managed care and healthcare arenas.

### The Current Therapeutic Landscape and the Health Plan Perspective for MS

The first agent for MS approved by the US Food and Drug Administration (FDA) was made available in 1993 and was quickly followed by the addition of 5 more agents (Figure 1).<sup>20-25</sup> Between 2005 and 2008, no additional agents were approved by the FDA, but between 2009 and 2013, the number of FDA-approved agents available to treat MS has nearly doubled.<sup>26-30</sup> One of the more profound differences between the first and second generations of approved agents for MS was the introduction of medications that could be administered orally. Prior to 2010 and before oral agents

■ **Figure 1.** Timeline Depicting the FDA Approval of DMDs and Other Agents for the Management of MS<sup>20-30</sup>



DMD indicates disease-modifying drug; FDA, US Food and Drug Administration; IFN, interferon; MS, multiple sclerosis. Several new agents have been approved since 2009, expanding the therapeutic armamentarium but challenging health plan developers and pharmacy and therapeutics committees.

for MS were available, clinicians and their patients could only select injectable first-line treatments from among the 3 available interferon-beta formulations (IFNs) and glatiramer acetate (GA).<sup>20-22,24,31</sup>

Improving clinical outcomes and QOL for patients with MS is a top priority for health plans. However, with the introduction of newer therapies, health plan decision makers are faced with growing complexity in the MS space. Already, the management of MS may require the use of several agents of various drug classes to combat comorbid conditions and complications, including agents for the management of migraine, antidepressants, narcotic analgesics, corticosteroids, antispasmodic agents, anticonvulsants, nonsteroidal anti-inflammatory drugs, and benzodiazepines.<sup>10</sup> Current health plan strategies for managing the optimal utilization of agents for MS include: (1) prior authorizations (PAs) that account for the appropriateness of the medication, the setting of care, and the duration of therapy; (2) initial clinical management with 1 or more preferred first-line agents; (3) the use of online “step edits” to automate clinical management; (4) case/therapy management for which patient compliance is of particular importance; (5) cost-effectiveness analysis, which is still a process in development; (6) benefit

designs with cost sharing by the beneficiary; and (7) risk evaluation and management programs.

Health plans are also sensitive to the needs of employers to attract and maintain a productive workforce. Although treatment guidelines for MS have been put forth by several institutions and organizations, these guidelines are not necessarily beneficial for developing a health plan’s clinical management program. Health plans need to consider important clinical issues by asking the right questions, examples of which can be found in the **Table**. When faced with the paucity of head-to-head comparative trials, those responsible for developing clinical management programs must rely on current clinical management strategies. Clinical algorithms may be considered more helpful when developing these clinical management programs, as guidelines tend to provide general statements or overviews of concepts, but algorithms will contain details and specific instructions for individual clinical decisions.<sup>32</sup>

One recent study was conducted in an effort to develop a uniform set of payer guidelines.<sup>33</sup> The study involved 14 panel members who were experts in managed care, 8 of whom were pharmacy directors and 6 were medical directors, representing 12 US health plans, 1 specialty pharmacy, and

**Table. Questions Regarding Important Clinical Issues Considered by Health Plans**

Who should be considered appropriate prescribers?
Is there a difference between new prescriptions and renewals?
Are there guidelines that can be used as the basis for clinical management?
What will the role in therapy be for the newer oral and infusion agents?
Are the IFNs approved prior to 2009 and GA still first-line treatments?
Can I have a preferred IFN?
When is it appropriate to switch therapy to another agent?
What is the role of the intravenous agents in therapy?
Are there patients who should not be started on an IFN approved prior to 2009 or GA?
How do we evaluate when a therapy is no longer effective?
GA indicates glatiramer acetate; IFN, interferon.

1 consulting company. All of the panelists were presently or previously involved in the formulary decision making process at their organizations. The panelists participated in 2 rounds of web-based questionnaires, with the first consisting of mostly open-ended questions and the second consisting of mostly closed-ended questions, before gathering for a live consensus meeting. A “consensus” was defined as a mean response of at least 3.3 or 100% of responses being either “agree” or “strongly agree” using a 4-item Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree). After 3 phases, the panelists reached consensus on 25 statements, which included<sup>33</sup>:

- The initiation of DMD therapy for patients with clinically isolated syndrome is a provider decision, but most patients with clinically definite MS should be treated with a DMD
- Both GA and a preferred IFN should be on a health plan’s formulary
- Patients with MS should have preferred access to platform therapies
- Access to non-preferred IFNs should be restricted by step therapy or the use of a preferred agent first
- Health plans should have a preferred high-dose/high-frequency IFN on formulary, but should take efficacy, safety, cost, and contracting into consideration when selecting the preferred high-dose/high-frequency IFN
- Access to natalizumab should be limited to use for the FDA-approved indication
- Access to fingolimod in combination with injectable DMDs should be limited until additional safety information is available
- Payers should identify the need for patient compliance and support while on DMDs

When considering the role of pharmacy and therapeutics (P&T) committees in health plans, institutions, and hospital systems, it is important to define a few common terms. A formulary is a continuously updated list of medications and related information that represents the clinical judgment of physicians, pharmacists, and other experts in the diagnosis, prophylaxis, and/or treatment of disease and promotion of health.<sup>34</sup> A formulary system is an ongoing process through which healthcare organizations establish policies regarding the prudent use of drugs, therapies, and drug-related products, and identify the agents that are most clinically appropriate and cost-effective to best serve the health interests of a given patient population. The P&T committee is responsible for managing the formulary system, and typically comprises plan medical directors, pharmacy directors, pharmacy staff, actively practicing physicians, and other healthcare professionals and staff who participate in the medication use process. Further, the P&T committee bases its decisions on 3 core principles: (1) safety; (2) efficacy; and (3) cost/value.<sup>34</sup> Generally, P&T committees will focus on the issues concerning safety and efficacy, and decisions can be categorized as clinically superior, clinically equivalent, or clinically inferior. Prior to 2009, all of the agents for MS were featured on many payers’ formularies and were readily available, with clinical management strategies typically consisting of a PA to verify RRMS and the prescribing physician. The addition of the newer agents since 2009 has introduced further complexity into the P&T decision-making process, and now those committees are looking to support their healthcare decisions with more relevant data. In the absence of adequate comparative data and clinical trials, committees are seeking to balance safety, efficacy, and the burden of therapy as one way of managing the MS formulary (Figure 2).

