

The Multiple Sclerosis Trend Report: Perspectives from Managed Care, Providers, and Patients

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To Our Healthcare Colleagues:

Teva Neuroscience and the National Multiple Sclerosis Society are pleased to present the *Multiple Sclerosis Trend Report: Perspectives from Managed Care, Providers, and Patients* as part of our ongoing efforts to inform those who live with MS and those who play key roles in diagnosing and treating it — including neurologists, nurses and case managers, managed care organizations, and specialty pharmacists.

It is the intent of Teva Neuroscience — in partnership with the National Multiple Sclerosis Society — to increase awareness and understanding of multiple sclerosis, and in so doing to improve treatment for patients with MS. Physicians, case managers, patients, and managed care organizations generously shared their time and their reflections in responding to the surveys summarized in this report. We anticipate that the candid responses provided by these respondents will lead to productive dialogue among all those who live with, treat, and finance the treatment of MS.

Today, more than 400,000 Americans face the prospect of losing functionality through the physical, cognitive, and psychological limitations caused by MS. Ongoing research affords the hope, and the sustainable expectation, that making the right choices for individual patients will help maximize the effective management of this disease.

The ability of the healthcare industry to stay current with new advances and new discoveries in the treatment of MS will lead to improved quality of life for patients with MS. In partnership with all who are working toward that goal, we look forward to the day when the medical community can declare that MS has been cured.

Special thanks go to all the survey participants whose efforts made this report possible. We welcome readers to share with us any thoughts this report may generate, and, alongside all who are assisting patients with MS and working toward a cure, we assure you that we will continue to support the treatment of patients who are facing the challenges of living with multiple sclerosis.

Sincerely,

Brendan O'Grady
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The Multiple Sclerosis Trend Report

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Executive Summary

Multiple sclerosis is a chronic disease of unknown origin that attacks the central nervous system — specifically, the brain and spinal cord. The course of MS, and its severity and symptoms, vary from person to person and are unpredictable. Symptoms may include numbness, weakness, spasticity, visual disturbances, cognitive changes, and bladder and bowel dysfunction, among others. The diagnosing of MS is complicated: symptoms may come and go; other diseases may mimic the symptoms of MS; and no single laboratory test can confirm the diagnosis.

The first medication approved by the FDA to affect the course of MS entered the market in 1993. Now there are a total of six MS agents, including two infused and four injectable. Numerous MS clinical trials are under way, including assessments of new classes of immunomodulatory therapies.

The Multiple Sclerosis Trend Report: Perspectives from Managed Care, Providers, and Patients

The National Multiple Sclerosis Society, in conjunction with a group of managed healthcare professionals, physicians, and academicians, developed several survey instruments in the spring of 2006 to research current issues in the care of multiple sclerosis patients, and to assess trends in the management of MS. The research surveys were distributed to managed care organizations; neurologists; those responsible for reimbursement, billing, and coding; specialty pharmacy companies; case managers; and MS patients themselves.

MANAGED CARE ORGANIZATIONS

The questions designed for MCOs targeted trends in managing treatment for MS. Eighty-two managed care executives participated in the research.

- More than two-thirds of the research respondents agreed or strongly agreed that a disease management program for MS patients improves outcomes and adherence, reduces disability, and contains costs; and further, that such a program could help to better identify the size and characteristics of the MS population in health plans
- Expanding the use of case management and disease management programs for MS could make the products offered by health plans more attractive to customers
- Of the MCOs that participated in the research, 90% currently contract with specialty pharmacies and 79% indicated that their members with MS will be required or encouraged to use a specialty pharmacy to obtain injectable drugs within the next two years
- Insurers tightly control — through prior authorization and moratoriums — new molecular entities, especially those in competitive categories or those whose use is largely off-label

- While biologics show promise and their use continues to increase, cost control for these products remains a concern
- As new MS drugs are introduced, insurers will be faced with the challenge of determining the cost benefit of drugs that may be more expensive than current drugs but also more effective
- Nearly all MCOs have formularies, mostly tiered models that allow some choice while designed to control costs and unnecessary utilization
- Sixty-seven percent of respondents reported that ensuring appropriate utilization of the drug in question is the most important objective of prior authorization requirements for biologic or injectable therapies
- Numerous strategies — including higher cost sharing with the patient, increased use of preferred categories, differential prior authorization rules to encourage the use of specific drugs, and delayed acceptance of new products — are in use, or under consideration, for managing biologic and other new classes of drugs

NEUROLOGISTS

The neurologists' survey research was based on the participation of 143 general neurologists and MS specialists currently in practice. It considered the provision of MS healthcare, including difficulties involved in diagnosis and treatment, reimbursement, the management of MS symptoms, and the use of disease-modifying therapies.

- Nearly two-thirds of the respondents said that insurance barriers interfere with their ability to diagnose and treat MS patients
- Many emphasized the need for more communication between insurers and practitioners, such as a panel of experts to consult with medical directors about new FDA-approved medications, agents for symptom management, the use of off-label prescriptions, and ancillary care such as physical therapy
- Neurologists would also welcome an increased role by specialty pharmacies in

the management of MS patients because of the numerous biologic and other MS drugs and symptomatic therapies on the market or in development

- Depression, including its causes and treatment, proved of particular concern, and neurologists felt that specialty-pharmacy case managers could help with self-assessment and screening tools for depression
- In addition, it was felt that specialty pharmacy programs could help ease neurologists' work load, which averages 48 hours of clinical practice and five hours of administrative work per week. Nearly two hours per week are devoted to reimbursement issues, and 74% of the respondents said they have had to hire additional staff to handle prior authorizations or payment issues
- More than two-thirds (70%) of the respondents reported that insurers at least sometimes try to restrict the use of infused disease-modifying drugs
- Neurologists combat these difficulties by acting as patient advocates, appealing claims decisions, and utilizing other, reimbursable treatments; a few respondents indicated that when they encounter difficulties, they refer patients to colleagues
- Results clearly show the desire of most neurologists to effectively care for their MS patients, despite the amount of time and other obstacles involved
- Finally, results indicate ample opportunity for insurers to assist neurologists with continuing education, and that the addition of insurer-supplied educational articles would enhance the value of an insurer's contract and prove an effective tool for keeping both doctors and medical directors on the cutting edge of MS treatment

NEUROLOGY REIMBURSEMENT AND CODING

This segment of the research canvassed 68 coding and reimbursement staff from doctors' offices.

- A key finding is that neurologists' offices would greatly benefit from more direct lines of communication with managed care organizations
- Respondents also desire consistency in explanations of claims denials; more accurate and timely dissemination of information on the telephone with insurance staff; and greater knowledge on the part of insurers of the differences between injectable and infusible MS disease-modifying agents and of the positive effects of symptomatic therapies
- Respondents thought that simplifying claims processing and easing the administrative time demands of those involved in treating MS patients will lead to better quality care
- Nearly 60% of the respondents remain on hold for 15 minutes or longer when contacting their insurer by telephone; another 10% never get through to a live customer service representative; and 19% must leave a message every time they place a call
- Treating MS patients is a labor-intensive activity, according both to doctors and their office staff
- Most practices (79%) do not use a billing service; 54% of the respondents maintain solo neurology practices, while 46% practice in a group setting
- Although nearly 60% of respondents said most of their contracts with MCOs are profitable, almost 30% said they are not
- Recent improvements in reimbursements have speeded claims payments and increased their accuracy, but there is room for improvement in communication between practices and MCOs
- Sorting out inconsistencies in claims payments, getting insurers to locate paper claims they have lost or misplaced, and obtaining straightforward and consistent answers to questions from MCOs are the most time-consuming issues related to billing and coding for MS patients
- Easier access to information, quick and simple answers to questions, and better access to customer representatives would improve profitability for providers
- Close to two-thirds of respondents (60%) indicated that managed care organizations should increase payment for procedures such as nerve conduction studies, while almost 30% believe insurers should increase payment for patient evaluation and treatment visits
- According to the neurologists surveyed, half of all insurers routinely ask for prior authorizations for non-drug-related therapies, and more than half (54%) require prior authorizations for drug therapies; moreover, despite the high rate of these requests, non-drug-related therapies are denied only 13% of the time, while drug therapy requests are turned down in 12% of cases, calling into question the need for and cost-effectiveness of such measures both for MCOs and for doctors

SPECIALTY PHARMACY

Owing to the current consolidation in this industry, the research sample consisted of 19 respondents. Professionals in the specialty pharmacy sector addressed questions on the management and distribution of MS drug therapies. While the results provide some pertinent insights, the small sample size precluded the ability to draw definitive conclusions.

- The role of specialty pharmacies in the management of MS is evolving as a potentially important one, because these companies have the potential to influence patient adherence, provide patient education, and improve the management of MS
- Because MS is not a highly prevalent disease, less than 10% of MCOs have fully developed MS disease management programs; however, given the national reach of most specialty pharmacies, the further development of disease management programs could benefit a significant portion of MS patients in the United States

- Ninety percent of responding MCOs currently maintain contracts with a specialty pharmacy for the distribution of MS injectables; moreover, two-thirds of participating neurologists indicated they would welcome a specialty pharmacy program that would assist in the management and treatment of patients with MS
 - Within specialty pharmacies, contact with MS patients is routine; 58% of the respondents said their organization contacts patients with MS every few weeks or every week, a rate similar to contact frequency for other diseases
 - The matters most frequently discussed between specialty pharmacies and patients with MS include medication usage (84%), side effects (79%), reimbursement (53%), disease symptoms (53%), and shipment issues (47%); interestingly, respondents indicated that patients discuss formulary issues only about 10% of the time
 - Specialty pharmacies said they put a significant amount of effort into patient education; 42% of responding pharmacies now offer web-based education in addition to traditional phone-based assistance
 - Most respondents (95%) said they believe many specialty pharmacies can add value to and enhance the ways in which MS specialists and neurologists deliver care to MS patients
 - Nearly half (47%) of the respondents reported that their pharmacy contracts directly with MS drug manufacturers, and all of those surveyed said they are capable of filling the entire line of MS drug therapies
 - In addition, specialty pharmacies offer prior authorization assistance, coordination of benefits from multiple payers, indigent patient programs, overnight medication delivery, patient education, reimbursement assistance, patient care coordination services, 24/7 patient support, and nursing support
- nurses. Questions were designed to assess the expertise, opinions, and typical practices of case managers involved in the care of MS patients. The respondents represented a wide range of practice settings, including MCOs and rehabilitation, acute care, and ambulatory care facilities. Many MCOs, in an effort to balance quality of care and cost, use case managers to evaluate the treatment needs of MS patients and to coordinate their care.
- Nearly 88% of respondents reported more than 15 years of clinical experience, and 87% worked in a case management setting for at least six years; more than three-quarters are certified in case management
 - Close to two-thirds (62%) of the case manager respondents practice in a health insurance or MCO setting
 - The primary mode of contact with patients for 63% is the telephone, while 31% reported that onsite contact with patients constitutes the main part of their practice
 - Most (97%) respondents “actively” manage MS patients — management is considered “active” if there is a callback or visit schedule; once stabilized, patients are often placed on an “inactive” status, in which they are still eligible for case management services but calls and visits are not scheduled unless needed
 - Close to 40% of the respondents reported 15 or more years of experience in managing MS
 - Approximately 39% of the respondents work in partnership with specialty pharmacies
 - Respondents reported that communication with MS patients occurs most frequently during the first three months of establishing contact and that this contact tends to decrease to once or twice a month thereafter
 - Respondents view their role in patient care as one of advocacy; they focus, therefore, on improving care and helping patients deal with MS symptoms rather than acting as gatekeepers for healthcare
 - Case managers said their most challenging issue in working with MS patients is adherence to treatment; other important

CASE MANAGERS

More than 75% of the 101 case managers who participated in the survey research are registered

concerns they help patients manage are emotions, fatigue, costs of medications, cognitive changes, transportation, and limitations in activities of daily living

- One of the most important services that case managers provide patients with MS is teaching, especially around the challenges of dealing with everyday activities
- Respondents expressed the need to enhance the availability of several case management tools, including education about MS — particularly patient-focused educational materials — and standards for quality of care, especially in relation to outcomes

PATIENTS

The patient survey research involved 1,935 persons with MS and focused on the diagnosis and treatment of MS, quality of life for MS patients, and insurance issues.

- More than 90% of respondents rely fairly heavily on their neurologist for treatment, assistance in obtaining medications, support, and education about their disease; therefore, the more that managed care organizations understand MS, the greater will be their ability to keep neurologists and their patients educated about the most up-to-the-minute research and information pertaining to MS
- Such education should help provide patients with access to more consistent and informed care and in turn should reduce costs for MCOs
- General neurologists diagnosed nearly two-thirds of respondents (63%), and MS specialists diagnosed more than a quarter of these patients (28%); the rest of the respondents (9%) received a diagnosis from an assortment of other medical practitioners, including family doctors and internists, ophthalmologists, neurosurgeons, and radiologists
- Just over half of the surveyed patients choose to be treated by general neurologists, and 38% by MS specialists
- Diagnosing MS more quickly and starting treatment as soon as possible could reduce costs for MCOs in the long run, since these changes could help to delay progression of the disease as well as its impact
- Sixty-four percent of patients in need of home care have it available to them in the form of hired help, a family member or a relative, a friend, or some other source; other sources include a nursing home, self-help, an assisted living facility, and state or federal services such as Meals on Wheels and hospice
- More than two-thirds (68%) of the patient respondents expressed satisfaction with their insurance coverage; many cited comprehensive coverage, overall affordability, and relatively low co-pays for expensive MS drug therapies as the major reasons for their satisfaction
- The remainder agreed that denials of prescribed drugs and the ensuing time-consuming appeals, the need for referrals to specialists, lack of patient information specifically related to MS, ignorance on the part of insurers about the differences between MS disease-modifying agents (particularly infusible drug therapies) and drugs that treat MS-related symptoms all translate into the message that the managed care industry — as a whole — does not fully understand MS as a potentially life-changing, chronic disease, and therefore does not allow doctors to treat it appropriately
- Many MS patients would welcome the development of a disease management program, and many of those surveyed enjoy the benefits of such programs already and cite their availability as a reason for satisfaction with their insurer; in contrast, many of the respondents cited dissatisfaction with their insurer owing to the lack of services offered by such programs
- The adage “knowledge is power” applies well to living with MS; those who have regular contact with MS patients and who can provide such knowledge are in a position to help patients diminish their symptoms and slow the progression of their disease



Managed Care Community

The task of managed care is to add value to the healthcare delivery system. Originally this meant reducing unnecessary hospitalizations, securing bulk purchase discounts, and improving care for common chronic diseases. Now that many of these commonly occurring diseases have mature management programs in place, managed care has started to focus on devastating but rarer diseases. This section of the report addresses current trends in managed care that affect the diagnosis and treatment of multiple sclerosis.

OVERVIEW

Of the 82 survey respondents, HMO/PPO medical directors comprised 28%, and HMO/PPO pharmacy directors accounted for an equal number. Clinical pharmacists totaled 22% of respondents, and the remaining 22% included managed care executives, managers of injectable drugs, pharmacy benefit management executives, and quality assurance staff members (Figure 1).

Close to 60% of the respondents hold advanced degrees, including MD (26%) and PharmD (32%); many also have a BS in pharmacy. The respondents have worked in the managed healthcare field for an average of 10 years, and have worked at their current positions for an average of five years.

Nearly three-quarters of the plans surveyed (71%) cover more than 100,000 lives, and 23% of these plans offer coverage to more than one million individuals (Figure 2).

HMO products cover more than half of the lives (51%) represented. PPO products account for 27% of members, and the remaining 22% subscribe to various other products, among them Medicare, Medicaid, and other government-sponsored plans; point of service (POS) plans; and exclusive provider organization (EPO) plans.

Approximately one-third of the respondents (32%) indicated that their plans are primarily Midwest-based, although plans from all geographic regions of the United States were represented.

Figure 1. You are . . .

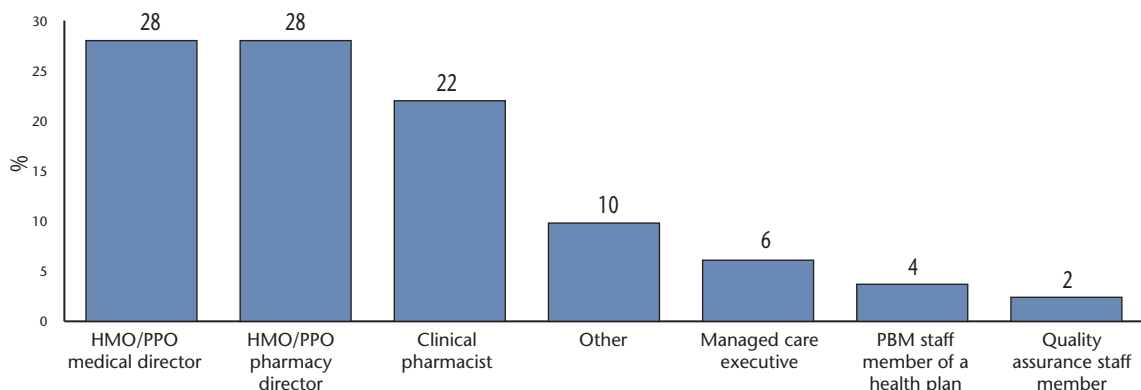
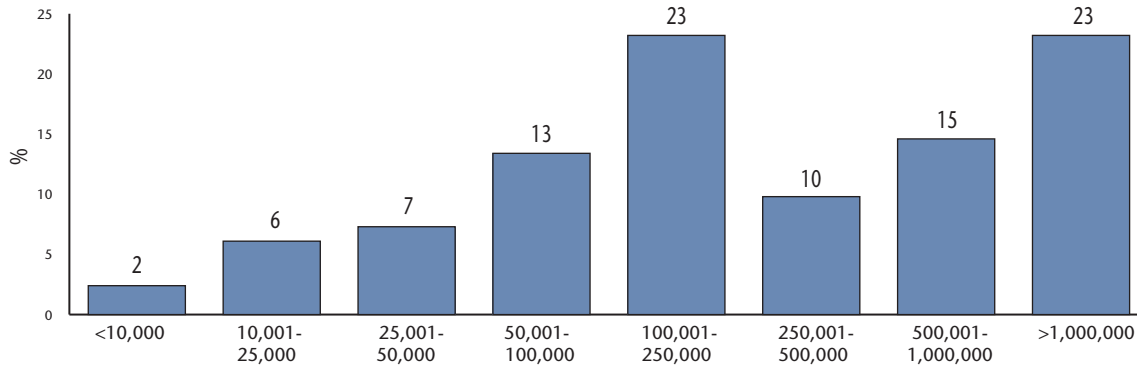
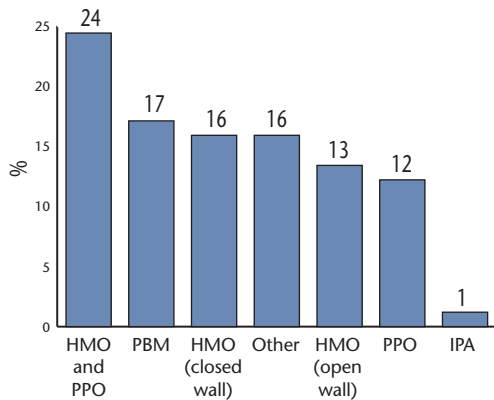


Figure 2. How many covered lives does your organization have?



About half of the MCOs represented (51%) are for-profit entities; 49% are non-profit. One quarter of the respondents characterized their organization as an HMO and a PPO. Twenty-nine percent defined their organization as either a closed wall HMO (16%) or an open wall HMO (13%). Twelve percent of those surveyed described their organization as a PPO. Sixteen percent of the survey participants classified their health plan as “other,” including Medicare or Medicaid plans (Figure 3).

Figure 3. Your managed care organization is best described as:



Twenty-seven percent of the survey respondents were unable to estimate the number of members within their organization who have been diagnosed with multiple sclerosis. Forty-one percent indicated that fewer than 101 of their members have an MS diagnosis. Figure 4 illustrates respondents’ estimates of the number of covered patients diagnosed with MS.

COMMENTARY

Nearly three-quarters of the respondents know the approximate number of individuals diagnosed with MS within their organization. These estimates accurately reflect the national prevalence of MS, estimated at approximately 400,000 individuals.

Seventy percent of members represented by the survey participants are fully insured (employers are required to pay premiums), while 28% derive coverage from self-insured employers’ groups, which bear the financial risk of paying for healthcare from their own funds (Figure 5).

Figure 4. Approximately how many of your covered lives have MS?

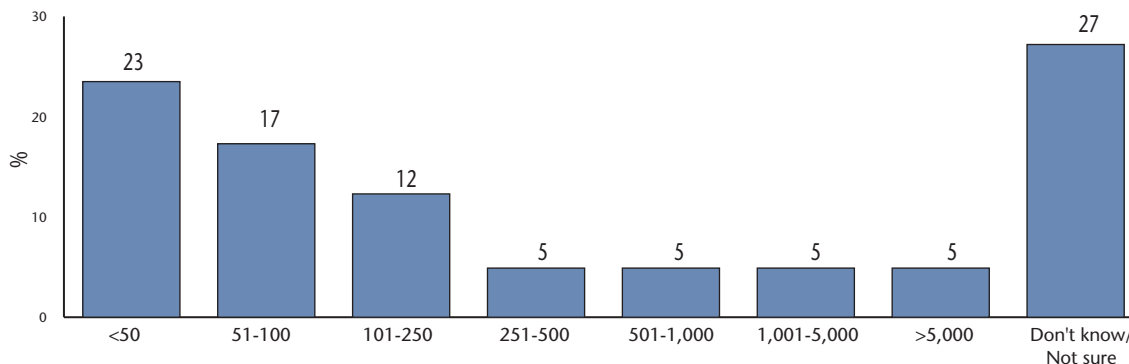
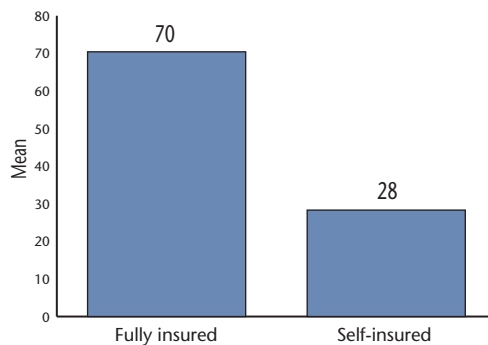


Figure 5. What percentage of your members are:



FORMULARY

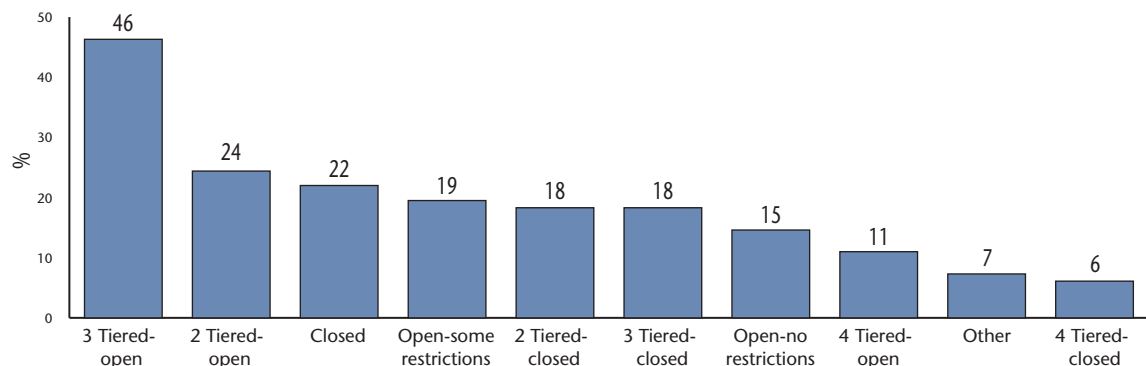
Almost all the respondents (96%) indicated that their organizations have formularies. Because MCOs have one formulary per therapeutic category, the survey asked respondents to choose the models that best describe their organizations' formularies. For the most part, respondents chose an average of two models to describe their formulary structures.

Almost half of all the respondents said their organizations use 3-tiered open formularies. Almost a quarter of the respondents indicated the use of 2-tiered open formularies, making them the second most common model. Both closed and open formularies that have some restrictions appear to be relatively common models among health plans, with 22% and 19% of respondents, respectively, using these terms as "best descriptions." Open formularies with no restrictions are rare (Figure 6).

Figure 7 illustrates the most common co-payment structures for prescription drug benefits; co-pays increase with the progression from tier 1 to tier 4 drugs.

Almost 80% of the respondents play an active role on their organization's formulary committee; 49% are voting members, while 29% can make recommendations to the committee (Figure 8). Ninety percent of the participants said their company's pharmacy and therapeutic committees (P&Ts) meet at least quarterly; 21% of these

Figure 6. Which of the choices below best describe your organization's drug formulary?



Managed Healthcare Terms

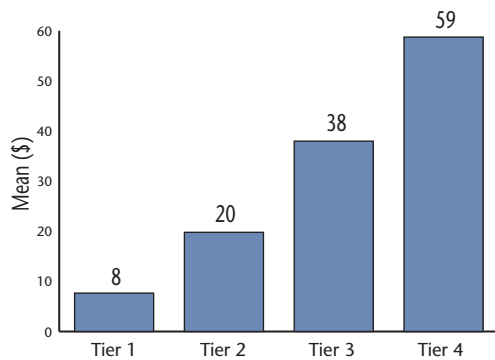
disease management: an integrated, comprehensive approach to healthcare that aims to reduce or prevent recurrence of symptoms, maintain optimal quality of life, and decrease the need for medical resources; disease management programs rely on pharmaceutical care, continuous quality improvement, adherence to practice guidelines, and case management. They are usually designed for patients with chronic illness, and they aim to reduce overall healthcare costs.

pharmacy benefit management company (PBM): a company that acts as a third-party administrator of prescription drug benefits.

self-funding: refers to a type of healthcare plan funded completely by employers who do not purchase insurance; the employer either administers the plan or contracts with an outside administrator for an administrative-services-only arrangement; also known as self-insurance.

specialty pharmaceutical services: organizations that specialize in providing health plan members with access to expensive, biologic agents used to treat specific, high-cost chronic diseases.

Figure 7. What is the most common co-pay structure (\$) for the tiers?



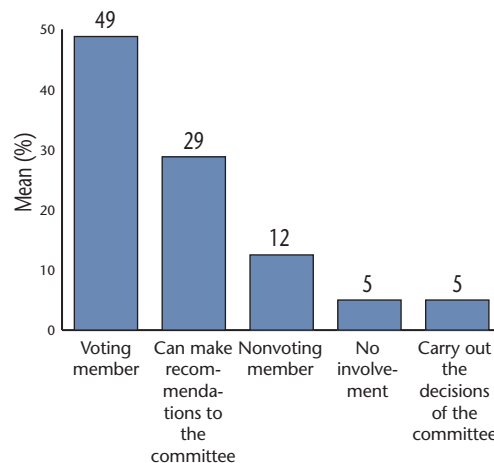
committees convene six times per year, and 16% meet monthly (Figure 9).

MCOs represented in the survey cover a range of 7,000 to 65 million prescription-eligible lives, with a mean of approximately 2.5 million covered lives.

Most organizations represented in the survey research offer two types of prescription drug plans. These offerings may include plans for commercial, Medicare, or Medicaid populations, or a combination of these. More than three-quarters of the respondents (77%) said their organization offers a plan for the commercial population. Just over half of the organizations (51%) offer a Medicare plan, and half offer a Medicaid plan.

Commercial plans cover 63% of represented lives; Medicaid plans cover 24%; and Medicare plans cover 12% of represented lives (Figure 10).

Figure 8. What is your involvement with the formulary committee?



Specialty pharmacy programs are used by 90% of the MCOs represented. Of the 90% of organizations that do have a specialty pharmacy program, 33% require the use of one or more contracted specialty pharmacies for most injectables (Figure 11).

A third of the surveyed MCOs may allow patients to acquire injectable drugs from retail pharmacy networks, but they encourage the use of one or more contracted specialty pharmacies as well. Twenty-nine percent of the respondents possess a limited network of specific specialty pharmacy vendors.

Forty-five percent of MCOs require a moratorium for a new molecular entity, while 55% do not (Figure 12). Ninety-four percent of the time, the length of the moratorium by those organizations that require one is six months.

Types of HMOs

staff-model HMO: in this model, the most direct form of managed care, physicians work at a centralized site that provides a full range of clinical services and possibly inpatient and pharmacy services as well.

individual practice association model (IPA): the IPA contracts with independent physicians who work in their own private practices, and see fee-for-service patients as well as HMO enrollees.

group model: the HMO contracts with a physician group, which receives a fixed payment per patient for services provided.

hybrid model: two managed care organizational models are combined into a single health plan.

network model: a group practice network that a single HMO administers.

point-of-service model (POS): allows patients to receive care either from physicians who contract with the HMO or from those who do not contract with the HMO. Patients are given an incentive to use contracted providers through the fuller coverage offered for contracted care.

Figure 9. Frequency of P&T Committee meetings:

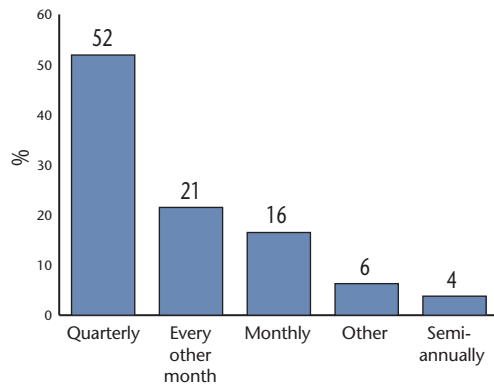


Figure 10. Indicate percentage of lives for each plan offered:

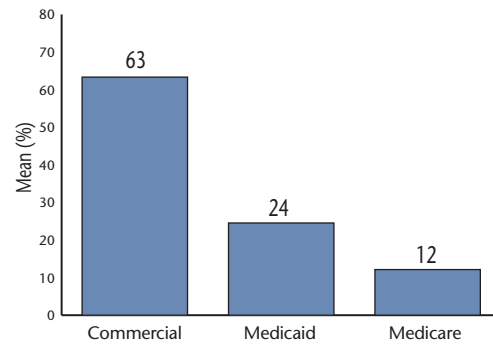


Figure 11. My organization:

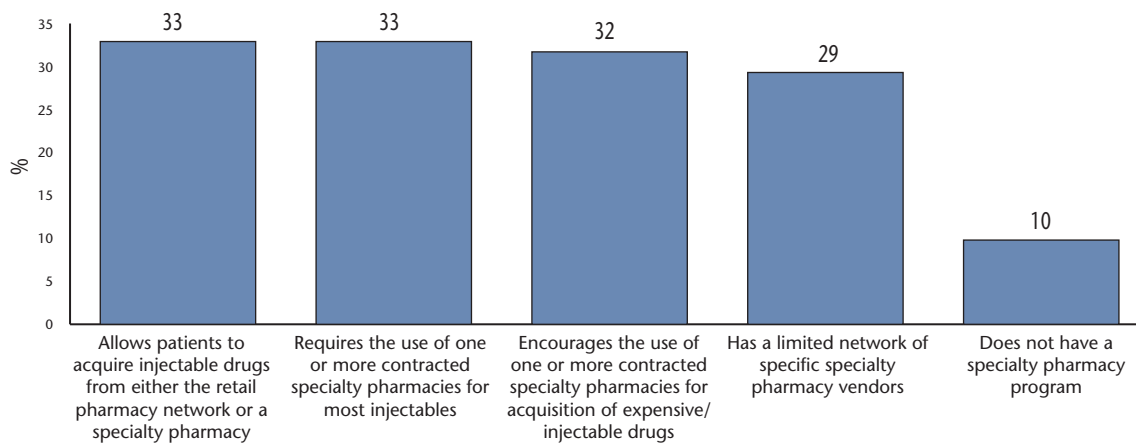
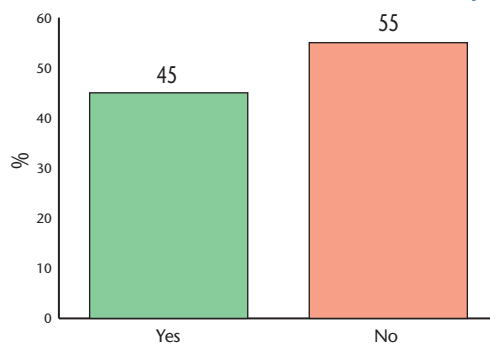


Figure 12. Does your organization require a moratorium for a new molecular entity?



Ensuring step-care therapy (whereby a patient must use the preferred product first before being authorized to access a second, non-preferred product), restricting the use of the drug to proven or common (compendium) diagnoses, confirming that appropriate lab work has been completed, and requiring that patients use the services of an MS specialist are of progressively lesser importance (Figure 13).

Eighty-five percent of the respondents said it is appropriate to confirm that a patient has failed conventional therapy before using an injectable biologic product whose long-term efficacy has not yet been proven. Two-thirds of the respondents believe that assessing patient compliance with conventional therapy is appropriate before prescribing an injectable whose long-term efficacy has not yet been proven. Sixty percent of the respondents indicated that patients should be encouraged to use a preferred biologic agent within the class or category before trying another injectable drug therapy (Figure 14).

REIMBURSEMENT STRATEGIES

When asked to rank, in order of importance, an organization's objective when applying a prior authorization requirement for biologic or injectable therapies, 67% of the respondents reported that ensuring appropriate utilization of the drug in question is the most important factor.

Limiting the use of the drug to FDA-approved indications ranks second in importance.

Figure 13. Ranking of objectives MCOs wish to achieve when applying a prior authorization requirement for biologic or injectable therapies (1 = highest rank; 5 = lowest rank).

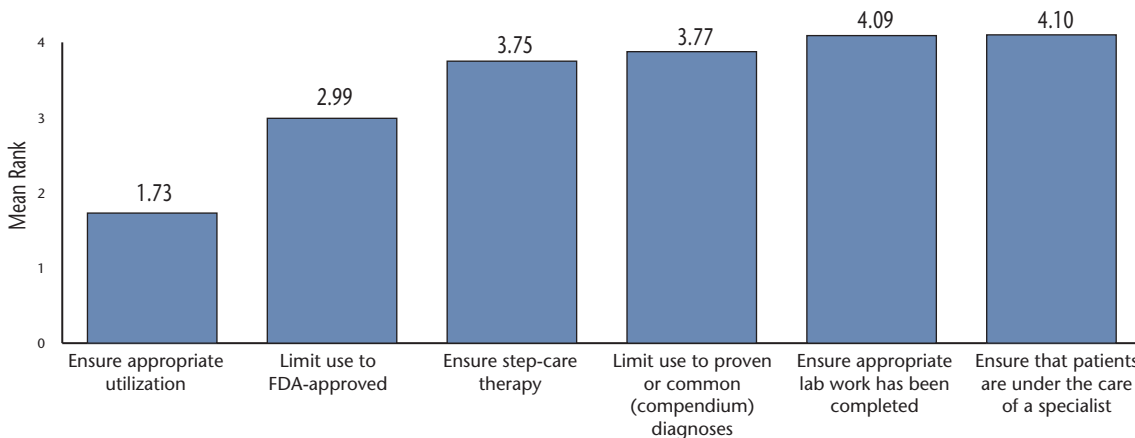
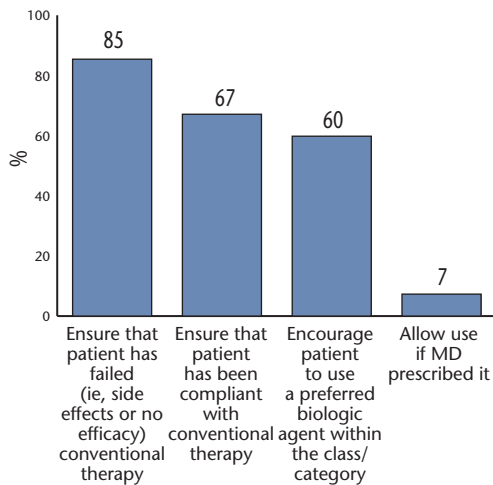


Figure 14. What action(s) is/are appropriate to manage the use of an injectable biologic product whose long-term efficacy has not yet been proven?



COMMENTARY

Biologics are a new class of drugs that show promising results, especially for chronic, debilitating conditions such as multiple sclerosis. The costs, however, can be staggering, and for MCO professionals, the costs of injectable drugs are a primary concern.

Nearly all MCOs represented in this research have formularies, and most have tiered models that allow some choice of drug therapy while attempting to control costs and unnecessary utilization.

Pharmacy and therapeutics committees meet regularly and frequently to review new medications. These meetings are essential,

as evidenced by the number of new drugs in the pipeline. More than 418 biologic drugs are now in development for the treatment of more than 100 diseases, including 210 medicines for cancer, 50 for infectious diseases, 44 for autoimmune diseases, and 22 for AIDS/HIV and related conditions. All 418 of these drugs are in human clinical trials or are under review by the Food and Drug Administration. Those that the FDA approves will be added to the 125 biotechnology medicines currently FDA-approved and available for use.

Biologics — especially those that are relatively new, in competitive categories, or subject to significant off-label use — are tightly controlled through prior authorization processes and moratoriums on new molecular entities.

For new biologic therapies, nearly half of the respondents said their organizations require moratoriums of about six months, a clear indication of a wait-and-see approach. During moratoriums, MCOs will either not cover the therapy in question or will cover it at a higher cost to the patient.

Ninety percent of the surveyed organizations have a specialty pharmacy program, suggesting that most MCOs find value in an integrated approach to the distribution and proper coding and billing of biologics.

BENEFIT DESIGN

Figure 15 illustrates the prevalence of various benefit design strategies for the management of biologic products used to treat patients with MS.

The figure also demonstrates MCOs' assessment of their intention to adopt these strategies in the near future.

The two most popular benefit design strategies for managing biologic products used to treat MS are as follows: (1) limiting product prescriptions to appropriate specialties (59%) and requiring prior failure on formulary-preferred drugs before approving the use of a nonpreferred product (69%). In addition to the MCOs that said they are already using these two strategies, about 23% plan to implement each of them within the next 12 to 18 months.

Forty-five percent of the surveyed MCOs currently use differential prior authorization rules to direct physicians to a preferred agent within a category; 35% said they will do so within the next 12 to 18 months.

Sixteen percent of the respondent MCOs already have in place a separate benefit design just for specialty therapies; 39% plan to introduce one within the next 12 to 18 months.

Thirty-two percent of the surveyed MCOs already have put in place tiered coverage with significant cost-sharing differentials (>\$30) between preferred and nonpreferred specialty therapies. Forty-two percent of the respondents said they plan to create this tiered coverage within the next 12 to 18 months.

Respondents indicated that setting a lifetime cap is a controversial strategy for managing the utilization of specialty or biologic products. Seventy-five percent of the organizations surveyed indicated they will not implement this strategy; 12% have already set these lifetime caps; and 12% said they will do so within the next 12 to 18 months.

The two most important factors MCOs consider when evaluating a therapy for MS are relapses and disease progression. All of the factors listed in Figure 16 are considered at least somewhat important in evaluating a therapy for MS patients, according to survey respondents.

What follows are highlights from opinion statements about biologic and injectable drug coverage, and about infused versus self-administered forms of biologic therapies:

- More than 75% of the survey participants agree or strongly agree that infused therapies are generally more costly than self-administered therapies
- Seventy percent agree or strongly agree that attractive discounts on injectables and biologics may result in preferred status on the formulary
- All but 8% of the respondents at least somewhat agree that self-injectable products may become increasingly

Figure 15. Indicate for each of the following how soon you think your organization will adopt various benefit design strategies to deal with relatively expensive biotech-derived MS products.

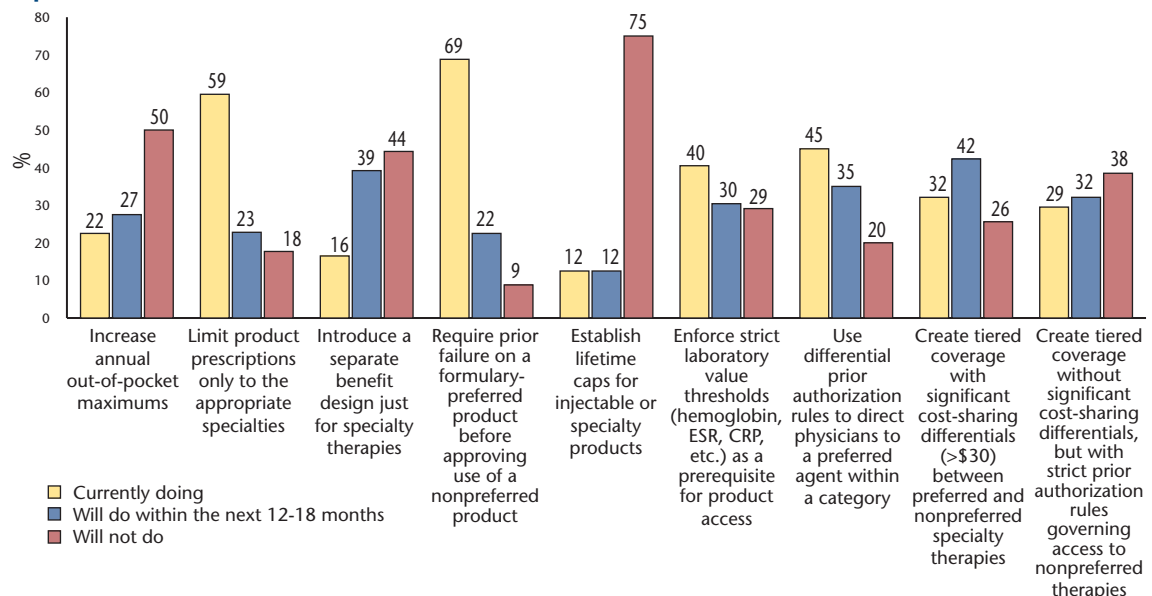
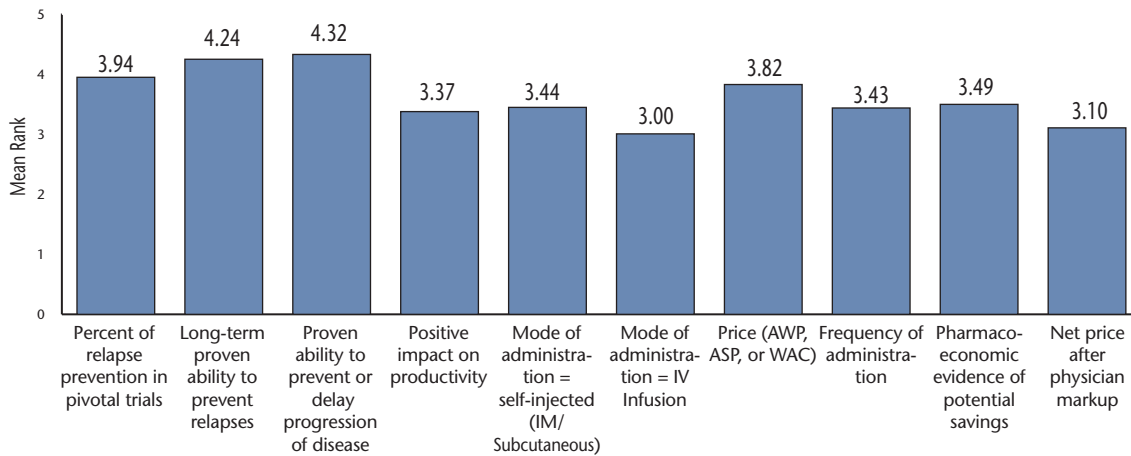


Figure 16. Rate the following factors regarding importance in evaluating a therapy for MS on a 5-point scale (1 = very unimportant; 5 = very important):



preferred over infusion products

- Respondents tended to agree overall that biologics and injectables that offer a clear efficacy advantage over traditional therapy may be placed in a favorable tier position
- Respondents showed little or no concern that falling reimbursements may cause contracted physicians to leave the network or limit their panel of patients from a particular organization

COMMENTARY

MCOs use, or are considering using, numerous benefit design strategies to manage the biologic and targeted therapy category of drugs.

These strategies include higher cost sharing with the patient, increased use of preferred categories, differential prior authorization rules to encourage the use of specific drugs, and delayed acceptance of new products.

Similarly, managed care professionals consider many factors — from cost to safety to mode of administration — when evaluating an MS therapy. However, the potential proven ability of a therapy to delay disease progression and prevent relapse is of paramount concern to MCOs. While treatment of MS is a complex issue, there are strong indications that the use of self-administered injectables will increase in the future as long as continued favorable results from studies of safety and efficacy are obtained.

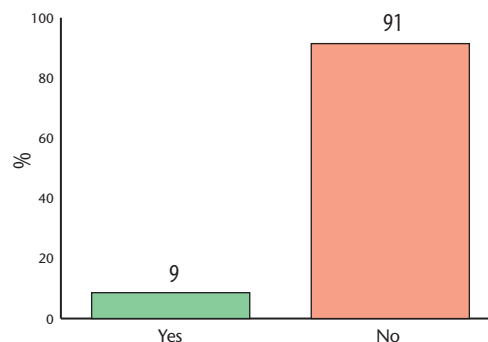
DISEASE AND CASE MANAGEMENT

Less than half of MCOs (43%) reported having at least some (but not fully developed) disease management capability. These MCOs have some components of a disease management program for MS in place, but they may lack the systems required to track outcomes and analyze the effectiveness of the program.

Fewer than 10 percent of MCOs recorded having a full, population-based disease management program for MS that includes reporting and clinical outcome tracking ability (Figure 17).

Out of all the MCOs that reported using at least some form of disease management program, more than twice as many MCOs developed these programs internally, rather than obtaining vendor-developed programs.

Figure 17. Does your organization offer a fully developed, population-based disease management program?



More than half of the surveyed MCOs (57%) offer case management services for MS patients. Eighty-nine percent of the organizations surveyed identify MS patients for case management through claims analyses, rather than a clinical event; this same proportion of the surveyed MCOs (89%) possess sufficient internal data-tracking capabilities to conduct claims analyses and identify MS patients for case management.

COMMENTARY

More than two-thirds of the survey respondents agree or strongly agree that a disease management program for MS would improve outcomes, increase compliance, and reduce disability.

The lack of comprehensive programs for MS patients conflicts with the desire of MCOs to use evidence-based care management programs to improve outcomes and reduce the use of avoidable unscheduled healthcare.

Opportunity exists for managed care companies to expand the use of case management and fully developed disease management programs to treat MS patients.