It is important to note that as benefits in a health plan are altered, patient and provider access will also change accordingly. Many plans have evolved from a typical 3-tier formulary (ie, generic, formulary, non-formulary) to a 4- or more-tier formulary (ie, generic, preferred branded, non-preferred branded, specialty).<sup>35,36</sup> Specialty drugs have varying definitions, but often, cost (>\$600/month) is an important determining factor in its placement on a formulary tier.<sup>37</sup> Drugs in the specialty tier will generally have higher patient out-of-pocket (OOP) costs and are usually coinsurance based. Newer benefit designs have increased member cost share through deductibles and coinsurance. Further, coinsurance tiers may or may not have a cap or maximum

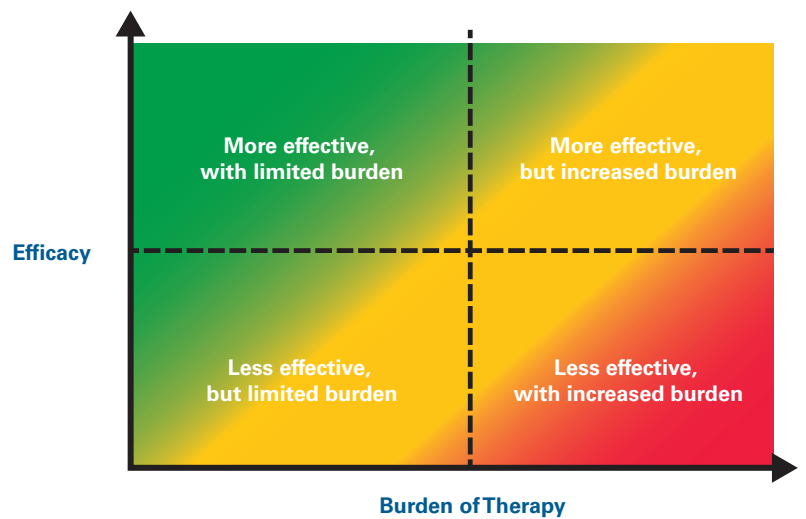
OOP limit, depending on the benefit design that is purchased by the client or beneficiary. It is important to remember that patients with MS will require lifelong therapy. Unfortunately, member cost-sharing practices, such as the absence of a cap on OOP expenses, may limit patient access to necessary treatments and create a substantial cost liability. A recent study showed that adherence to therapy is likely to decrease as member OOP costs increase, such that a 10% increase in cost sharing leads to an 8.6% decline in adherence.<sup>38</sup>

### Summary

The cost of providing health plan benefits and insurance coverage for MS therapy is one of the fastest growing sectors of healthcare spending today. The increasing complexity of the MS market is accompanied by increasing complexity for payers. Employers are aware of the rapidly growing costs of DMDs distributed through specialty pharmacies and have requested the development of actionable plans that put forth comprehensive management strategies. These plans must balance appropriate access to treatments for MS with the need to manage the high price tag of the therapeutic category. As management strategies for MS evolve, payers are constantly seeking population-based solutions to manage the disease.

As noted in articles 1 and 2 in this supplement,<sup>39,40</sup> optimal therapies for MS must be tailored to individual patients, and current treatment guidelines maintain an essential role in managing initial treatment decisions and switches in therapies when needed. However, during a time in which the therapeutic environment and drug pipeline for MS is rapidly evolving, further research and application of prognostic indicators and treatment biomarkers in clinical practice will provide the necessary guidance and insight to formulate standardized treatment algorithms for MS and drive best practices that correlate with the dynamic picture of MS. Further, improved comparative studies will allow payers to differentiate agents from within the same drug class and to determine, on a population basis, which agents will work best for whom, under which circumstances, and the most cost-effectively, thus driving improved treatment efficacy, safety, adherence, and ultimately, reduced overall costs. As the clinical landscape for MS continues to expand and grow in complexity, the managed care arena must adapt accordingly and promote the prudent utilization of costly therapeutic

■ **Figure 2.** Potential P&T Scenario for the Management of MS



MS indicates multiple sclerosis; P&T, pharmacy and therapeutics.

Factors affecting the burden of therapy include convenience, monitoring, tolerability, and safety.

agents to achieve optimal clinical and economic outcomes for both patients and providers.

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**Funding source:** This activity is supported by educational grants from Bayer HealthCare Pharmaceuticals; Biogen Idec; EMD Serono, Inc; Genzyme Corporation; and Questcor Pharmaceuticals, Inc.

**Author disclosure:** Dr Owens reports serving as a consultant/paid advisory board member for Biogen Idec, Genzyme Corporation, and Novartis. He also reports meeting/conference attendance sponsored by Biogen Idec and Genzyme Corporation.

**Authorship information:** Concept and design; critical revision of the manuscript for important intellectual content; administrative/technical support; and supervision.

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