Moreover, specialty pharmacies that can claim disease management capability for MS patients may possess an advantage in acquiring contracts.

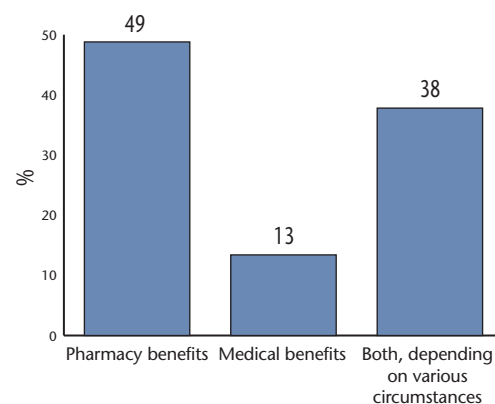
Specialty pharmacies have become an integral component of MS drug distribution, and half of the survey respondents said they prefer to contract with a specialty pharmacy vendor that already has a program in place for MS patients.

Specialty pharmacies may be the best locale for disease management programs, as they serve a large percentage of MS patients in the majority of health plans surveyed.

Nearly half (49%) of the MCOs surveyed cover injectable MS drugs under pharmacy benefits. Thirteen percent reimburse for injectable MS drug therapies solely under medical benefits, and 38% cover injectables for MS treatment under both, depending on various circumstances (Figure 18).

As the following highlights indicate, the acquisition and distribution of injectable MS

Figure 18. Self-injectable MS products are covered under:



drugs is governed by a wide variety of rules, and additional changes are under way:

- Forty-two percent of the respondents require patients to use a specialty pharmacy; 55% encourage patients to use a specialty pharmacy; and 41% anticipate that they will require members to use a specialty pharmacy within the next 24 months
- Thirty-nine percent of the surveyed MCOs indicated that patients may obtain a three-month supply of their medication through mail order; 23% said their members will be able to do so within 24 months
- Thirty-four percent of the respondents said they encourage their patients to use mail order to obtain injectable MS drugs; 8% of surveyed MCOs require patients to use mail order

The significant role of specialty pharmacies in the acquisition and distribution of injectable medications is underscored in the managed care survey results. Respondents indicated that within the next two years, they will encourage or require 79% of their members with MS to use a specialty pharmacy to obtain injectable drugs.

Mail order is a popular means of acquiring medications, and 62% of respondents either currently allow their MS patients to obtain a three-month supply of injectable drugs by mail or will allow them to do so within the next two years. A three-month supply of medication assists with compliance for chronic conditions like MS, in which long-term drug use is indicated.

CONCLUSION

Managed care is paying increasing attention to the disease of multiple sclerosis, but the intensity of the focus varies widely across plans. Eight percent of the surveyed plans have mature disease management programs in place; less than half of the respondents have a partially developed disease management program; and 27% of the plans do not track even the absolute number of members with MS within their organization. At the same time, few of the surveyed plans have fully developed outcome improvement programs in place.

The primary focus of MCOs surveyed centers on controlling the cost of medications for MS. This outcome is not surprising, given the per-patient per-month costs of the drugs used to treat patients with MS.

The trend toward moving the MS class of drugs to the pharmacy benefit — with its data-rich environment — along with the dominant use of specialty pharmacies by the survey respondents, forecasts an increasingly important role for specialty pharmacies in the active management of multiple sclerosis.

TWO PRIORITIES: COST AND USE



*The Comments of Bruce Niebylski, MD
Senior Associate Medical Director
Health Alliance Plan of Michigan
Detroit, MI*

Detroit-based Health Alliance Plan (HAP) considers cost and appropriate use of MS drugs the leading factors in determining which medications to cover for treatment of the disease, according to Bruce Niebylski, MD, senior associate medical director for HAP.

“Cost plays a role, but first we want anybody who has MS to have access to the right medications, while also ensuring that they will benefit from them,” Niebylski says. “In addition, we limit product prescriptions to the appropriate specialty — neurology.” One in 500 members of HAP is an MS patient.

HAP contracts with BioScrip, a specialty pharmacy, to manage seven classes of drugs — including those for MS — in order to take advantage of the best discounts. HAP is not alone in its reliance on specialty pharmacy; as many as 90% of MCOs that responded to the survey in this report follow suit.

BioScrip makes staff available for one-on-one training of MS patients who feel they need to learn more about the use of a medication, and the company has a mail service as well. As Niebylski explains, HAP and BioScrip have complementary interests: “We share our guidelines on appropriate use, which are developed by MS experts, with BioScrip, which in turn utilizes prior authorization based on clinical information.”

HAP places four of its five MS disease-modifying drug therapies on tier 3 of its three-tier formulary. Coverage falls into the pharmacy bucket, as do all biotech drugs — where drug use can be tracked more efficiently. The fifth MS disease-modifying drug, Tysabri®, is considered a medical benefit; requests for Tysabri® still require a prior authorization, but the drug does not have a tier associated with it.

HAP’s tier 3 co-payments range from \$30 to \$50, and the insurer does not anticipate adding a specialty tier. “It’s a Detroit thing,” Niebylski observes. “Our health plan was

created for the United Auto Workers, and it already offers one of the richest and lowest-cost benefits in the country.”

HAP employs two other strategies to control the cost of MS drugs: step therapy and the elimination of any incentive for physicians to prescribe an MS-infusible drug. “We will pay for the physician to give the infusion but not for a percentage of the cost of the drug,” Niebylski says. “Instead, the physician must use the drug supplied by us.”

Unlike 32% of the surveyed MCOs already doing so and another 42% planning to within the next 12 to 18 months, HAP does not implement tiered coverage with significant cost sharing differentials. But the company is in step with 75% of the surveyed MCOs in not setting a lifetime cap for injectable or specialty products.

HAP plans to launch a disease management program for rare diseases, including MS, in the first half of 2007; to do so, it will bring on board Accordant, a health management company. Slightly less than half of the MCOs surveyed in this report said they have at least some kind of disease management program; and more than twice the number of respondents who have such a program said they developed them internally rather than contracting with an outside vendor.

WORKING OUT FROM THE CENTER



The Comments of Ben W. Thrower, MD

Medical Director

Shepherd MS Institute

Atlanta, GA

As medical director of the Shepherd MS Institute, Dr. Ben Thrower says he feels “fortunate to work as part of a multi-disciplinary team.” All therapeutic endeavors in MS fall into one of three categories: relapse management, symptom management, or alteration of the disease course. For each of these groups, there is a host of potential providers, medications, and interventions. MS centers offer the advantage of pooling these resources and allowing for coordination of care.

A key player on the MS team is the case manager. Case managers can prove invaluable in coordinating financial assistance, community resources, and access to care. These needs contribute to the perception that caring for patients with MS is time-consuming. “Most community neurologists don’t have immediate access to case management services, and a ‘therapy optimization program’ via specialty pharmacies can help fill some of this need,” says Thrower.

Many MS centers, such as Shepherd, have a strong rehab focus. “The role of rehabilitation and wellness in MS cannot be overemphasized,” Thrower notes. “Appropriate use of therapy may minimize symptomatic medication use and prevent secondary complications. For instance, energy conservation techniques taught by occupational or physical therapists can help lessen fatigue, the number one MS symptom complaint.” While 97% of community neurologists surveyed said they referred to PT, OT, and speech therapy, only 16% used PT/OT, stretching, and other exercise for spasticity management.

“The comprehensive MS center,” Thrower says, “may also offer research, aquatics, counseling, driving evaluations, cognitive testing, pain management, and urological services. Most centers serve as an educational resource both for patients and providers. The center should partner with community neurologists as needed. For example, the center may assume total neurological care for the patient, provide periodic consultative services, or just offer ancillary services such as therapy.”

Barriers to comprehensive MS center care do exist, Thrower acknowledges. “The MS community and providers may simply not be aware of services offered at a center. Managed care organizations may also prove problematic. I would hope that MCOs and Medicare realize that while comprehensive care could prove more costly up-front, it should reduce complications, equipment needs, and ER visits in the long run. In my experience, MCOs vary in their knowledge and flexibility in working with the MS community itself, which tends to be Internet savvy and well-informed. The MS community tends to seek a partnership in their care, rather than a paternalistic relationship,” he says.

“MCOs have generally acknowledged the importance of starting one of the standard immunomodulatory drugs. I do see some requiring needless annual reauthorization for what could be a lifetime therapy,” Thrower observes. “Another challenge with MCOs,” he adds, “is that they may authorize a service, but only with a provider who is inexperienced with MS. Two areas that come to mind are therapy and imaging. Not all therapists are comfortable working with the specialized needs of the MS community. For instance, ignorance of the unique cognitive deficits or exertional symptoms common in MS can make the difference between success and failure in therapy.” In the area of MRI, notes Thrower, many technicians are unaware of recommendations for standardization of MRI technique by the Teaneck, New Jersey–based Consortium for MS Centers. “This lack of awareness can lead to suboptimal MRIs that may need to be repeated, adding time and expense for someone,” he says.

Tracy Walker, a nurse practitioner at the Shepherd MS Institute, concurs that there is room for increased awareness in MCOs’ handling of reimbursement for MS services. “The current thinking in managed care is, How can we lower costs; how can we avoid paying for anything for one to two years? While it is true that patients may shift from one plan to the next every couple of years or so, inadequate care costs everyone in the long run. The MCOs need to realize that they may see one tough patient move on to another plan, only to be replaced by another patient who was denied preventive care by a competing MCO,” says Walker.

In conclusion, Walker and Thrower agree that working with the MS community is both rewarding and challenging. MS centers, community providers, and third-party payers all play a role in the health of the person with MS. Specialty pharmacies can certainly add value by improving knowledge of and access to therapy.

BEST PRACTICES: MCO FORMULARY



The Comments of Bonnie J. May, RPh, MBA

Injectable Clinical Pharmacist

Fallon Community Health Plan

Worcester, MA

Fallon Community Health Plan in Worcester, Mass., like many of the other MCO survey respondents, hosts an open, three-tier formulary; however, Fallon places Betaseron[®] (interferon beta-1b), Copaxone[®] (glatiramer acetate injection), and Avonex[®] (interferon beta-1a) on tier 2, while Rebif[®] (interferon beta-1a) has landed on tier 3. Bonnie May, injectable clinical pharmacist for Fallon, says that in this case, it is a question of pricing. “We consider the mechanisms of actions for these drugs to be similar,” says May, “and since all of them are targeting remitting-relapsing stages of multiple sclerosis, price is the differential.” Tysabri[®] (natalizumab), which requires prior authorization, is the only MS drug that falls under the medical benefit at Fallon.

When evaluating a drug for formulary, Fallon rates safety and efficacy at the top of the list, says May, followed by three other factors: price, compliance, and a comparison with other MS drugs on the market. “Although we will not accept prescriptions for drugs that have not proved safe, sometimes we get caught between a rock and a hard place and receive pressure from a physician or the marketplace to approve the drug,” she admits.

To encourage safety, Fallon enforces laboratory value thresholds and monitoring parameters, such as periodic MRIs, as a prerequisite for continuing therapy. Fallon also turns to its P&T committee for assistance in determining which drugs should go on formulary. May says that although there are no neurologists on the committee, Fallon willingly listens to the opinions of respected, local neurologists.

May says Fallon is not planning to add a fourth tier or a specialty pharmacy tier in the near future. “We want to keep member satisfaction high, and adding a tier may increase co-payments,” she notes. Occasionally Fallon uses an external specialty pharmacy provider, when a member has difficulty accessing a drug at the local pharmacy. But May says that Fallon encourages its members to visit pharmacies in the network.

At Fallon, members pay \$10, \$20, and \$50 for tier 1, 2, and 3 drugs, respectively. May says that the gap between co-payments for tiers 2 and 3 may create an incentive for some members to try one of the less expensive drugs first.

To keep costs down and maintain appropriate utilization, Fallon relies on prior authorization and step therapy. The goal is to make sure that only those patients who have remitting-relapsing MS will receive drugs aimed at treating that stage of the disease, compared to patients in a more progressive stage, who would not benefit from these same agents. She expresses concern about physicians who may think more is better, adding that Fallon sometimes develops distinctive prior authorization rules that direct physicians to a preferred agent within a category. “To steer market share, we may require prior authorization for one drug and not for the other,” May explains.

Fallon has placed no constraints on what type of physician may prescribe drugs for MS through the plan, nor does it require physicians to obtain products from a particular source in order to improve the reimbursement rate. At the same time, May says, Fallon is moving in the direction of obtaining some MS agents from a specialty source.



Neurologists

The neurologists' survey considers the provision of MS healthcare — including complexities involved in diagnosis and treatment, reimbursement patterns, the management of symptoms, and the use of disease-modifying therapies.

Respondents totaled 143 currently practicing general neurologists and MS specialists. Though most respondents said they are generally confident in their ability to diagnose MS, 96% noted barriers to diagnosing and treating MS, including economic and clinical issues as well as problems with insurance carriers.

Because it is difficult to predict the course of this neurological autoimmune disease in any one individual, doctors routinely prescribe various disease-modifying agents, conduct frequent neurological exams, periodically request MRIs, and prescribe various medications or therapies in efforts to manage the progression and symptoms of MS.

The complexity of treating MS patients became evident as surveyed neurologists pointed out a number of issues regarding the reimbursement of injectable therapies for MS patients, along with the variety of difficulties encountered in the reimbursement of infused disease-modifying agents; 73% of respondents reported that insurers at least sometimes try to restrict the use of infused disease-modifying drugs.

Sixty-six percent of the surveyed neurologists said they are willing to be interviewed or to participate in a panel discussion on MS best practices in regard to diagnosis, treatment, and management of the disease.

Respondents indicated that they would welcome an enhanced role on the part of specialty pharmacies in the management of MS patients, owing to the various biologic products and other MS drugs in the pipeline, and because additional treatments for managing symptoms are under development.

Specialty pharmacy case managers and pharmacists can assist neurologists in providing self-assessment tools for patients, including screening tools for depression. It is still a matter of debate whether the depression that many MS patients experience is caused by the disease itself, is a result of side effects of disease-modifying agents or other medications, is of an inherent nature, is situational, or a combination of these. Identifying the causes of depression can play an important role in treating MS, and one medication may prove more effective than another, depending on the origin of the depression and patients' other MS-related symptoms.

Specialty pharmacy programs can also assist in easing neurologists' time constraints — a common problem for physicians who evaluate patients with MS. Respondents to the survey said they average 48 hours of clinical practice and five hours of

administrative work per week, along with devoting nearly two hours per week to reimbursement issues. Nearly 75% of those surveyed have had to hire additional clerical staff to handle prior authorizations or payment issues.

Neurologists handle difficulties in treating their patients with MS in a variety of ways: they act as advocates for their patients, appeal claim decisions, and use treatments that are reimbursable. A few indicate that they refer their patients to colleagues.

This survey makes clear the desire of neurologists to effectively care for their MS patients, despite the amount of time and other impediments that can be involved.

And while many neurologists prefer to obtain their continuing MS education by reading journal articles and attending meetings, the survey suggests there is ample opportunity for insurers to assist physicians with this task. The addition of insurer-supplied educational articles could enhance the value of an insurer's contract and prove an effective tool for keeping both doctors and medical directors on the cutting edge of MS patient treatment.

OVERVIEW

Respondents to this survey are practicing neurologists who are currently managing patients with MS. Eighty-five percent of the respondents are board certified; all but two of the remaining 16% are board eligible.

Nearly half (48%) of the neurologists surveyed practice in a group setting, while 37% represent solo practices. The other respondents maintain offices that are affiliated with a hospital or a university. Respondents who work in group settings have been in practice for an average of 13 years.

Neurologists participating in the survey represent half the states in the nation, and except for 12% who practice in rural areas, are about evenly

divided between urban and suburban settings.

Respondents have been in practice from one to 44 years, with a mean of 18 years. Their average age is 50, and 51% are planning to retire within the next 14 years (Figure 19).

During the past two years, 73% of the respondents experienced either no change in income or a drop in earnings (Figure 20).

One-third of the respondents employ one or more physician assistants or nurse practitioners; an additional 13% plan to do so within the next two years.

The practices represented in the survey follow a mean of 1,635 patients (median = 1,500). Each physician manages an average of 152 MS patients (median = 80). A couple of the practices surveyed manage more than a thousand patients with MS.

RESULTS

Surveyed physicians report that in regard to the four subcategories of MS — relapsing remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and progressive relapsing (PRMS) — nearly two-thirds of their MS patients (65%) are currently classified as relapsing remitting (Figure 21).

Physicians who responded to this survey are quite comfortable with their ability to diagnose MS (Figure 22). However, 59% indicated that barriers to diagnosing and treating MS in their practice — primarily economic concerns, clinical issues, and difficulties with insurance carriers —

Figure 19. In how many years do you intend to retire?

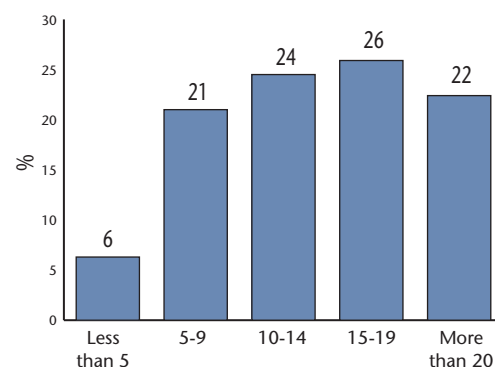
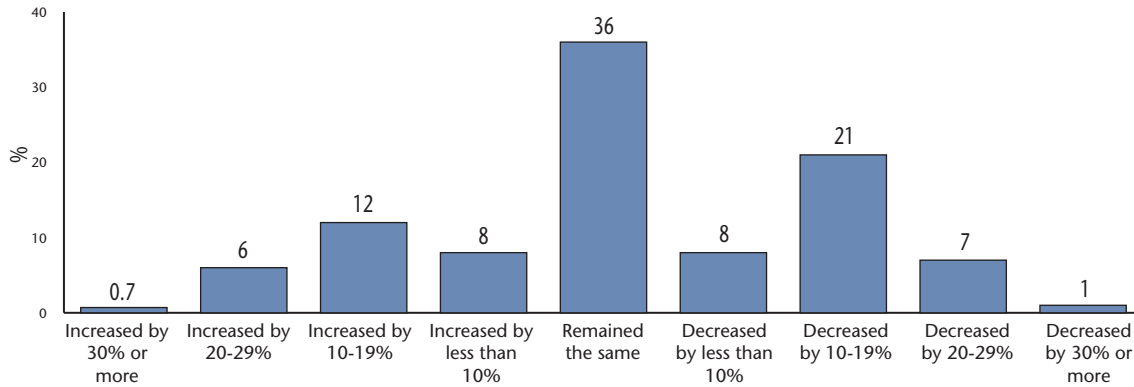


Figure 20. How has your take-home income changed over the last two years?



interfere with more effective management of the disease (Figure 23).

Besides the major economic, clinical, and reimbursement concerns, respondents pointed to the resource-intensive nature of MS as another important barrier in diagnosing and treating patients with MS. Other challenges include medication coverage, patient fear of treatment, issues with benefit managers, and the lack of specific biologic markers.

Most of the physicians surveyed (90%) are aware of the McDonald criteria for diagnosing MS. Seventy-one percent of those who are aware of the McDonald criteria actually use them, with the majority favoring the 2005 revision.

More than a third of the respondents (36%) indicated that they either are not aware of or do not use the McDonald criteria. Of those who do not use the McDonald criteria in diagnosing MS, most (63%) use both clinical and objective findings to make these diagnoses (Figure 24).

The respondents use cranial MRI (27%), spinal MRI (27%), or lumbar puncture (26%) when

diagnosing MS; 20% indicated that they use evoked potential tests, including visual (VEP), somatosensory (SEP), and brainstem auditory (BAEP), among others.

Twenty-nine percent of the respondents personally interpret MRIs; 21% rely on a local radiologist and 50% collaborate with an MS center for interpretation.

Figure 22. What is your level of comfort in diagnosing MS?

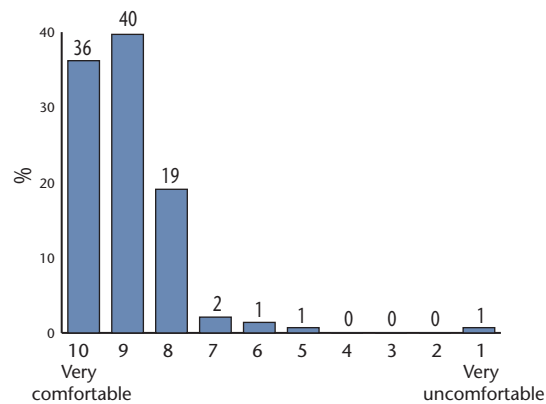


Figure 21. What is the distribution of MS patients in your practice by the following diagnoses?

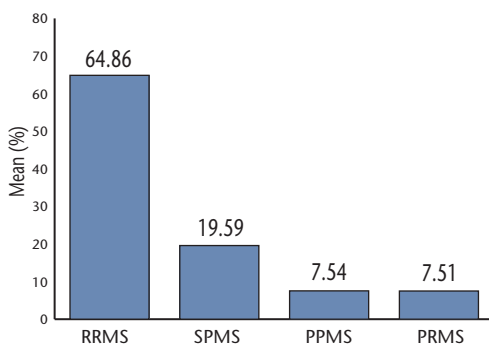


Figure 23. What are barriers to diagnosing and treating MS?

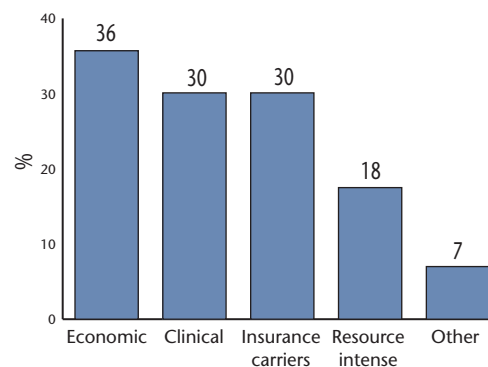
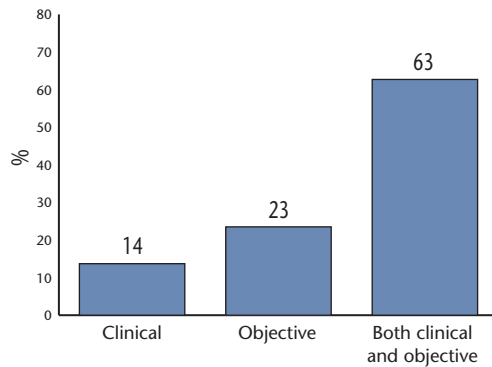


Figure 24. What criteria [other than McDonald] do you use for diagnosing MS?



COMMENTARY

Nearly three-quarters (73%) of the respondents prescribe infused disease-modifying drugs (DMDs), other than corticosteroids, in treating MS patients. About one in every three of these respondents offers infusion services in the office.

Among infused DMDs, respondents most frequently prescribe the chemotherapy drug Novantrone® (mitoxantrone for injection concentrate), used to treat more progressive MS cases; IVIg and Cytoxan® (cyclophosphamide) are the next two most frequently prescribed infused DMDs (Figure 25).

Nearly three-quarters (74%) of the surveyed neurologists at least sometimes encounter difficulties with carriers in obtaining reimbursement for infused DMDs; only 10% never encounter reimbursement issues for these agents (Figure 26).

Practitioners vary in their approach to handling reimbursement barriers for infused DMDs: 55% advocate for their MS patients or appeal decisions, or both; 17% use other treatments; and 3% refer patients to a colleague or choose another option.

More than two-thirds of the respondents (71%) reported that insurers at least sometimes try to restrict the use of infused DMDs (Figure 27).

Respondents who do use infused DMDs to treat MS administer these agents to an average number of 11 patients each.

Respondents said they prescribe injectable DMDs – most frequently Avonex® (interferon beta-1a) and Copaxone® (glatiramer acetate

injection), at approximately 30% of patients each – more often than infused therapies.

Figure 28 details respondents' use of injectable DMDs for their patients with MS.

Figure 25. Other than corticosteroids, which infused disease-modifying agents do you prescribe?

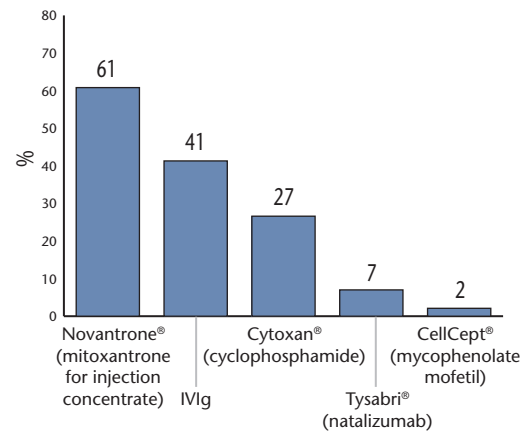


Figure 26. Do you ever encounter difficulties with carriers in obtaining reimbursement for infused disease-modifying agents?

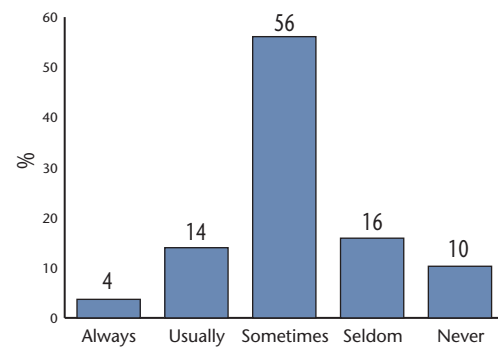


Figure 27. How frequently do plans try to restrict the use of infused disease-modifying agents?

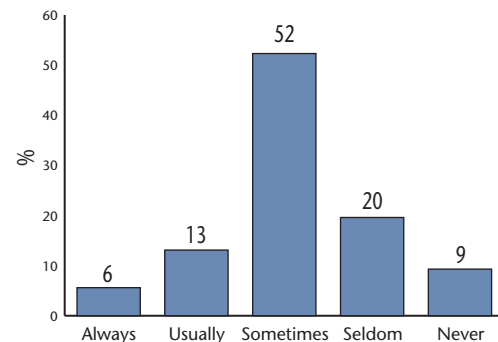
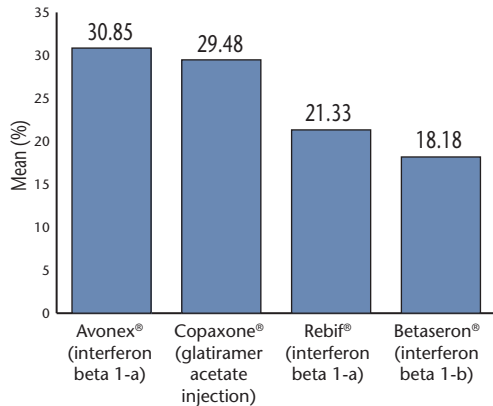


Figure 28. Of the five immunomodulators available, what percentage of your MS patients are on each?



Approximately 30% of the respondents' patients obtain their injectable immunomodulatory drug therapy from retail pharmacies; 31% obtain these agents from traditional mail order pharmacies. Nearly 40% receive self-administered immunomodulators from specialty pharmacies.

Most of the neurologists surveyed (95%) use infused corticosteroids to treat MS. Most steroid therapy is used to treat acute relapse; however, respondents estimated that they also prescribe corticosteroids on a periodic or scheduled basis for 9% of their patients. More than 70% of the respondents said they seldom or never encounter reimbursement difficulties when prescribing infused corticosteroids (Figure 29). Those who do encounter difficulties usually appeal the decision (54%).

Many respondents said they provide infused corticosteroids in a variety of settings. A quarter of those surveyed provide infusions in the hospital — both for inpatients and outpatients — and at home; 20% make infusions available at their clinic or office.

Most respondents (97%) prescribe speech, physical, or occupational therapy for their patients with MS. Almost one-third (32%) sometimes experience difficulties in obtaining coverage for prescribed PT/OT/speech therapy, while 45% and 16%, respectively, seldom or never do (Figure 30). These difficulties most commonly involve limits on coverage (71%) (Figure 31); 75% of respondents said they usually appeal a decision that restricts coverage.

Just over half the neurologists (51%) surveyed reported that plans sometimes attempt to restrict

Figure 29. Do you encounter difficulties with carriers in obtaining reimbursement for infused corticosteroids?

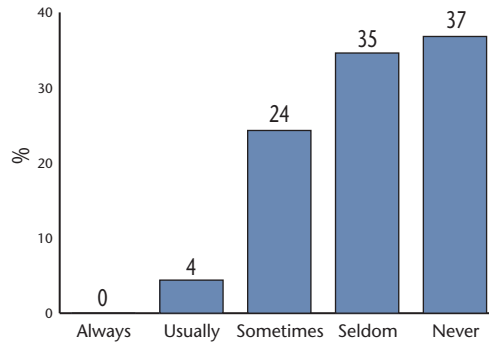


Figure 30. Do you encounter difficulties with carriers in obtaining coverage?

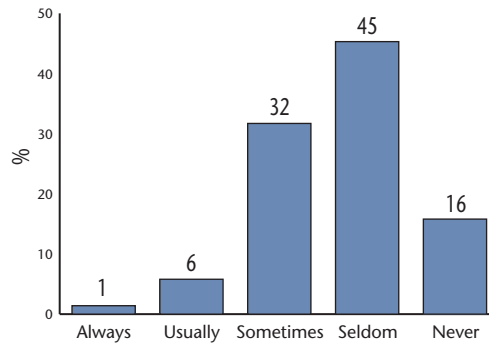
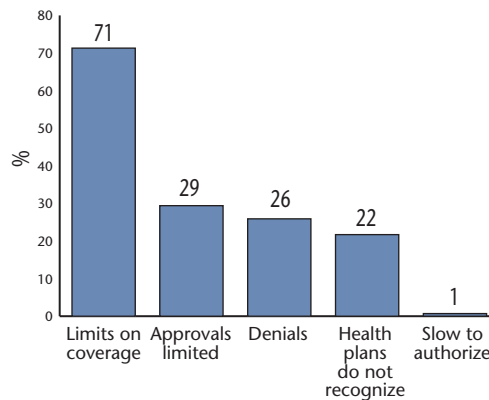


Figure 31. What kinds of difficulties do you typically encounter?

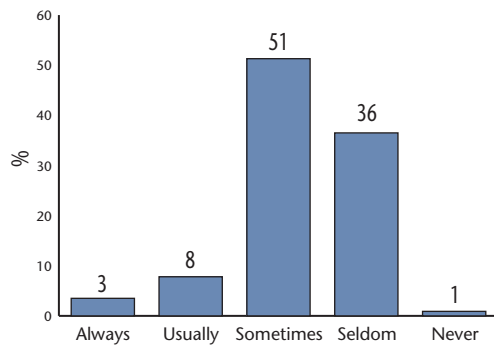


PT, OT, or speech therapy; 36% said that plans seldom attempt to restrict the use of these services (Figure 32).

MANAGING MS

Figure 33 represents methods of assessing the efficacy of immunomodulatory therapy for patients with MS. In a multi-response question, 28% of respondents said they use the EDSS scale. Respondents more commonly perform

Figure 32. How frequently do plans try to restrict the use of PT/OT/speech therapy?



neurological exams (57%), obtain serial MRIs (78%), or see patients on a regular basis (87%) to judge the efficacy of immunomodulatory treatment. Figure 34 represents the range in percentage of MS patients for whom survey respondents are able to complete an annual EDSS assessment.

Respondents were asked about their possible use of a patient self-assessed EDSS in place of the physician-completed EDSS. Eighty-six percent said they would use such a self-assessment tool if one were available (Figure 35). This result appears to highlight the importance of periodically assessing the progression of disability while acknowledging the difficulty and time involved in employing the physician-rated EDSS or similar measures.

Only 13% of the respondents have access to a central databank (electronic medical records) to track the clinical status of their MS patients.

Seventy-five percent of the respondents said they rely on medication to treat MS patients with bladder dysfunction; 25%

refer patients to urologists for specialty care. For bowel dysfunction or MS-related bowel symptoms, 38% of the respondents prescribe medications for their patients; 17% refer patients to a gastroenterologist; 14% urge the use of dietary modifications and fiber; and 9% advocate bowel training.

Thirty-four percent of the respondents prescribe drugs for erectile dysfunction, while more than 25% prefer other medications; 32% refer patients to counseling or educational services or to behavioral therapy for sexual dysfunction, a problem commonly encountered by patients with MS.

For the treatment of spasticity, 54% of the physicians surveyed choose baclofen (an additional 3% recommend use of a baclofen pump); 17% prescribe Zanaflex® (tizanidine hydrochloride) and 7% recommend Botox® (Botulinum Toxin Type A). An additional 17% advocate the use of physical therapy, exercise, stretching, and massage.

More than two-thirds of the respondents indicated that they treat their patients' depression themselves in most cases, while 22% refer their patients to counseling services, psychotherapy, or other specialists. Treatments of choice include various antidepressants; 30% of the respondents prescribe selective serotonin reuptake inhibitors (SSRIs), such as Prozac® (fluoxetine hydrochloride) or Zoloft® (sertraline hydrochloride), and 9% choose other, unspecified antidepressants.

Respondents prefer certain treatments for MS neurogenic pain. Fifteen percent prescribe Neurontin® or its generic equivalent, gabapentin;

Figure 33. What techniques do you use to assess efficacy of immunomodulatory therapy?

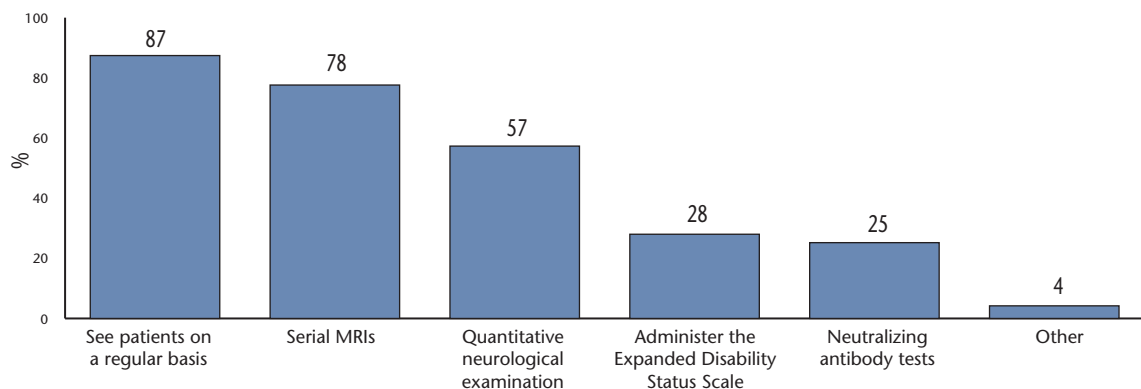


Figure 34. What percentage of your MS patients have you performed an EDSS for at least once in the past year?

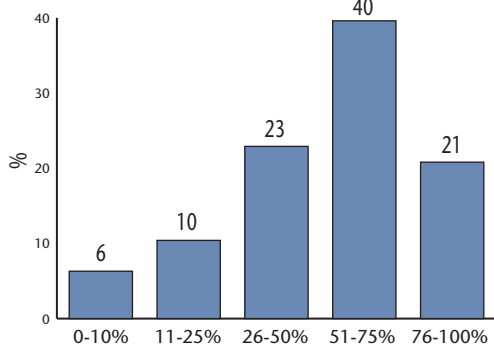
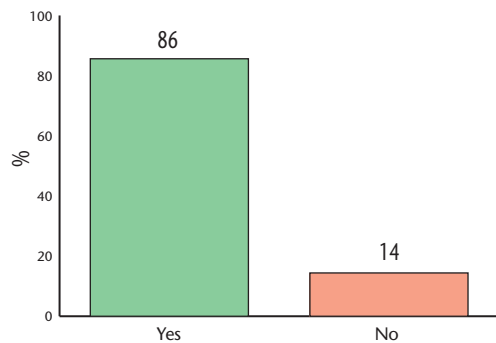


Figure 35. If a patient self-assessment EDSS tool were available, would you use it?



3% refer their patients to pain management services.

Overall, the neurologists surveyed do not feel that patient compliance is a significant problem in the treatment of MS patients (Figure 36).

In open-ended responses, physicians said they use patient education, frequent follow-up, counseling, family support, and an MS nurse or an interdisciplinary team, among other strategies, to improve patient compliance.

Asked if they rely on a patient's primary care physician (PCP) to manage non-MS-related illnesses in their patients with MS, 29% of the respondents said they always do; 44% said this is their usual practice; and 19% said they sometimes do. Less than one percent responded "never." For MS patients who have no PCP, about half the respondents reported that they assume this role (Figure 37).

The wide variety of symptoms that typify MS make it difficult to manage, but improved

Figure 36. How much of a problem is patient compliance with regard to treatment of MS symptoms?

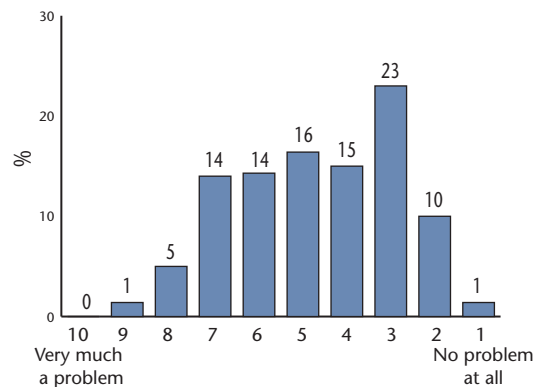
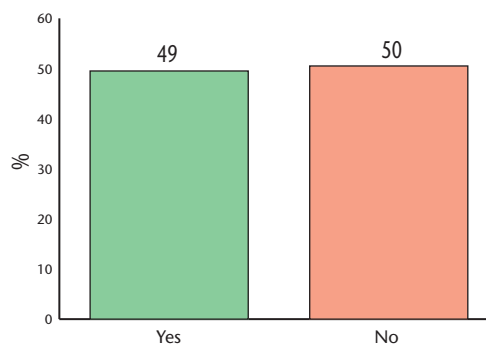


Figure 37. For those patients who do not have primary care physicians, do you typically handle non-MS-related illnesses?



management is required to minimize the clinical, financial, and social impact of the disease. One very important symptom is depression. Many valid tools exist to assess depression, but most of the neurologists surveyed (82%) do not use a standardized tool for this purpose.

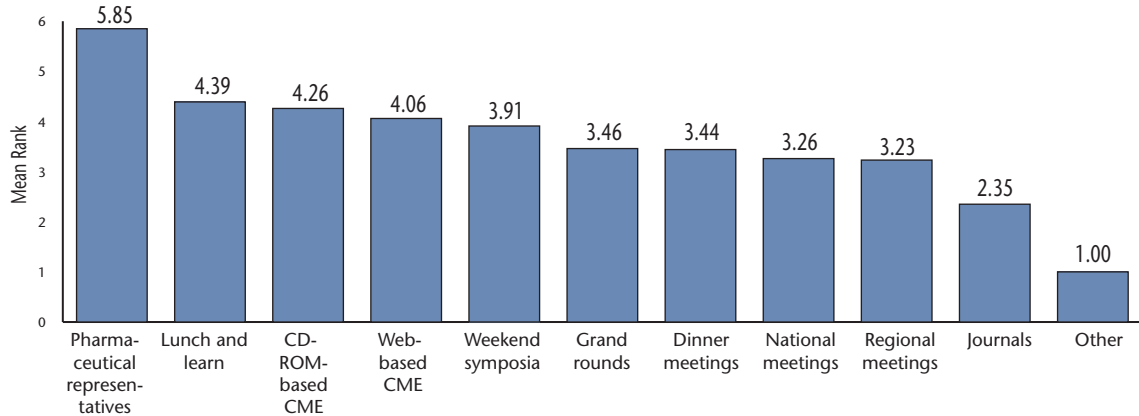
Similarly, only 13% of the respondents use a standardized form with which patients can regularly self-report their MS symptoms.

COMMENTARY

Neurologists indicate that they not only determine the course of disease-modifying therapy for their patients with MS, but that in more than two-thirds of cases, they determine the course of therapy for MS symptoms, rather than refer their patients to a specialist. When necessary, they also assume the role of PCP.

Given these myriad responsibilities, it is often impractical for neurologists to use complex, time-consuming tools like the EDSS.

Figure 38. What is your preferred mode of continuing education? (1 = most preferred)



Neurologists already receive only limited reimbursement for the time they devote to managing treatment for patients with MS.

DAY-TO-DAY PRACTICE TRENDS

The final survey questions addressed the daily care and management of MS patients. Responses reflected neurologists' desire to effectively care for their MS patients, along with their practice preferences and the challenges encountered in treating individuals who have been diagnosed with MS.

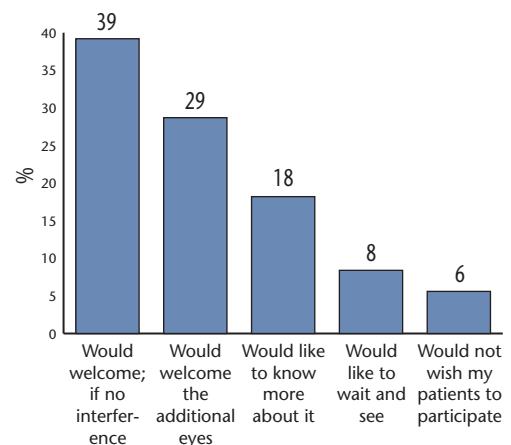
Respondents spend an average of 3.5 hours per week on continuing medical education. Journals, regional and national meetings, and grand rounds are preferred learning venues (Figure 38).

When considering the “profitability” of caring for MS patients in comparison to caring for other patients in their practice, neurologists acknowledged that, in general, working with MS patients is less profitable. In indicating their level of satisfaction with reimbursement for MS care by commercial carriers, a total of 66% of respondents chose the number 5 or below on a scale of 1 to 10, with 10 representing “very satisfied” and 1 representing “very unsatisfied.”

Sixty-four percent of the neurologists surveyed would prefer not to take on more MS patients.

More than two-thirds (68%) of the respondents would welcome a specialty pharmacy program to assist them in managing the treatment of their MS patients (Figure 39). A description of a hypothetical program of this kind follows the figure.

Figure 39. How would you view a program administered by specialty pharmacies?



Therapy Optimization Program

Administered by specialty pharmacy distributor case managers or pharmacists who, while arranging the mailings of a patient's medication, periodically call the patient to inquire about or make recommendations on the following:

- MS symptoms
- Relapses
- Changes in disability
- Depression
- Compliance
- Routine preventive care, such as flu shot reminders
- Assistance with reimbursement from insurer
- Assistance with reimbursement if insurance is not available
- Communication with the neurologist

Neurologists are quite enthusiastic about this type of program, and many offered suggestions for its development. Here are a few examples:

- Involve neurologists in developing and assessing the program
- Make the program noncommercial; assess the motive of its sponsor
- Do not increase the workload of physician office staff
- Include a role for case managers
- Include people who are knowledgeable about reimbursement issues
- Eliminate the use of forms

CONCLUSION

Neurologists would favor the creation of therapy optimization programs, administered by specialty pharmacies and centered on the expertise of neurologists, case managers, and reimbursement professionals. In providing neurologists with screening tools for depression, tools for patient self-assessment, and access to case managers experienced in MS patient care, these programs could improve the management of MS treatment, in part by easing the time constraints many neurologists face in evaluating and treating MS patients.

Such programs could also increase educational opportunities for neurologists who treat patients with MS, because survey results show that neurologists prefer to continue their MS education through journals and meetings, including regional and national meetings and grand rounds.

This survey reflects neurologists' desire to effectively care for their MS patients despite the resource-intensive nature of such care, and despite the belief on the part of 30% of respondents that insurance carriers represent a barrier to treating their MS patients.

Because the efficacy of disease-modifying drug treatment for any given MS patient is determined primarily through regular appointments, clinical neurological evaluations, and serial MRIs, it makes sense that fewer existing barriers to claim coverage for such services would better enable neurologists to track disease progression and symptom management among their MS patients.

The neurologist survey reveals that most of the respondents would prefer not to take on new MS patients. Alongside this outcome, it indicates that reducing barriers to diagnosis and treatment would enhance the ability of neurologists to provide their MS patients with the highest level and quality of care.

LACK OF TRAINING HURTS DOCTOR-PATIENT RELATIONSHIPS



*The Comments of Lisa I. Iezzoni, MD, MSc
Professor of Medicine, Harvard Medical School
Associate Director, Institute for Health Policy
Massachusetts General Hospital*

About 54 million Americans have some type of disability,* so it stands to reason that most physicians will see people with disabilities in their practices. However, physicians receive little training about how people with disabilities live their daily lives.

How does the lack of training affect doctor-patient relationships? Dr. Lisa Iezzoni addressed this issue in a perspective published in the *New England Journal of Medicine* in September 2006. She has conducted a Society-funded research project examining insurance issues and is now conducting a study of mobility aid use among people with MS. She brings an additional perspective to this question: she has MS.

** Cited in "The Surgeon General's Call to Action to Improve the Health and Wellness of Persons with Disabilities."
U.S. Department of Health and Human Services, July 26, 2005. Available at www.surgeongeneral.gov.*

This is what she has observed:

- Physicians tend to ignore their patients' disabilities. "It's the elephant in the room — present, but unmentioned," writes Dr. Iezzoni.
- Physicians tend to "medicalize" disability as an illness. They may focus on one problem and not the bigger picture of wellness and care.
- Physicians, like society in general, tend to marginalize people with disabilities and make uninformed assumptions. People with disabilities believe that physicians do not recognize that they can lead rich and fulfilling lives.

A Better Understanding

How can these obstacles to understanding be overcome? By talking. Dr. Iezzoni concedes that extra time for talk is harder to come by in the managed care environment. However, she believes her fellow healthcare providers can do better if they make no assumptions and instead ask questions. Better communication will increase a physician's knowledge and enhance the quality of medical care, she stressed.

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*The Comments of R. Philip Kinkel, MD
Director, Multiple Sclerosis Center
Beth Israel Deaconess Medical Center
Associate Professor of Neurology
Harvard Medical School*

Emotional distress and adjustment disorders are common in MS and tend to occur in response to the perceived loss or threat that patients experience mainly at the time of diagnosis, at times when symptoms become persistent rather than intermittent, and with the development of significant disability. Major affective disorders, such as depression, anxiety/panic disorder, and bipolar disorder, are observed more often in MS than in other chronic diseases. This is best characterized in studies that reveal a lifetime prevalence rate of major depression of approximately 50 percent. Imaging studies suggest that involvement of certain regions of the brain by MS may account for the increased rate of depression in this condition compared to other chronic and disabling conditions. However, identification of these major affective disorders in MS may require extra vigilance. This is due to the overlap often observed between symptoms of affective disorders, particularly major depression, and common MS-related symptoms such as fatigue, diminished attention and concentration, and pain. Physicians should have a very low threshold for exploring emotional issues, referring patients to a psychologist or neuropsychologist and initiating treatment.

Emotional lability, so-called pathologic laughing and crying, is less common than depression, but equally disabling. This tends to occur with extensive frontal lobe white matter disease.

SURVEYING THE RESULTS



The Comments of Ben W. Thrower, MD

Medical Director

Shepherd MS Institute

Atlanta, GA

“The neurology survey results provide some interesting perspectives on the management of MS in the community setting. We know that caring for the person with MS is time-consuming and that it is usually not a money-making proposition,” says Dr. Ben W. Thrower, medical director of the Shepherd MS Institute in Atlanta. Noting that nearly three-quarters of surveyed neurologists have seen stagnant or declining incomes, Thrower adds that “these two factors may explain why two-thirds of surveyed neurologists have no desire to see higher numbers of MS patients.”

The group of community neurologists surveyed indicated with some of their responses that they are likely to be representative of their peers. Most of their MS patients fall into the relapsing-remitting category. The two most commonly prescribed immunomodulatory therapies were reported as Copaxone® (glatiramer acetate injection) and Avonex® (interferon beta-1a). “These findings are consistent with national trends in terms of MS categorization and treatment,” notes Thrower.

“Some of the findings on monitoring efficacy of therapy were a little surprising to me. The use of serial MRIs by 78% and of EDSS by 28% were both higher than I expected,” Thrower says. As of yet there is no consensus on the use of routine MRI in monitoring MS. The EDSS takes longer to perform and score than a typical brief neurological exam, adding to the time already needed with the MS patient. “These numbers are actually encouraging to me,” says Thrower. “I would argue that the use of serial MRI may prove valuable in identifying suboptimal responders to therapy, especially in individuals who appear clinically stable. Serial MRI may also help determine which patients are non-adherent to therapy,” he adds.

Survey results may have also pointed out areas for improvement in MS care. “Only 16% of respondents use physical therapy, exercise, and stretching in the management of spasticity, while the majority used Lioresal® (baclofen) and Zanaflex® (tizanidine hydrochloride). Stretching, exercise, and physical therapy really should be the first line of spasticity management,” says Thrower. Similarly, only 14% of neurologists surveyed suggest dietary modifications and fiber for the management of MS-related bowel symptoms.

In summary, notes Thrower, “Surveys such as this one may provide needed information about the way MS is managed.” Most MS care in the United States is given in the community setting, not in a comprehensive MS center. Understanding the trends in community MS care and the potential challenges, Thrower believes, may help MS centers, specialty pharmacies, pharmaceutical companies, and MCOs partner more effectively to provide optimal comprehensive medical management of the person with MS.



Neurology Reimbursement and Coding

The survey on neurology reimbursement and coding as they apply to MS indicated some improvements in communications between providers and MCOs while illuminating obstacles to better service for patients with MS. Many providers face a range of difficulties in obtaining payments from MCOs for the treatment of patients with MS, and close to a third of providers say that most of their contracts with MCOs do not make a profit. The majority of providers experience difficulties when contacting managed care representatives for answers to billing questions. MCOs, in turn, may need to articulate the constraints they face in processing requests from providers. While demonstrating that some progress has been made, the survey of 68 coding and reimbursement staff from doctors' offices highlights many areas in which an exchange of information and ideas might lead to streamlined systems and reduced costs both for providers and for MCOs.

OVERVIEW

Fifty-four percent of survey respondents maintain solo neurology practices, while 46% practice in a group setting. These practices employ an average of three full-time neurologists, five non-clinical administrators, and between two and three full-time billing employees. Most practices surveyed (79%) do not use a billing service.

Respondents said that most (91%) of their patients pay part or all of their bills through their insurance. These numbers have not changed significantly over the past two years. Capitated agreements, which cover 28% of patients, have increased 3% from two years ago.

Most respondents (69%) reported some improvement in their interactions with MCOs; for example, claims are paid faster and with greater accuracy. However, 31% reported no improvement in the payment of claims. Fifty-three percent said that when they have to file a paper claim, the claim frequently is not paid because the carrier states that it was never received. Eighty-five percent of respondents indicated some level of difficulty in obtaining answers to their questions when they place phone calls to managed care representatives.

Nearly 59% of survey respondents reported that most of their contracts with MCOs make a profit; 29% said they do not; and about 12% said they don't know (Figure 40).

Sixty-nine percent of respondents said they know how much each plan should pay, and that they get paid correctly; 23% know the allowables but do not know if they are paid correctly. Seven percent have no familiarity with the fee schedule allowables for their plans (Figure 41).

More than half of the respondents (53%) reported success in appealing incorrectly denied claims; 39% said it's hard to say what happens because the carriers are inconsistent.

Figure 40. The majority of contracts we have with managed care plans are:

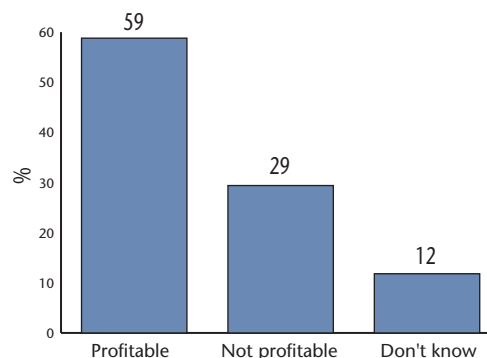
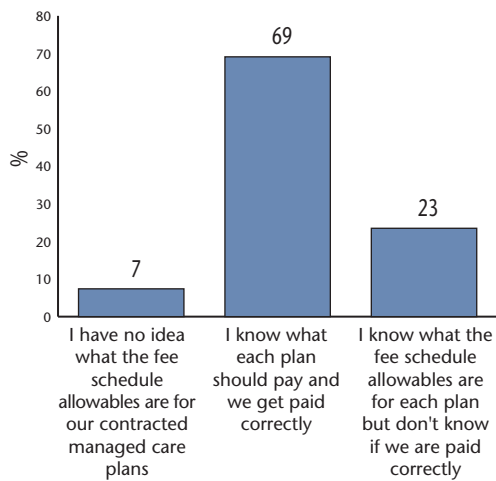


Figure 41. Which of the following is most true?



RESULTS

Fifty-nine percent of those polled listed Medicare as the best health plan for timeliness and adequacy of payments, percentage of claims paid cleanly on the first pass, and customer service. Forty-three percent indicated that most of their managed care contracts pay at the same level as Medicare; 22% reported that most of these contracts reimburse at levels below Medicare. A third noted that most of their managed care contracts pay above the Medicare fee schedule (Figure 42).

Responses show that, on average, half of non-drug treatments require prior authorization by managed care plans; of that number, 13% are denied. Similarly, 54% of survey respondents indicated that MCOs request prior approvals for drug treatments and that 12% of those are denied.

Sixty percent of respondents said that managed care companies should increase payment allowables for neurological assessments such as electromyography and nerve conduction studies. Twenty-nine percent said that MCOs should increase payments for evaluation/management visits; 10% said that reimbursement for drugs and for supplies should be increased (Figure 43).

Forty-seven percent of the respondents try to negotiate fee schedules with contracted carriers and are sometimes successful; 26% never negotiate fee schedules; and 26% try to negotiate them and are generally unsuccessful (Figure 44).

Figure 42. Do you feel that the majority of your managed care contracts pay (eg, contract allowables) ...

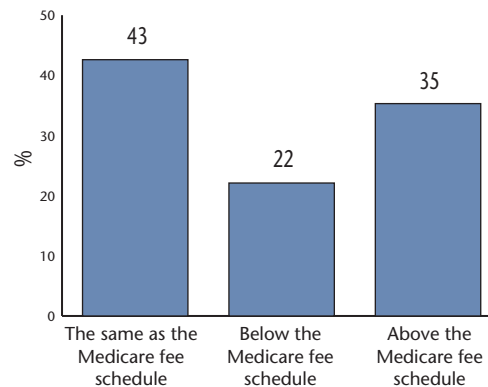


Figure 43. For which services do you feel the payment allowables should be increased?

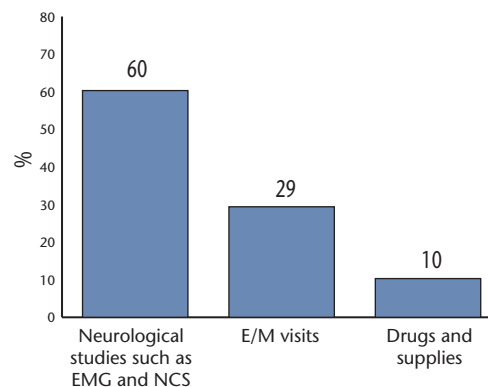
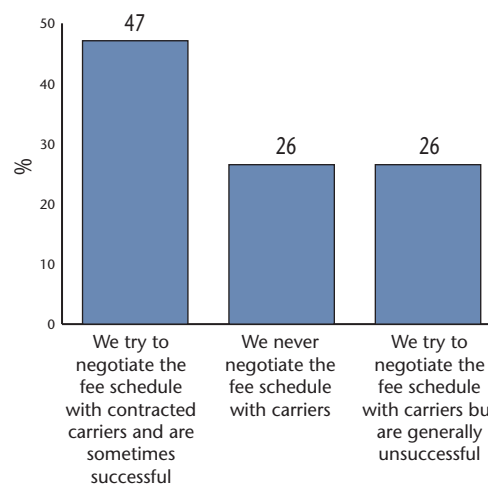
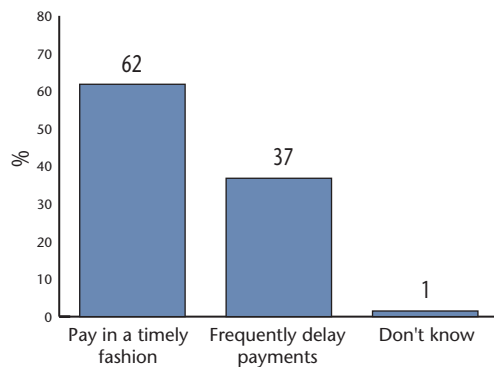


Figure 44. Which of the following is most true?



Eighty-seven percent of respondents indicated that most plans accept electronic claims; 62% said that most managed care plans they contract with pay in a timely fashion; and 37% said most of their plans frequently delay payments (Figure 45).

Figure 45. The majority of the managed care plans with whom we contract ...



Thirty-five percent of respondents said that most plans pay their claims within 30 days; 62% said they have to wait 31 to 60 days for payment. Three percent said they have to wait more than 60 days for payment.

More than half the respondents (53%) said that when they appeal an incorrectly paid claim, it usually gets paid; 38% said their carriers are inconsistent in regard to appeals for incorrectly paid claims. Nine percent said that MCOs regularly deny their appeals (Figure 46).

Forty-four percent of respondents reported easy access to their carriers' coverage policies and criteria for medically necessary services. Thirty-seven percent said their carrier is inconsistent in regard to these issues; 19% said they do not know how their carriers make decisions with respect to these provisions (Figure 47).

When asked about the best way to access carrier information, 15% of respondents said there is no easy way to access information on such matters as policies and documentation guidelines. Thirty-eight percent said the best way to access carrier information is by contacting a carrier representative; 35% go on the carrier website for such information; and 12% consult carrier bulletins and provider manuals (Figure 48).

Fifty-seven percent of respondents said they are frequently kept on hold for 15 minutes or longer when calling a representative of a managed care plan. Nineteen percent said they leave a message and hope the carrier calls back. Almost 9% said there is no way to speak with anyone directly; 15% said they easily reach a representative on the phone (Figure 49).

Figure 46. When I appeal an incorrectly paid claim, it is usually:

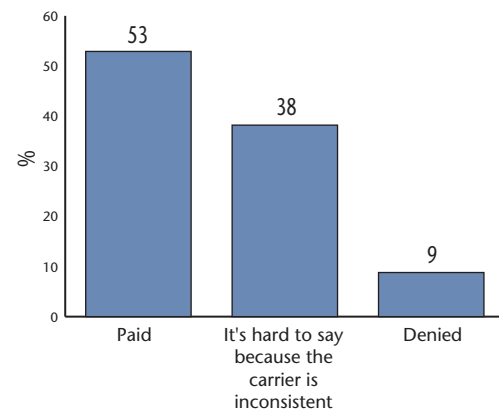


Figure 47. Regarding coverage policies and providing medically necessary services, the following is most true:

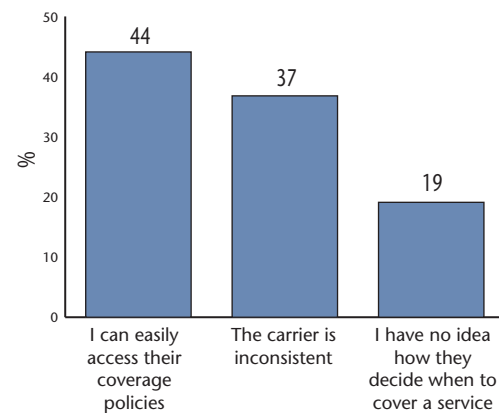
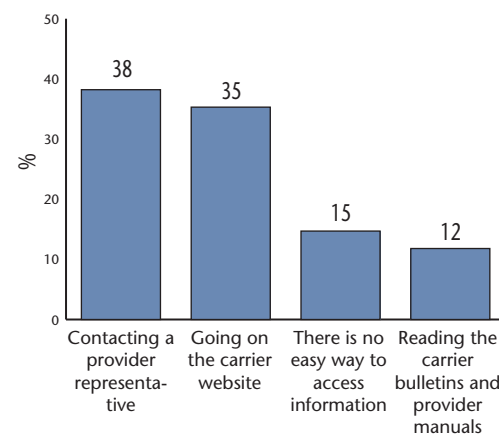
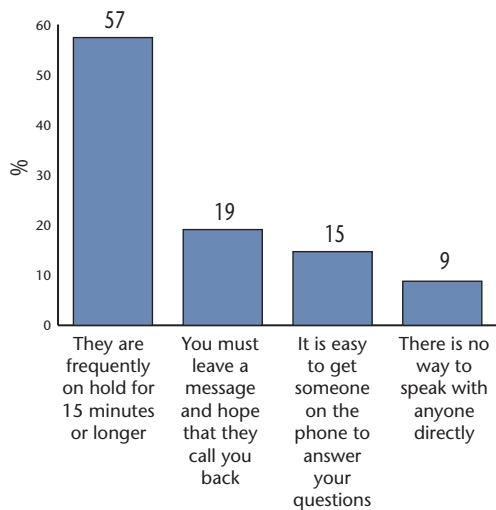


Figure 48. The best way for staff to access carrier information (policies, documentation guidelines, etc.) is by:



Sixty percent of respondents said that information given over the telephone by their carrier is generally reliable; 30% said that

Figure 49. When staff need to speak with a representative from a managed care plan:



provider representatives frequently dispense incorrect information on the phone. Another 10% said that contacting their carrier is unproductive and so they rarely try.

Seventy-two percent of respondents said they take the extra step of requesting a hearing if they do a review of a claim appeal and it is denied. Twenty-five percent said they must accept the ruling of the managed care company, as their practice has no other recourse. Three percent of the respondents were unfamiliar with the due process.

Most respondents (81%) verify patient eligibility online; 75% said they verify claim status online. Over half (55%) noted the complexity of the credentialing process for new providers, and 77% said the credentialing process for new providers takes too long. Fifty-eight percent said that obtaining a referral or authorization is easy for their managed care patients, but 43% noted difficulties in this regard.

New patients wait almost three weeks for an appointment on average, while established patients wait just under two weeks. Despite new patients' wait times, only 21% of neurological practices surveyed plan on adding a PA or NPP (non-physician provider) to their staff.

Twenty-nine percent of practices surveyed employ at least one PA or NPP. Almost two-thirds (65%) noted that in order to bill for tier services, PAs and NPPs must be personally

credentialed with MCOs. Twenty-five percent said that contracted carriers do not recognize these physician extenders for purposes of billing.

Forty percent of respondents said that managed care organizations reimburse PAs and NPPs at the same rate as MDs or DOs.

Forty-five percent described the process of billing managed care plans for physician extenders as easy; an equal number said that the level of billing difficulty varies by plan. Ten percent said the process is complicated.

COMMENTARY

Although survey results demonstrate recent improvements in managed care reimbursement, respondents say there is room for improvement in communication between neurology practices and managed care organizations.

Many neurology practices continue to face challenges in the profitability of their contracts, the appeal of claim denials, and the negotiation of contracts. Easier access to information, quick and simple answers to questions, and better access to customer representatives would facilitate improved relations between MCOs and providers, along with other steps to streamline processes and increase transparency.

CONCLUSION

Improved communication is the key to better relationships between neurology practices and MCOs. Better exchange of information may increase profitability on both sides. Less than satisfactory communication sometimes leads neurology practices to conclude that they are being overlooked or ignored by MCOs. For example, neurologists need to understand why MCOs have difficulties with paper claims, many of which are reportedly never received. Neurologists need a more detailed explanation of claim denials, and they need MCOs to better explain how to successfully refile a previously denied claim.

Neurology practices may be unaware of the limitations faced by some MCOs, including the time needed to implement the changes required to attain or retain profitability. However, managed care needs to do more to understand why neurology practices find

their communication with MCOs burdensome, especially in obtaining answers to questions from managed care representatives and in trying to streamline referral and reimbursement processes. More open and consistent communication between providers and MCOs should foster a smoother relationship that, in the end, will reduce obstacles to profitability for both and will ultimately benefit the lives

of MS patients. Better communication is only the first step, however, and both parties must compromise and cooperate to improve services for patients.

BRINGING CONSISTENCY TO THE MIX



*The Comments of Michael Kaufman, MD
Medical Director
Multiple Sclerosis Center
Carolinas Medical Center
Charlotte, NC*

The survey data in the *Multiple Sclerosis Trend Report: Perspectives from Managed Care, Providers, and Patients* seems to illustrate a lack of uniformity in the ways in which many MCOs handle customer service telephone inquiries, according to Dr. Michael Kaufman of the Multiple Sclerosis Center at the Carolinas Medical Center in Charlotte.

What strikes Kaufman is that “calls are not monitored for uniformity” in the same way in which calls within his own MS center are followed. “All calls between physicians and other physicians or patients that are handled through our answering service are overseen and reviewed internally,” he says.

“Every single call is monitored and routinely listened to by administrators here,” Kaufman explains. Staff gets called in the next day and told if a call wasn’t handled properly, he adds.

As for claim review and reimbursement, Kaufman notes that he is usually successful in his efforts to appeal a claim on behalf of a patient, but not before making a personal call to an MCO’s medical director.

“Usually I can be successful, but what’s odd is that I may be talking to a medical director who is a cardiologist, or a neurologist who specializes in epilepsy,” Kaufman points out. “The person making the decisions is often very unsophisticated” in his or her knowledge of MS, he adds. But once Kaufman makes contact with the medical director and discusses a particular patient’s claim rejection, he is rarely turned down, he says.

Kaufman cites the example of a medical director who defended a rejected claim on the basis that an MS patient had not had a spinal tap to aid in his diagnosis. When Kaufman asked if the insurer would approve a spinal tap and, assuming its result was positive, if that would make a difference, the medical director agreed to approve the previously rejected claim.

These kinds of appeals are very labor intensive, Kaufman notes, and time could be better spent treating patients than by enlightening medical directors about the details of multiple sclerosis on a patient-by-patient basis.

“What I think would be really helpful is for the industry to hire a group of consultant medical directors” or to partner with organizations like the National Multiple Sclerosis

Society and patient advocacy groups to keep pace with changes occurring in the utilization of therapies, Kaufman suggests.

For example, if the managed care industry had an expert panel on MS on which to rely, medical directors and others might make faster, more knowledgeable decisions when processing claims and reimbursements. In turn, administrative costs would be reduced, Kaufman believes.

In addition, the advent of new MS disease-modifying agents — many of which are in the pipeline and destined for eventual FDA approval — will make it even more difficult for those without more specific knowledge of MS in managed care settings to make decisions concerning approvals for drug therapies.

A perfect example is monoclonal antibody medications, such as Tysabri® (natalizumab) and Rituxan® (rituximab) — both of which are administered by infusion. Natalizumab is FDA-approved, but only in certain cases, and rituximab (currently in Phase III clinical trials) is exhibiting Phase II data that makes it an appealing choice for patients who have failed other therapies, according to Kaufman.

Insurers may deny either of these MS drug therapies — and steer MS patients toward injectable drugs — because such infusible medications tend to be almost twice as expensive as injectable MS drug therapies.

But MS neurologists who treat a greater number of MS patients regularly are familiar with these drugs and their potential benefits, as are doctors who are connected with the NMSS. These physicians know what MCOs often do not — that although this class of drug may be more expensive, it may be administered, and therefore billed, at a less frequent rate, and its potential benefits in delaying disease progression may result in future cost savings in MS patient care.

This is the case with the infused drug Novantrone® (mitoxantrone for injection concentrate), which has a maximum dosage of 100 to 140 milligrams per meter squared, owing to potentially harmful long-term side effects. Mitoxantrone costs twice as much as most injectable MS drug therapies, and like rituximab, another intravenously administered treatment that may be approved for use in MS, it can be administered as infrequently as two to four times per year.

The promise of these potentially toxic and developing treatments to better prevent disability in MS may materialize in savings in expenditures for ancillary care and in prolonged productivity for patients with MS. Injectable therapies are less expensive than these agents in the short term, but may prove to be less cost-effective in the long term.

“We need to rely on the people who do this the most,” such as MS specialists, Kaufman emphasizes. “Insurance companies are making rules, patient advocacy groups are making rules, and physicians are trying to make judgments — all without much consistency,” he says.

Kaufman agrees with managed care that certain items have to be validated periodically, but not each and every time a claim is filed. In addition, explanations for claim rejections are rarely forthcoming without a time-consuming phone call to a medical director.

Drugs for MS symptom management, such as Provigil® (modafinil) for MS-related fatigue, are routinely denied by certain MCOs, while other MCOs have no problem approving them. “This is a drug we find very helpful in combating MS-related fatigue” among patients, Kaufman notes, and managed care should provide a more consistent explanation for its denials.

“There is a reason to practice cost-effective medicine,” particularly in the realm of treatment for MS patients, Kaufman says. “In my area, insurers have come a long way, as we used to have more denials than we do currently,” he notes. But better education of medical directors through the advice and experience of the NMSS and MS center physicians — who provide “the bulk of the care to MS patients — will be a more cost-effective and more efficient method” with which to best serve both MS patients and managed care organizations in the future, Kaufman concludes.



*The Comments of Lisa I. Iezzoni, MD, MSc
Professor of Medicine, Harvard Medical School
Associate Director, Institute for Health Policy
Massachusetts General Hospital*

A survey of 983 U.S. residents nationwide with MS, ages 18 through 64, suggests that financial and health-plan-policy-related concerns significantly affect their access to disease-modifying medications. Research in other diseases documents that increasing medication costs that patients themselves must pay can decrease patient adherence to prescribed drug regimens. The concern is that this might also happen for people with MS who could potentially benefit from these expensive, disease-modifying drugs. Even persons with health insurance coverage may have trouble affording their MS medications. Furthermore, our survey findings suggest that dealing with financial and other insurance policies may compound the stresses already confronting persons with MS.*

** Iezzoni LI, MD, MSc; Ngo LH, PhD. Health, disability, and life insurance experiences of working-age persons with multiple sclerosis. Multiple Sclerosis 2007;13:534. Iezzoni LI, MD, MSc; Ngo LH, PhD; Kinkel RP, MD. Working-age persons with multiple sclerosis and access to disease-modifying medications (survey). April 2007.*



*The Comments of June Halper, MSCN, ANP, FAAN
Executive Director, Consortium of Multiple Sclerosis Centers
Founder, MS Center, Teaneck, NJ
Founder, IOMSN*

The following are important issues in MS: There is a shortage of neurologists coming into the MS field; numerous nurses are leaving the field of MS care. These positions remain empty. We don't have another generation of care providers coming along. A lot of this has to do with poor reimbursement for the amount of care we're providing. New patients require neurological expertise, nursing, counseling, and rehabilitation services, and the care we provide far exceeds the reimbursement we receive. The amount of work required for one patient is extraordinary. A private neurologist with a small staff is challenged by the needs in MS. Another real issue is the people with more progressive MS. People with progressive MS require frequent monitoring and reassessment that may not be covered under their insurance.



Specialty Pharmacy

Specialty pharmacies are playing an ever-increasing role in managing and dispensing medication for those rare or chronic diseases that are treated with expensive targeted and biologic therapies, such as MS. They supply drugs directly to patients and provide a more intense level of patient contact than a retail setting would typically offer. Pharmacists, nurses, and other professional clinical staff advise and monitor patients via telephone and mail, develop web-based patient education and support programs, and even provide in-home administration for certain drugs. Such services, referred to in the industry as “high touch,” increase both the cost and the efficacy of therapy. Some manufacturers of complex biologic products have designated specialty pharmacy as their preferred distribution method in order to gain control over the storage and administration requirements of these products.

In providing education on medication usage, side effects, disease progression, and reimbursement to this comparatively well-educated patient sector, specialty pharmacies aim to address barriers to successful MS therapy. They also provide management programs for payers and manufacturers, including prior authorization and strategies for maximizing patient compliance and adherence.

Specialty pharmacy companies have grown rapidly and are in a massive wave of consolidation, which encompasses related industries such as pharmacy benefit management (PBM) and home infusion companies. As a result of this consolidation, MS patients are currently being served by many different models of specialty pharmacy, with varying management philosophies.

The survey questions that follow address the practices and attitudes of people who work in specialty pharmacy. Nineteen professionals in this sector responded. The impact of several years of consolidation currently limits the ability to obtain a statistically large enough sample of qualified participants for this trend report. Therefore, this section of the report covers only general trends, and draws general conclusions about the involvement of specialty pharmacies in managing MS.

OVERVIEW

On average, respondents to the specialty pharmacy survey have about seven years of experience within this industry; several have more than 15 years of experience. Most respondents (63%) represent companies that do business nationally; the rest work with organizations that serve the Midwest, Southwest, Northeast, Mid-Atlantic, Southern, and Western regions of the United States (Figure 50).

About half (47%) of the respondents reported that their pharmacy contracts directly with MS drug manufacturers (Figure 51). Forty-two percent of the respondents stated that a pharmacy benefit management company owns their pharmacy, reflecting the consolidation and vertical integration that is occurring within this industry. Only 5% of the respondents represent pharmacies that are owned by managed health plans directly. Thirty-seven percent of the respondents represent independent

Figure 50. What region(s) of the country does your organization primarily cover?

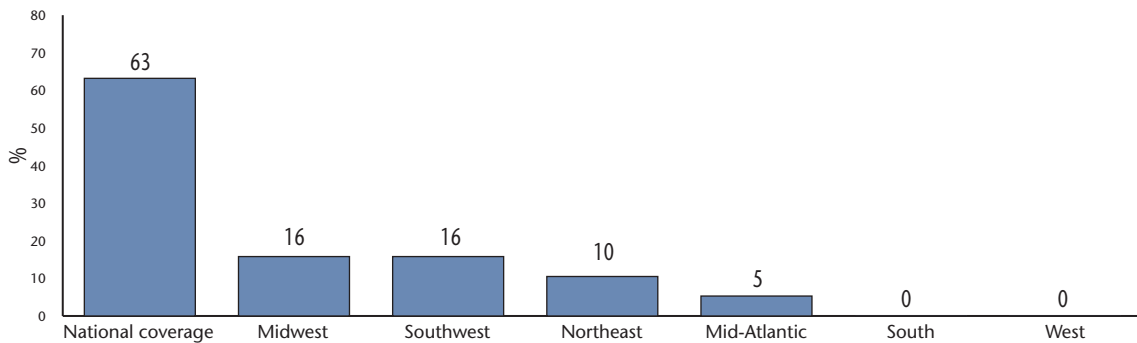


Figure 51. Does your pharmacy contract directly with MS drug manufacturers for pricing and rebates?

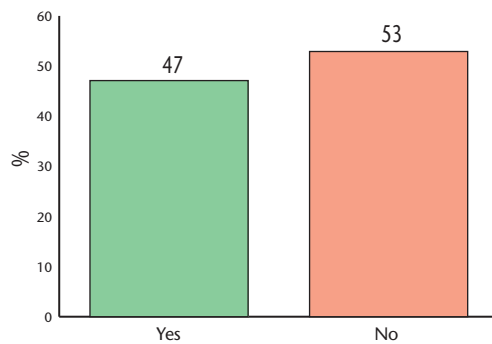
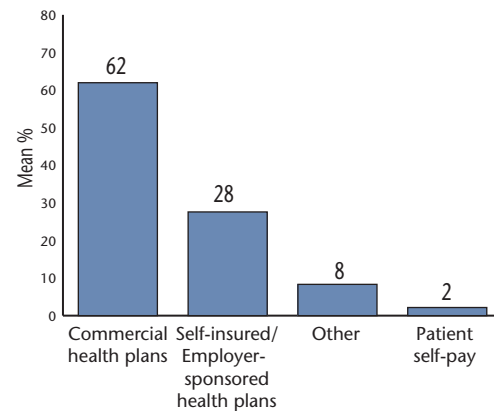


Figure 52. What is the distribution of your MS prescription revenues by source of payment?



specialty pharmacies. A few of the respondents represent specialty pharmacies that also operate neighborhood retail pharmacies, such as CVS.

RESULTS

The respondents reported that nearly 8% of all the prescriptions they fill are for MS. Most of the revenue generated by this drug category comes from commercial plans (62%), with most of the rest (28%) coming from self-insured or employer-sponsored health plans. Only 2% of revenue reflects patient self-pay (Figure 52).

The services that respondents' organizations offer reflect the personal nature of this complex set of drugs. Specialty pharmacies offer prior authorization assistance, coordination of benefits from multiple payers, help with patients qualifying for manufacturer- or government-sponsored benefits, overnight medication delivery, patient education services, indigent patient programs, patient insurance reimbursement support, 24/7 patient support, and nursing support to answer questions. Figure 53 lists some of these services.

Fifty-eight percent of the respondents reported that their organization contacts patients with MS every few weeks or every week (Figure 54). This frequency is comparable to the incidence of organizational contact for other chronic, degenerative diseases. Specialty pharmacy professionals confer most often with patients in regard to medication usage (84%) and side effects (79%), reimbursement (53%), disease symptoms (53%), and shipment issues (47%) (Figure 55). Survey respondents indicated that they discuss formulary with patients only 10% of the time.

Eighty-nine percent of the surveyed specialty pharmacies provide education services to members. Forty-two percent of specialty pharmacies surveyed now offer web-based education, in addition to the traditional phone-based education that most of the respondents (89%) said they offer.

Figure 53. Do you provide reimbursement support services, such as:

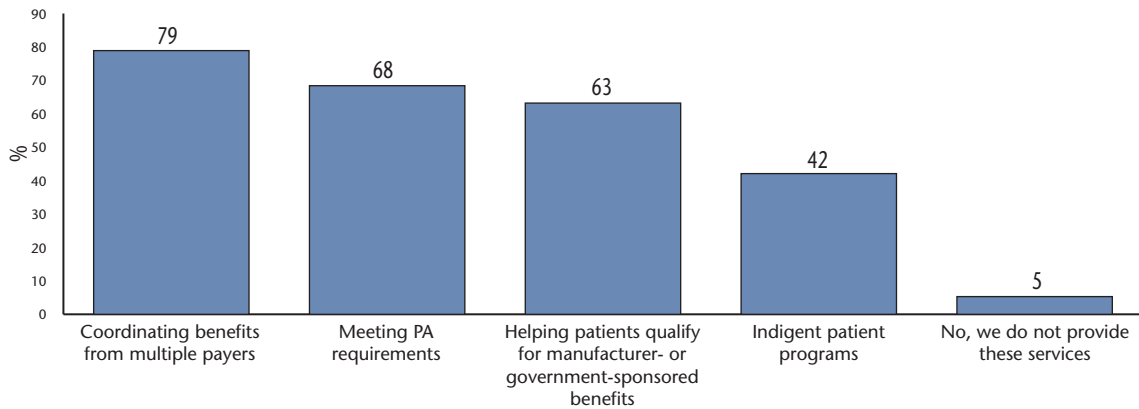
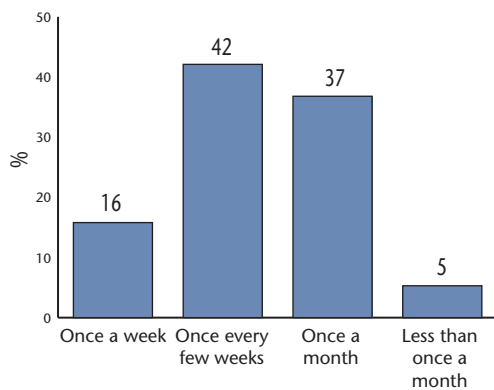


Figure 54. About how frequently does your pharmacy have contact with a given MS patient?



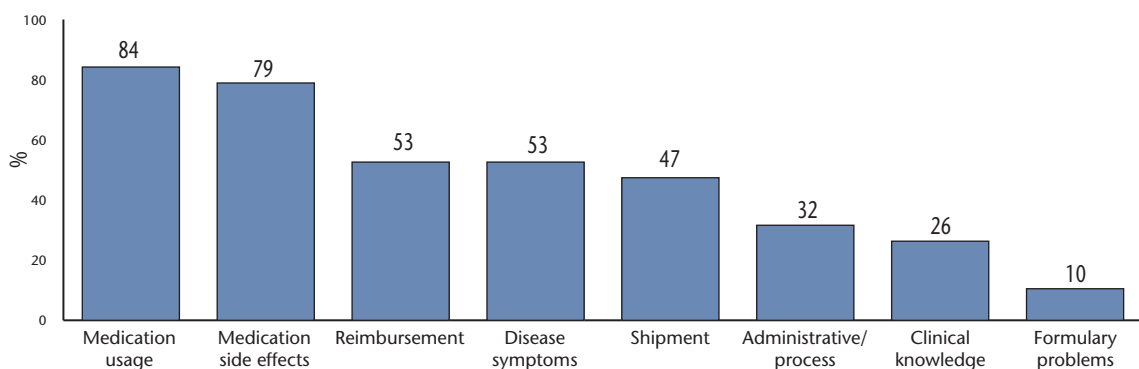
COMMENTARY

Coordination of reimbursement and other funding sources can be a major issue in MS care because of the high cost of some of the drugs used to treat the disease. As their disease progresses, MS patients often are unable to administer their own injections. Specialty pharmacy staff either go to the patient's home to administer the medication or play an active

role in training a rotating set of family members and unskilled or less skilled caretakers in the home setting. This type of training can keep disabled patients out of the nursing home much longer, which is desirable not only in terms of cost but for quality of life. Certain popular MS drugs must be refrigerated or mixed right before administration, or both. In such instances, untrained patients or caretakers may mistakenly believe they are compliant with medication instructions, and when storage or administration errors are made, the pricey drug is wasted. Manufacturers are eager to avoid this scenario because it will suggest both to doctors and patients that the drug is not working, when in fact it was rendered ineffective by improper storage or administration. Specialty pharmacies can glean more accurate and favorable outcomes data for manufacturers by assuring proper usage.

Nearly 80% of the respondents stated that their organization offers monitoring for patient compliance. This monitoring is fairly evenly divided between patients opting in (46%)

Figure 55. What issues arise most frequently during contacts with MS patients?



and patients opting out (54%). Nearly half of the 80% of respondents who have a patient compliance monitoring program said the data collected within these programs is shared with insurance health plans; 32% share the data with prescribing physicians, and 21% share the data with PBMs (Figure 56). Eighty-four percent of the respondents said their organization offers refill reminders or automated reordering, or both. Given the multitude of services offered by specialty pharmacies, nearly all of the respondents believe that their organization can add value to or enhance the ways in which MS specialists and neurologists deliver care to MS patients (Figure 57).

Nearly half of the respondents (47%) believe that patients are being forced into 90-day mail order pharmacy plans (Figure 58).

All pharmacies represented said they can fill the entire line of available MS products. Seventeen percent of the respondents said

Figure 56. With whom do you share results?

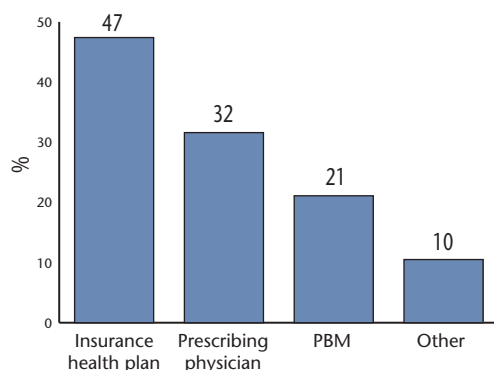


Figure 57. Do you believe specialty pharmacies can add value to or enhance the ways in which MS specialists/neurologists deliver care to MS patients?

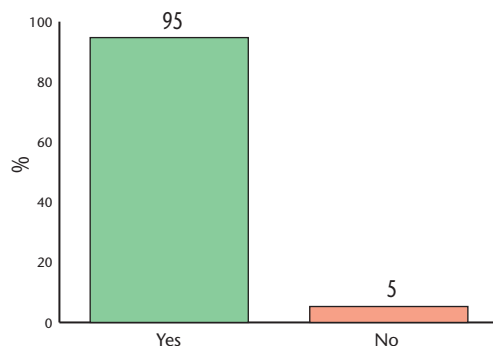
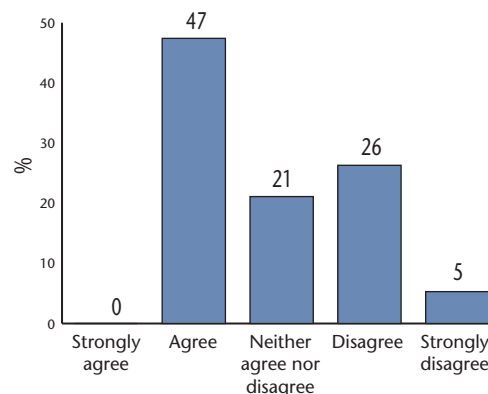


Figure 58. Indicate your level of agreement or disagreement with the following statement: In MS, more and more patients are being forced into 90-day mail-order houses.



their organization tries to move market share for manufacturers.

CONCLUSION

Representing 8% of all prescriptions, MS drugs are a key therapeutic category served by the specialty pharmacy industry. As this industry adapts to the wide-scale consolidation of recent years, it is embracing new technologies and data that will enable even tighter management of MS therapy costs. This will allow specialty pharmacies to better meet the needs of their managed care clients, which account for 62% of their MS drug revenues. At the same time, new capabilities and larger specialty pharmacy vendors are likely to drive improved patient access and product utilization, thereby elevating the value proposition of specialty pharmacy for all stakeholders in the MS realm.



Case Managers

Over the past several decades, case managers have fulfilled an ever increasing role in meeting our health system goals of improving quality of care and overall outcome and of achieving high levels of patient education and compliance for those with chronic conditions. This recognition has led to the inclusion of case managers in this trend report. A survey designed to assess the expertise, opinions, and demographic profiles of case managers involved in the management of patients with MS was distributed to the case management community.

The 101 respondents comprised a group of healthcare professionals with expertise in providing case management interventions in a managed care practice setting. The great majority of the respondents were registered nurses who have 15 years or more of experience in healthcare and who are familiar with the continuing care needs of chronically ill patients.

As treatment options for multiple sclerosis have expanded, hope for delay in disability has often been realized; at the same time, the associated costs of treatment have risen. These costs can strain the ability of patients to finance treatment and the capacity of managed care organizations to extend benefit coverage for MS services. Many MCOs, in trying to balance cost and quality of care, have adopted a case management approach for evaluating the treatment needs and goals of patients with MS. Respondents to the survey represented the full range of case management practice settings, from health insurance and managed care organizations to rehabilitation facilities and acute and ambulatory care.

OVERVIEW

Of the 101 case managers who participated in the survey, more than 77% identified themselves as registered nurses. Forty-four percent of the respondents have a baccalaureate degree in nursing, and nearly 8% have an advanced degree in nursing (Figure 59).

Sixty-two percent of the respondents have been practicing case management for more than 10 years; 87% have been working in a case management setting for at least six years (Figure 60). Nearly 88% of the respondents reported more than 15 years' experience in clinical practice, and 94% have been in clinical practice at least 10 years (Figure 61). More than 77% of the respondents said they have received certification in case management.

Most of the respondents (62%) practice in a health insurance or MCO setting. Twenty-four percent of the respondents practice in an acute care setting. Representation in the remaining

Figure 59. Which type(s) of healthcare degree(s) do you have?

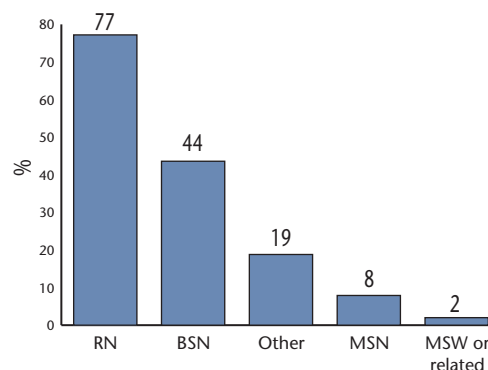


Figure 60. How many years have you been practicing case management (CM)?

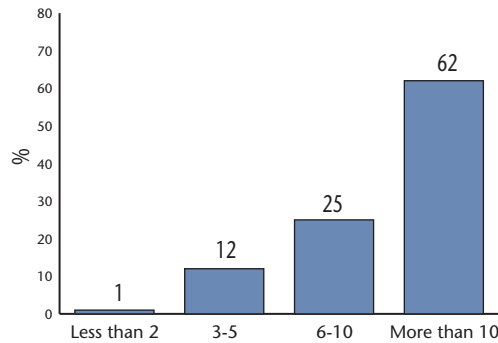
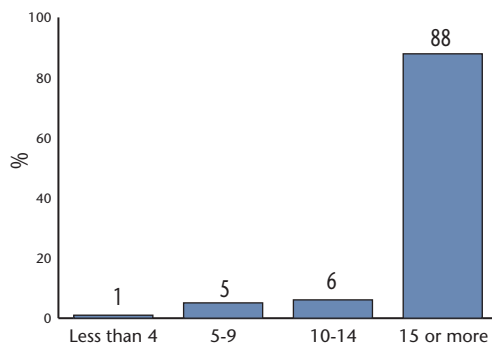


Figure 61. How many years have you been in clinical practice?

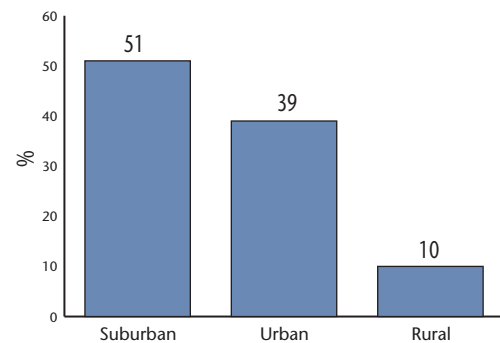


care environments drops sharply to 4% and below (Figure 62).

Respondents represented 33 U.S. states. The most common practice locale was suburban (51%), followed by urban (39%) and rural (10%) (Figure 63).

In parallel to the practice setting, 63% of respondents said their primary mode of contact with patients is via telephone; 31% of respondents said their practice consists

Figure 63. Which setting best describes your practice?



mainly of direct, on-site contact with patients; and 6% employ both means of contact more or less equally (Figure 64).

When asked to select the three most frequent diagnoses in their practices, respondents listed more than 90 diseases. The ten most frequently selected were diabetes (37%), cancer (28%), congestive heart failure (28%), chronic obstructive pulmonary disease (16%), coronary artery disease (12%), cardiovascular disease (12%), asthma (8%), cardiac disease (8%), multiple sclerosis (7%), and renal failure and stroke (7%). Seven percent of respondents listed renal failure and stroke.

Respondents indicated that they spend an average of 30 hours per week with patients (Figure 65). The median overall patient caseload is 60. The mean caseload of MS patients each respondent manages is about six, while the range in number of MS patients for the entire case manager survey population is one to 75.

Figure 62. Which choice best describes your practice environment?

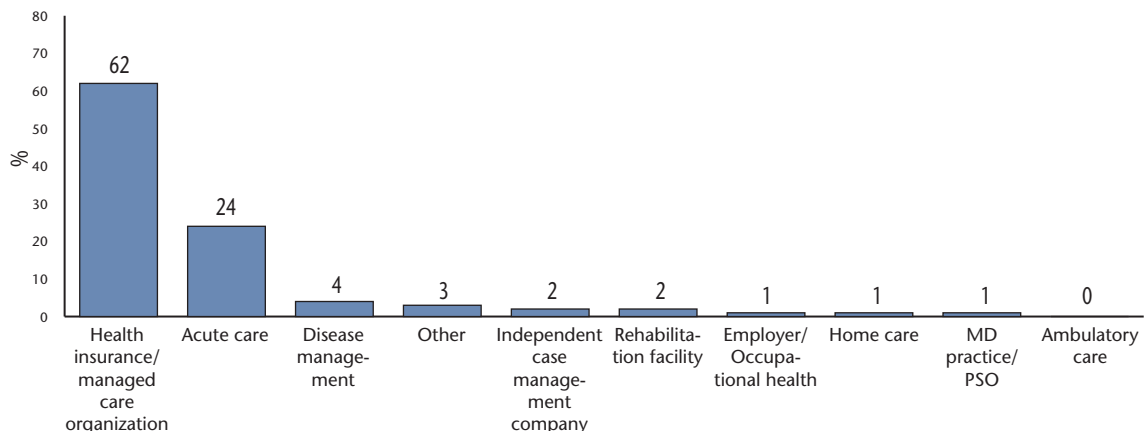


Figure 64. Does your practice primarily consist of ...

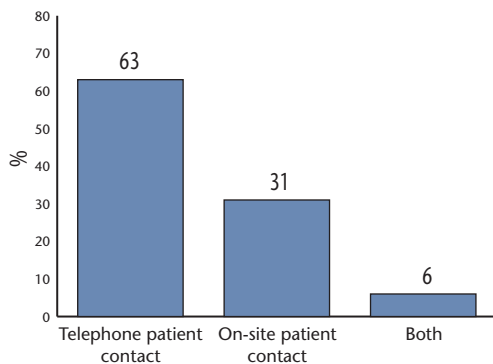
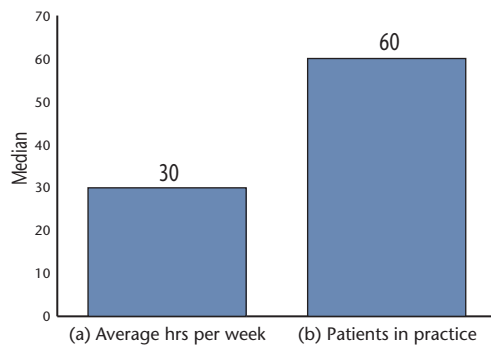


Figure 65. (a) On average, how many hours per week do you personally spend seeing patients and dealing with clinical issues? (b) How many patients do you have in your practice?



RESULTS

Ninety-seven percent of respondents said they are managing patients with a confirmed diagnosis of MS.

Nearly 40% of respondents said they have been managing interventions for patients with MS for 15 years or more. Only 13% have four years' or less experience with MS patients (Figure 66).

About 39% of respondents said they co-manage their MS patients with specialty pharmacies; about 61% do not (Figure 67).

About 11% of respondents said that during the first three months of case management, they have contact with MS patients three or more times a week; 37% have contact once or twice a month; 28%, once or twice a week; and 14%, less than once a month (Figure 68).

Respondents gave the primary reason for contact with MS patients during the first three months of treatment as follows:

Figure 66. About how many years have you worked with MS patients?

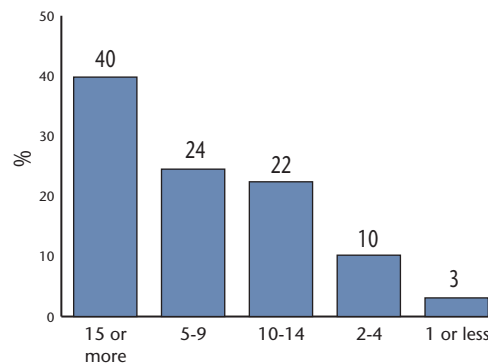


Figure 67. Do you co-manage your MS patients with specialty pharmacies?

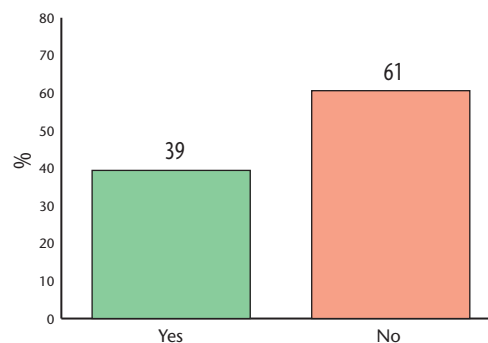
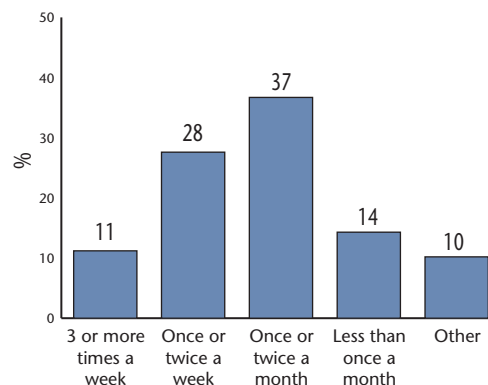


Figure 68. Typically, how frequently do you have contact with an MS patient within the first 3 months of an assignment?



MS-related symptoms	70%
Activities of daily living	62%
Access to and quality of care	45%
Emotional reactions/depression	45%
Fatigue	43%
Drug administration/compliance	37%
Bladder/bowel problems	29%

Drug-related adverse reactions	27%
Work-related issues/questions	26%
Memory and cognitive problems	23%

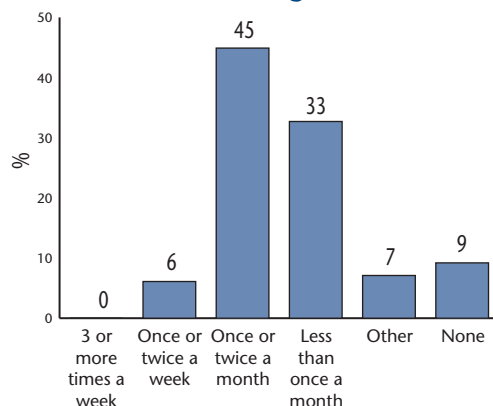
Respondents indicated a decrease in the frequency of patient contact after the first three months of intervention. About 45% said that after this time, contact occurs once or twice a month. Only 6% of respondents said they have contact with MS patients once or twice a week after the first three months of care. Nine percent of respondents said they have no contact after the first three months of care (Figure 69).

Respondents also said the primary reason for contact with MS patients changes as time progresses. After the first three months of care, the main reasons for contact are as follows:

MS-related symptoms	49%
Emotional reactions/depression	43%
Activities of daily living	42%
Fatigue	40%
Drug administration/compliance	35%
Access to and quality of care	33%
Drug-related adverse reactions	26%
Family/social relationships	25%
Bladder/bowel problems	23%
Work-related issues/questions	23%

Most case managers who responded to this survey view themselves as advocates for their

Figure 69. Typically, how frequently do you have contact with an MS patient after the first 3 months of an assignment?



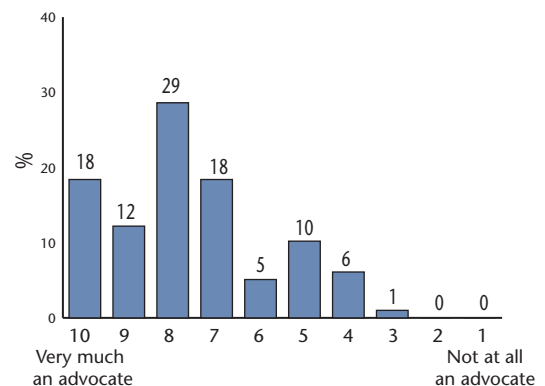
MS patients (Figure 70); they strive to improve the outcomes of care. Rather than play the role of gatekeeper to patient access to care, they help their MS patients deal with their symptoms, family and work issues, and activities of daily living.

Respondents were asked to list the three most difficult or frustrating issues that affect their interactions with their MS patients. From a list of more than 200 issues, the top two emerged as compliance and depression, with emotional reactions and fatigue tied for third; the cost of medications, memory and cognitive issues, transportation needs, and activities of daily living followed closely behind.

Respondents were asked about their management plans for patients, including durable medical and adaptive equipment; lifts; orthotics; safety; bowel and bladder programs; visual aids; pain management; complementary integrative medicine; home healthcare interventions (skilled nursing visits, direct provision of care, home health aides); physical, speech, and OT therapy; psychosocial assessment; neuropsychological evaluation; psychological support; and management of sexual dysfunction.

Respondents indicated that the provision of durable medical and adaptive equipment is an important component of most case management interventions for their MS patients. The most commonly provided devices are associated with mobility or safety. In a clear reflection of the disabling nature of MS, 95% of respondents said they have included a wheelchair in their

Figure 70. On a scale of 1 to 10 (10 = highest ranking), to what degree do you perceive yourself as being an advocate of your MS patients?



continuing care plan for their MS patients (Figure 71).

Respondents identified home healthcare services as a significant component of their case management plans for patients with MS. Perhaps as a reflection of the key role case managers play in educating patients, 94% of respondents said they incorporate “teaching” support services in their management plans for MS patients. Between 80% and 90% of respondents identified the next most frequently incorporated home health services as pain management through pharmaceutical intervention; physical therapy; occupational therapy; psychological support; skilled nursing visits to assist with injections, self-catheterization, and a home evaluation; and a psychosocial assessment involving referrals to community services, a financial evaluation, and referrals to SSI or SSDI. Seventy percent

of respondents said they manage the provision of assistance with the activities of daily living. (Home health aides as well as other home care services are arranged for and approved for payment by the case managers who work for MCOs.) Less than 50% of the respondents said they use home health aide workers specifically to provide homemaker services such as food preparation.

In a multi-response question, respondents identified pharmaceutical interventions as the most common form of pain management for their MS patients (82%); biofeedback (21%) and guided imagery (19%) were the next most commonly identified forms of pain management. Support groups were listed as the primary form of complementary therapy (80%); massage (38%) and meditation (28%) were the next most commonly cited types of complementary therapy (Figure 72).

Figure 71. Which of the following devices have you incorporated into a case management plan for a patient with MS?

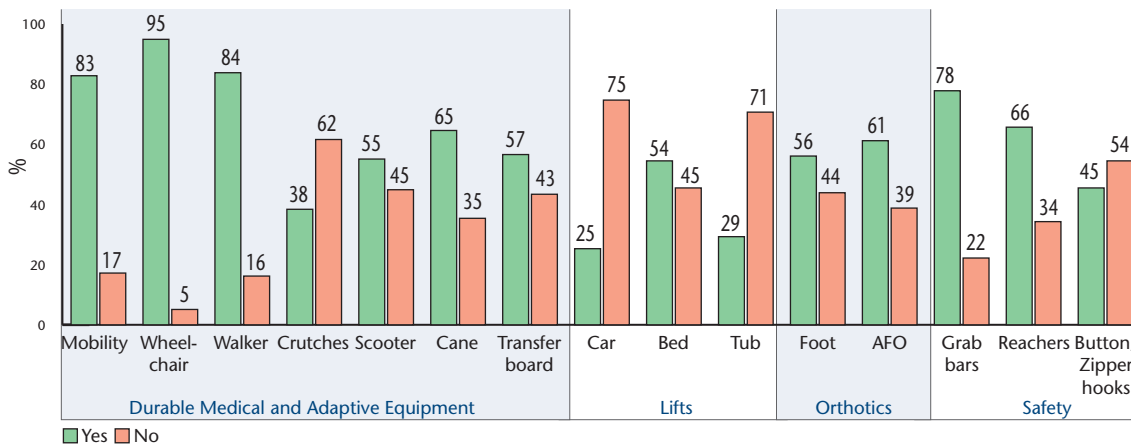
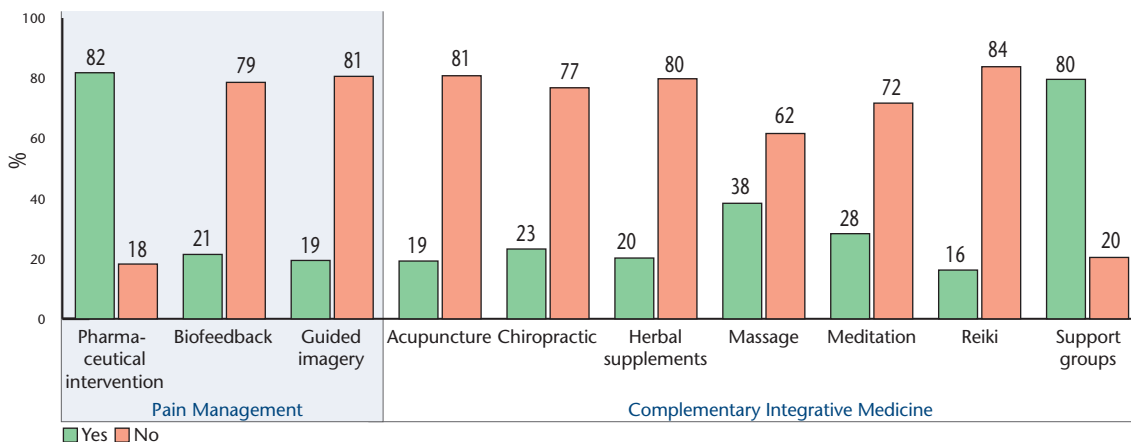


Figure 72. Which of the following services have you incorporated into a case management plan for a patient with MS?



COMMENTARY

As pharmaceutical therapies began to more effectively target the frequency and intensity of exacerbations of MS, the face of chronic disease management for the patient with MS began to change. Case managers who once focused on negotiating the cost of pharmaceutical therapies or encouraging compliance with plan formularies began to look more intensely at the long-term outcomes of care.

Case managers also focused more intently on advancing patient education. Their patients became informed consumers and more health literate. Many patients began to ask for therapies by brand name (43%) (Figure 73), and case managers responded by advising patients to speak with their prescribing physician (33%) or by passing them on to the prescriber themselves (52%) (Figure 74). This opportunity to open the pathways for communication may well be the reason that almost half of the survey respondents indicated an ability to influence the prescribing of a specific pharmaceutical product (Figure 75).

However, the ability to obtain a specific prescription does not guarantee patient adherence. Respondents reported that patients continue to express concerns regarding access to prescribed injectable MS drugs. The access barrier most frequently reported by patients is cost (65%); the second most common barrier to access, patients tell their case managers, is approval by payers (54%) (Figure 76).

The three highest-rated case management tools or services provided by manufacturers of MS drugs were associated with education and outcomes. Forty-five percent of respondents indicated a need on their part for further education about MS; the establishment of standards for outcomes and the provision of educational materials about MS for patients were both cited by 25% of respondents (Figure 77).

CONCLUSION

This survey offers an insider's perspective on the case management community and interventions for patients with MS.

Figure 73. How often do patients request injectable MS drugs by brand name?

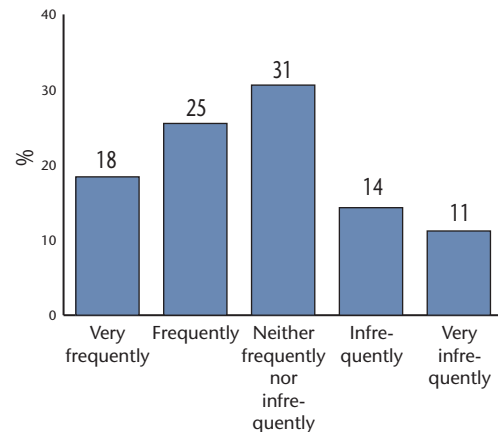


Figure 74. How do you handle these requests?

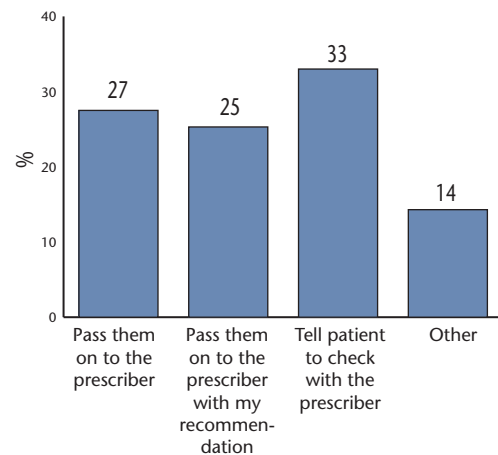
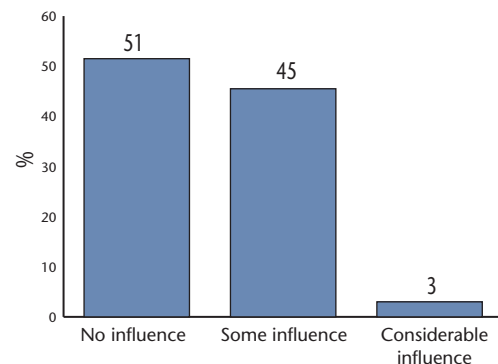


Figure 75. How much influence do you have in prescribing specific drug products, either initially or as a recommended change?



Case managers work in partnership with MS patients to address not only their symptoms but also the emotional reactions and depression that often accompany their disease. Bringing to bear a comprehensive, holistic view of

Figure 76. What are the most frequent complaints of MS patients regarding access to the injectable MS drug products they are prescribed?

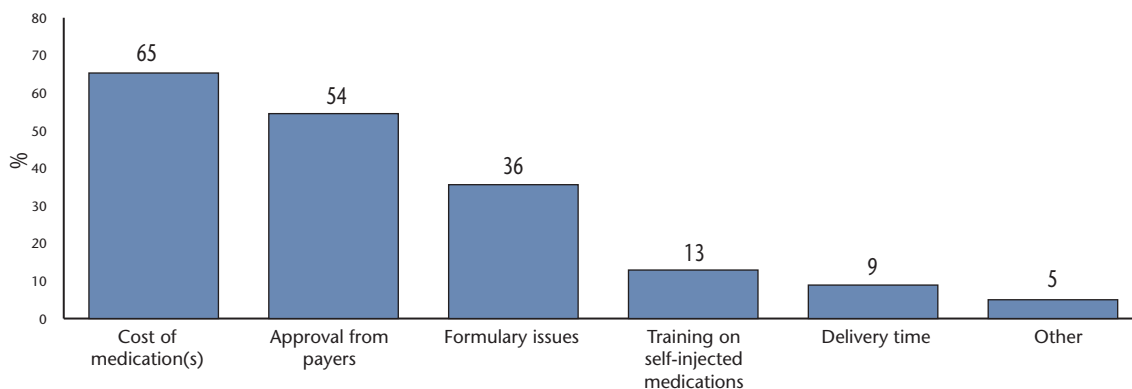
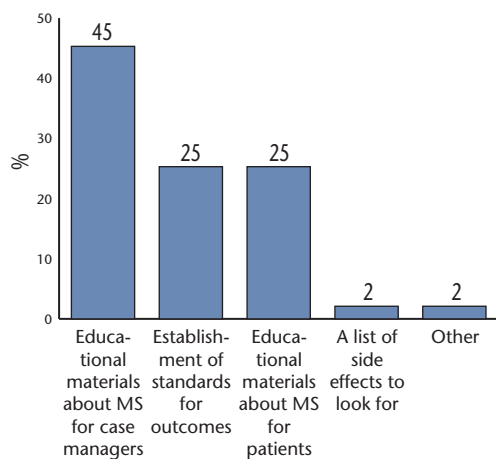


Figure 77. If you could get one of the below-listed tools or services that manufacturers of MS drugs provide, which one would it be?



MS, respondents described the focus of their interventions as advocacy. Advancing adherence to the prescribed treatment plan is one important aspect of that advocacy. To facilitate adherence and achieve established goals, case managers assess and reassess patient needs and coordinate, facilitate, and advocate for the delivery of necessary services. MS presents an ever changing set of clinical challenges, and respondents emphasized the importance of working with patients from a variety of perspectives to enhance their independence and productivity. The persistent focus on advocacy distinguishes case management from other medical or cost management strategies.

Most of the case managers who were surveyed reported a commitment to timely conversations with patients and their families as a way of sustaining consistency and continuity in the

assessment process. These discussions occur as frequently as three times a week during the initial three-month assessment process and usually occur once or twice a month thereafter.

The commitment to communicating with patients and their families assists case managers in gathering accurate data on primary disease symptoms; the patient’s ability to perform activities of daily living; the patient’s emotional state; degree of fatigue; drug administration and compliance; and access to care. As the case management extends beyond the initial review and assessment, primary reasons for contact begin to shift away from essential access to care and toward more comprehensive provision of care. Despite their commitment to advocacy, however, case managers must work within prevailing guidelines for the coverage of medically necessary services, including durable medical equipment and supplies, rehabilitation therapies, and pharmaceutical products. Many practices cannot consistently support coverage for all services and pharmaceutical products for all patients. To assist their patients in obtaining treatment, case managers often seek alternative sources of support, such as charitable organizations and public funding. Case managers also work within a delivery system that relies on specialty pharmacies to manage certain injectable drugs and biologic therapies. In many cases, establishing a relationship between the specialty pharmacy and the managed care organization presents its own set of challenges. For that reason, more than 61% of respondents said that co-managing pharmaceutical products obtained from a specialty pharmacy lay outside the scope of their practice.

One case manager who practices in a managed care environment offered perhaps the most succinct summary for this section of the report:

“My role does not include denial of benefits or reduction in services. I work in partnership with my patients and their entire treatment team to advance the achievement of quality treatment outcomes. Sometimes that means I try to remove the barriers that prevent or restrict the delivery of necessary care. One of those obstacles can be full funding for all components of an established treatment plan. When a payer is unable to provide benefit coverage for a service or pharmaceutical product, I look to publicly and privately funded resources to fill that gap. I provide patients and their families with education that empowers them to engage in self-advocacy. And I continually focus on helping patients receive the most appropriate and best-quality care. I am a patient advocate. That is why I am a case manager.”



Clay Walker, National Ambassador for the National MS Society's 2005 MS Cycling Series, shown here with his cycling team.

Patients

Employment and quality of life — and the relationship between the two — are among the top concerns of patients with MS today. The patient survey highlighted the dilemma of more than two-fifths (43%) of MS patients who leave the workforce owing to the progression of their disease or to symptoms such as fatigue that prevent them from sustaining full-time jobs.

Early treatment is essential in slowing disease progression, and delaying the progression of MS is key to helping more patients extend their work lives, sustain their economic and professional contributions, and lead more fulfilling lives. Survey results indicate that prerequisites for early treatment include insurer approval for disease-modifying agents and for prescriptions for medications to treat symptoms such as fatigue. Prior authorizations by doctors, drug denials, and high co-payments and deductibles often represent obstacles to early treatment.

Patients would also like to see more aggressive development of disease management programs, as they understand that these help insurers to better educate themselves about the complex nature of MS. Patients believe that increased knowledge of MS among insurers, combined with the availability of agents to delay disease progression and treat symptoms, will lead insurers to approve more prescriptions and tests now, and will reduce costs for MCOs in the long term, when treatment of more progressed forms of MS is more costly.

Most of the 1,935 patients surveyed are satisfied with their insurance coverage, mainly because it is comprehensive, is affordable overall, and has low co-pays for high-price medications. However, more than a fifth of those surveyed said they are burdened with such difficulties as denials of claim reimbursements, frequent requirements for prior authorization, and high co-payments or deductibles; when asked about the least satisfactory aspect of their insurance coverage, respondents cited lifetime caps on medications and many other obstacles to treatment.

OVERVIEW

Most respondents to this survey received a diagnosis of multiple sclerosis from an MS specialist, general neurologist, or primary care physician; the remainder received a diagnosis from an ophthalmologist, a neurosurgeon, a radiologist, or hospital or other medical facility staff.

The time between diagnosis and participation in the survey varied widely, with 40% of respondents reporting that they received a

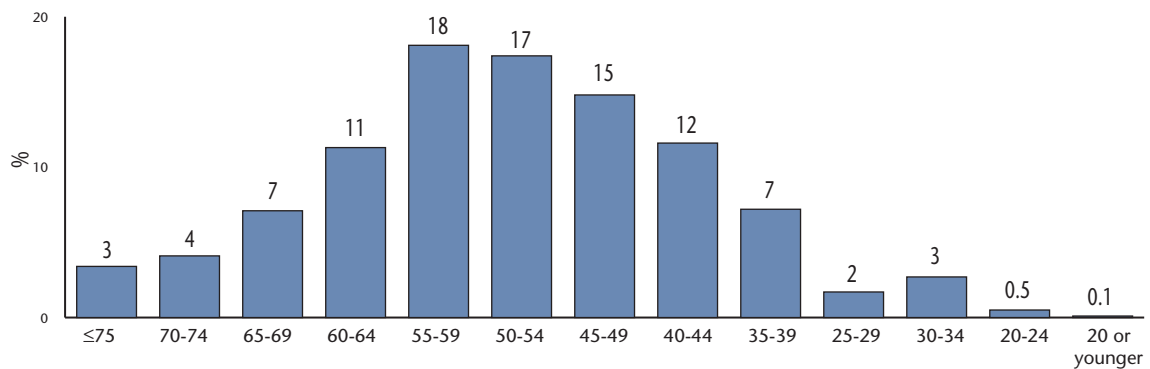
diagnosis of MS within the past ten years: < 2 years, 3%; 2-5 years, 15%; 5-10 years, 36%; 10-15 years, 20%; 15-20 years, 14%; and > 20+ years, 26%.

More than four-fifths of the respondents (81%) were female.

Most respondents (87%) were between 35 and 69 years of age; more than half (60%) were 50 or older (Figure 78).

Married MS patients comprised 63% of those surveyed; single and widowed patients

Figure 78. Into which age group do you fit?



accounted for 13% and 5%, respectively. Patients who were separated, divorced, or living with a partner totaled 18% of the respondents.

This was a highly educated sample; 19% of respondents have a master's or a doctoral degree or its equivalent; 33% have a bachelor's or associate's degree; 25% attended college but did not obtain a degree; and 21% have a high school education. Only 3% of respondents said they had not finished high school.

Respondents reported a wide range of annual income: close to one-quarter (23%) earn \$20,000 or less per year; 33%, \$20,000 to \$50,000; and 44%, more than \$50,000.

Fifty percent of the respondents receive health insurance from their employer; 37% are covered by some form of Medicare or Medicaid, or both. Eight percent of the respondents obtain their insurance privately; 3% are covered through the Veterans Administration (VA) or Tricare; and 2% have no health insurance (Figure 79).

Among those whose health insurance is provided through an employer or is bought

privately, 52% are covered by employer-provided or privately purchased PPO health plans; 45% have HMO plans; and 2% and 0.4% have indemnity or ASO health plans, respectively (Figure 80).

Note: At the time this patient survey was administered, Tysabri® (natalizumab) was not commercially available, and therefore was not included in the survey. Tysabri falls within the category of monoclonal antibodies, one of the new generation of infusible disease-modifying agents, now on the market in a limited fashion. Tysabri further falls within the category of those newer treatments that are referred to in the managed care survey in this report; that is, drugs for which it may be more difficult to obtain insurer approval, at least until there is additional data on safety, efficacy, and clinical experience. As with other such drugs, many of which are still in clinical trials, such as Rituxan® (rituximab), patients are not only likely to have more difficulty in obtaining reimbursement, but they will probably have higher co-pays, at least for the time being.

Figure 79. Your health insurance coverage is being provided through which of the following?

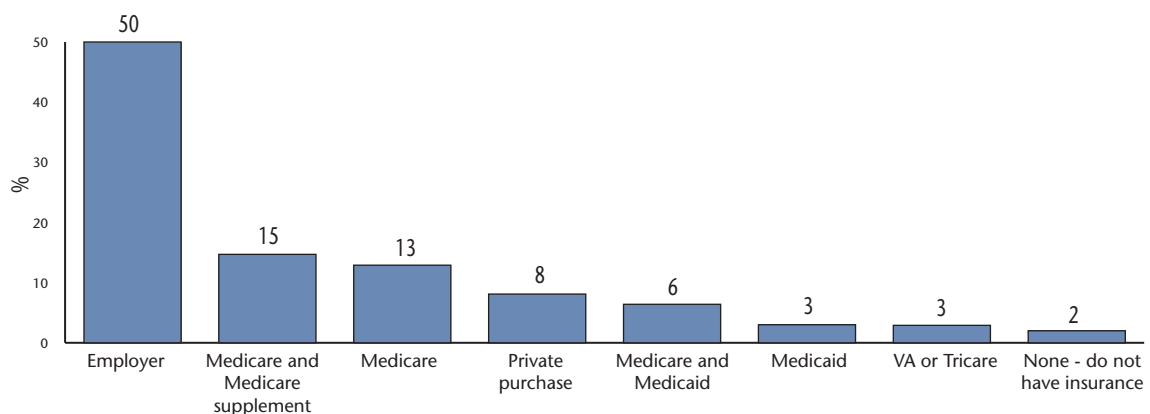
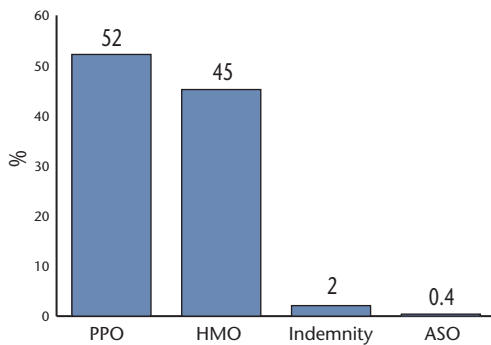


Figure 80. If your health insurance is provided through your employer or is bought privately, it is of which type?



RESULTS

Thirty-seven percent of respondents said it took six months or less to receive a definitive diagnosis of MS after their symptoms started. Fifteen percent had to wait between seven and 12 months to receive a diagnosis of MS; 32% waited between one and six years for a conclusive diagnosis; and 16% waited six years or more.

Sixty-three percent of the respondents were diagnosed by general neurologists, and 28% by MS specialists. Family physicians and internists made the diagnosis in 5% of those surveyed. Three percent of the respondents said they had been diagnosed by “other medical practitioners” (Figure 81). Among these others were ophthalmologists, who made the diagnosis for 26% of this group; neurosurgeons (9%); radiologists (6%); VA hospitals, other hospitals, and various emergency room medical personnel (5% each); the Mayo Clinic and neuro-ophthalmologists (3% each); and a host of other medical facilities and specialists (between 1% and 2% each).

More than two-thirds of respondents (69%) reported that magnetic resonance imaging (MRI) was used to establish an MS diagnosis; the remainder said that their diagnosis was not made on the basis of MRIs.

Fifty-two percent of respondents said they are treated for their MS by general neurologists; 38%, by MS specialists; 8%, by family physicians or internists. Of the remaining 2%, many seek treatment through other venues, such as nurse practitioners, emergency room staff, a

spinal cord specialist, homeopathic physicians, a doctor of osteopathy, an ophthalmologist, or alternative practitioners (Figure 82), while some are receiving no treatment and others said they are treating themselves.

The frequency with which physicians order MRIs to follow the course of their patients’ MS varies considerably, according to respondents: once annually, 15%; every other year, 14%; twice yearly, 3%; and every now and then (no set time), 31%. Fourteen percent of the respondents said their physicians never order MRIs for them, and 4% said they don’t know how often their physician orders an MRI.

Twelve percent of respondents said they experience difficulties with health plan reimbursements for their MRIs. Of this 12%, more than half (55%) noted that a high co-payment and/or deductible represents a major obstacle to receiving MRIs; 21% pointed to lack of coverage as the main reason MRIs are difficult to obtain; and 15% cited insurance plan denials as their biggest problem. Most of the remaining

Figure 81. Who confirmed your diagnosis of MS?

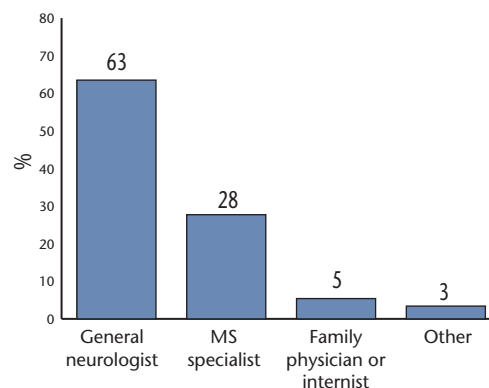
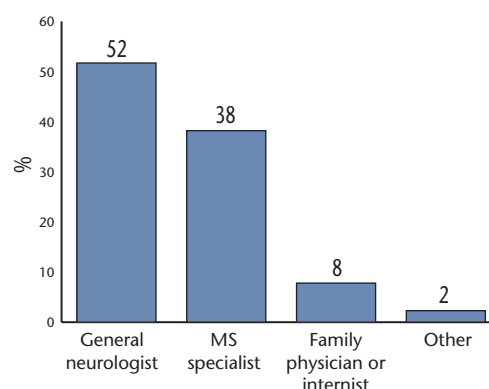


Figure 82. Who is treating you now for MS?



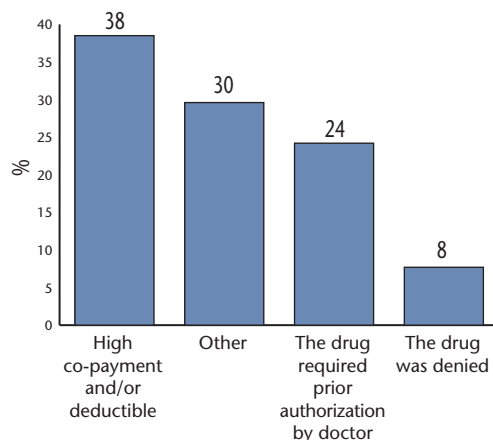
8% of respondents, categorized in the survey as “other,” reported difficulties with obtaining reimbursement.

Nearly two-thirds of the respondents (63%) are currently being treated with an MS immunomodulatory drug. Avonex® (interferon beta-1a) is the drug most widely used by respondents (40%); Copaxone® (glatiramer acetate injection) is the next most widely used drug (32%).

Among the 63% of respondents currently on one of the MS immunomodulatory drugs, 22% reported difficulties with drug therapy reimbursement by their insurance plans. These problems include high co-payments and/or deductibles (38%), difficulties with prior authorization (24%), and denials for drug coverage (8%) (Figure 83). Other obstacles include the following:

- Insurer ceased drug coverage
- Drug no longer on formulary
- Insurer refused to cover drug for seven months, then approved it
- Patients reached insurance cap
- Patients required to receive shots in doctor’s office only
- Medicare makes drug too expensive
- Patient was never reimbursed

Figure 83. Of the 63% of respondents who said they are currently taking an immunomodulatory drug, 22% are experiencing difficulties in obtaining reimbursement for these drugs, including:



More than two-thirds (68%) of respondents who are taking an immunomodulatory drug have been on more than one immunomodulatory injectable drug for MS, while 32% are taking only one such drug therapy.

Combination therapy (two immunomodulatory drugs simultaneously) was reported rarely in this group. Ninety-four percent of respondents who had been prescribed more than one immunomodulatory drug started treatment with the second drug after discontinuing the first.

Use of infused disease-modifying drugs (other than corticosteroids) for MS was also uncommon in this group — only 7% said they are taking one of these agents.

Infused disease-modifying agents currently on the market and administered to respondents include the following:

Agent	% of Respondents Administered To
Novantrone® (mitoxantrone for injection concentrate)	2.7%
IVIg (immunoglobulin)	1.4%
Cytosan® (cyclophosphamide)	1.2%

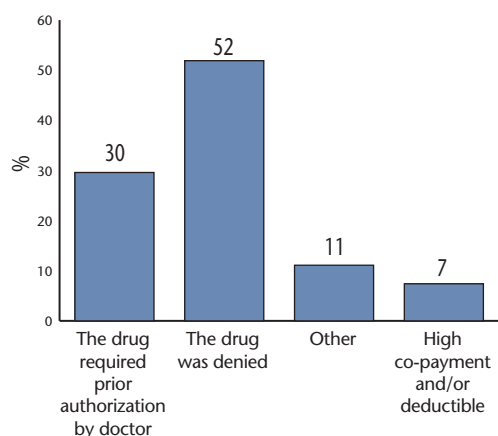
One surveyed MS patient reported enrollment in a study for the infused disease-modifying drug Rituxan® (rituximab).

Approximately one-fifth (21%) of respondents receiving an infused drug treatment for MS reported difficulties in obtaining reimbursement; problems included requirement for prior authorization (30%), denial of coverage for the drug (52%), a high co-payment and/or deductible (7%), and “other” (11%), such as “would not pay for three days of infused drugs” and “Denied, told Novantrone® was for cancer, not MS” (Figure 84).

More than half of the respondents (58%) said they were able to overcome the insurer’s denial.

Eighty-three percent of the survey respondents have not taken an antibody test to determine whether their medication is effective.

Figure 84. Of the 93% of respondents who said they are taking infused disease-modifying drugs for MS, 21% said they are encountering difficulties in obtaining reimbursement for these drugs, including:



COMMENTARY

Antibody tests are sometimes necessary for patients taking the injectables Avonex® (interferon beta-1a), Betaseron® (interferon beta-1b), and Rebif® (interferon beta-1a), which are interferon drugs, but not for Copaxone® (glatiramer acetate injection), which is not in the interferon class of MS drug therapies. There currently exists no need for antibody tests for infused MS medications.

An antibody test is administered to determine whether the medication has been rendered ineffective owing to the buildup of antibodies in the blood. Doctors request the administration of an antibody test when a patient who has been on an interferon drug for a certain period of time is either no longer experiencing that medication's side effects or is showing definite signs of disease progression while on the medication.

Asked how they would define a drug's lack of effectiveness, respondents said that increased frequency of relapses was most important and intolerable side effects (such as flu-like symptoms) were least important. Full results in terms of mean ranks for the total sample of respondents are as follows (most important = 1; least important = 5): frequency of relapses, 1.94; progression as measured by MRIs, 2.78; EDSS, 3.05; laboratory tests such as neutralizing antibodies, liver function tests, 3.35; and side effects, 3.39.

Respondents were asked to rank four aspects of their medication in order from most to least important. Most important, respondents said, is the effectiveness of the medication in treating MS. The next most important factor, they said, is affordability. Avoidance of negative side effects and ease of administration, though considered significant, placed third and fourth, respectively.

Although patients consider the effectiveness of disease-modifying drugs the most important issue, it is often difficult for them to determine whether their drug is working. Since these agents slow or halt disease activity rather than restore function, success may be indicated by the fact that nothing obvious is happening. Over the long term, as patients observe that their disease is not getting worse or is progressing more slowly than before, patients are more likely to feel that treatment is working.



Respondents cited their primary sources of information on MS as follows: MS organizations such as the National Multiple Sclerosis Society, 45%; neurologists, 21%; MS specialists, 10%; the Internet, 9%; MS support groups, 6%; MS nurses, 3%; and primary care physicians, 3%. An additional 5% reported using one or more of a variety of sources, such as pharmaceutical company educational materials and programs, alternative medicine practitioners, physical therapists, medical journals, friends, and family.

Nearly two-thirds (64%) of respondents said their health insurer does not offer a disease management program for MS patients. Twenty-five percent said their insurer does provide a disease management program, while 11% said they did not know whether their insurer provides such a program.

Healthcare organizations and drug companies often offer disease management programs to patients free of charge to assist them in understanding their disease or condition, and to suggest ways to manage their illness, reduce complications, and maintain treatment compliance. Among the 25% of respondents whose insurers do offer a disease management program for MS, 69% said that a program nurse does contact them.

Only 31% of the respondents said they expect to get all the information they need about MS from their neurologist. Fifty-four percent of the respondents said they “strongly agree” with the statement “My neurologist functions as a patient advocate by assisting me in obtaining the medications, treatments, support and information I need to help me manage my condition.” Another 28% of those surveyed said they “agree” with that statement, while 19% disagreed or strongly disagreed.

Approximately one-fifth (21%) of respondents use alternative treatments to manage their MS, including acupuncture, massage therapy, yoga, physical therapy, chiropractic care, reflexology, reiki, meditation, water exercise, evening primrose oil, estrogen, vitamins, herbs, minerals, fish oils, marijuana, Botox®, liquid oxygen, and many more.

Of the respondents who use alternative treatments to manage their MS, 80% said their neurologist is aware that they use these treatments.

In addition to prescribing disease-modifying drugs, neurologists prescribe medications to treat the symptoms of their MS patients. Almost two-thirds of respondents (64%) reported that they receive some form of symptomatic treatment. These treatments target symptoms

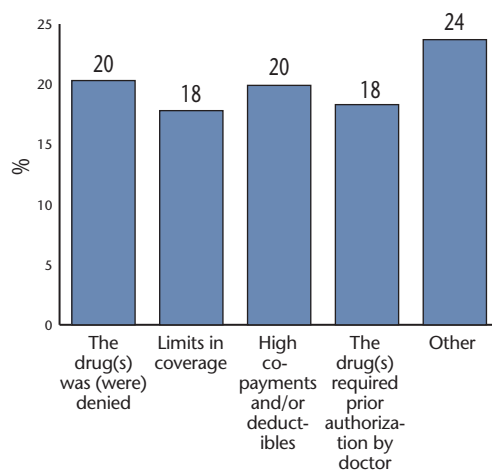
such as spasticity, optic neuritis, fatigue, depression, and sexual dysfunction.

Among respondents who are receiving some form of pharmaceutical treatment for symptoms of MS, approximately one in five (20%) experiences some form of difficulty in obtaining reimbursement for these drugs. The many problems listed include denial of coverage (20%), limits in coverage (18%), high co-payments and/or deductibles (20%), need for a doctor’s prior authorization (18%), and other issues (24%), such as refusal to reimburse for a non-FDA-approved drug or a drug not on formulary (Figure 85).

MS AND QUALITY OF LIFE

When asked in a multi-response question about the effect of MS on their social life, 35% of those surveyed reported a major negative effect; 34%, a minor negative effect; and 21%, little or no effect. Seventeen percent said they had lost old friends, while 15% reported making new friends. Five percent reported a minor positive effect; 4%, a major positive effect. Nine percent of the 1,935 respondents surveyed listed “other” effects of MS on their lives, including the following excerpts:

Figure 85. Of the 64% of respondents who said they are being prescribed medications to treat “other” symptoms of MS (eg, urosepsis, spasticity, optic neuritis, fatigue, depression, sexual dysfunction), 20% said they are experiencing difficulties in obtaining reimbursement for these medications, including:



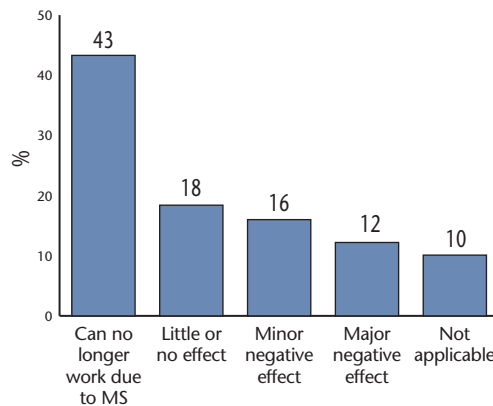
- Ability to be my old self
- Affects my self-worth
- Afraid to date because of MS
- Alcohol use
- Being bedridden for 9 years you are forgotten
- Can no longer compete in my sport, a major part of my social life
- Cannot walk, bathe, dress, or write by self
- Caregiving gets rough at times for my wife
- Closer to family
- Confined to a wheelchair
- Depression has played a major role in negative impact
- Desperately isolated
- Divorced; son taken by ex-husband

- Drained savings for testing; I run an in-home child care; I must keep positive and working
- Faithfulness
- Fear misunderstanding from others
- Find men afraid of me
- Fired because of MS
- Had to move; can't earn a living
- Had to retire early, but feel better that I did (physically)
- Have altered every aspect of my life to remain functional; hesitant to make commitments
- Hibernate after work
- I adapted to changes positively; learned that what is really important is to live better with less
- I am an MRI supervisor now, so I can truly empathize with the patients having scans
- I can bike, kayak — going camping and kayaking in Galapagos in 2007
- I can't dance anymore
- I can't go to many places due to access
- I don't tell many people that I have MS
- I feel worthless; I went from working 12 hours a day to zero
- I must pick and choose what I want to do in a day to recover from exhaustion
- I stay home and do not travel for vacations
- I went to college because of MS
- It resulted in a personal revelation and evolution, but exhausted and in pain
- Limp; use cane
- Low sex drive — fatigue
- Made dating difficult
- Marriage ended due to ex-spouse's extreme fear of my disability
- Mood swings impact me; I fall frequently, and it puts people on edge
- Most people don't understand
- MS support group has really helped
- My old social life was intense athletic endeavors that I am no longer capable of
- No one really understands what the fatigue is really like
- Now I can spend time with my grandchildren
- Physical limitations so deep that daily responsibilities are not met
- Planning for future can be scary
- Realized I'm an introvert and happier
- Retired early; sex life went to hell
- Robbed of life almost ...
- Ruined my life!
- Since few people understand MS, I am constantly having to define it to people
- Since I am no longer employed, I am no longer asked to participate in charitable organizations
- Started my own business to control my time
- The plus is that I am a stay-at-home mom, but I use a wheelchair and can't drive
- Try to do the best I can but totally incapacitated
- Unable to do activities, children
- Varies depending on symptoms
- We were part of a close group of very active friends; now my husband can go and I can't
- Wife left for fear of me being crippled; she could not deal with it
- Zero stamina = no job = no income = poverty

Thirty percent of respondents indicated that MS is having or has had little or no effect on their marriage. Nine percent indicated that their MS has led to separation or divorce, and an additional 10% of respondents said their MS is having or has had a major negative effect on their marriage. Twenty-eight percent said their MS is having or has had a minor negative impact on their marriage; 22% said the question was not applicable; and 0.2% of respondents reported a positive effect of MS on their marriage.

On the subject of employment, 43% of the respondents said they can no longer work, owing to the effects of MS; 18% reported little or no current effect on their employment situation; and 16% reported a minor negative effect. Twelve percent reported a major negative effect, while 10% said the question was not applicable to their current situation (Figure 86).

Figure 86. What effect is MS having, or has MS had, on your employment?



When asked what effect MS is having or has had on their schooling, 60% of respondents said the question was not applicable. Twenty-one percent indicated that MS is having or has had little or no effect on their schooling; 8% reported a minor negative effect; 6%, a major negative effect; and 5% said they can no longer attend school owing to their MS. Only 0.2% of the respondents reported a positive effect on their schooling from MS.

More than one in five respondents (22%) reported a current need for home healthcare. Among this group, 64% said they have someone available in their home to provide the care. Among the 36% who have no one available in their home to assist, hired help is the primary source of care (4% of total number of respondents); 2% of respondents who have no one available in their home to provide care receive it from a family member or relative; and 1% receive this help from a friend. The 3% of respondents who indicated “other” for providing care in the home listed the following sources, among others:

- Nursing home
- None

- Assisted living facility
- State agency
- Meals on Wheels
- County-funded agency sends help
- In a retirement home
- Applied to CNA from insurance
- Through Medicare/Medicaid
- The visiting nurse service certified a nursing assistant
- Homemaker service from Council on Aging
- Husband must do everything and try to work too
- Get along as best I can
- Need help cleaning; I can care for myself
- In-home healthcare
- Community long-term care
- Cystic Fibrosis Agency pays for 28 hours per week of care
- My landlord has power of attorney and is caregiver
- UCP Attendant Care program
- Have no arrangements
- Assisted living when absolutely necessary
- My roommate is IHSS certified and is paid to help
- Held hostage by the law
- I have nobody
- Attendant care program through Accessibilities
- None; I improvise or ignore
- Hospice
- Rehab/care center
- I get by on my own as best I can
- Home health helps out greatly
- Hospital Family Care
- MS Society
- Church volunteers

- Friend pays for homemaker
- 24/7 home aide

On a scale of 10 to 1, with 10 ranking the highest level of satisfaction, respondents indicated their level of satisfaction with their insurance coverage as follows: rank of 10, 23% of respondents; 9, 17%; 8, 18%; 7, 10%; 6, 8%; 5, 8%; 4, 5%; 3, 4%; 2, 2%; and 1, 4%.

Asked to pick the one most satisfactory element of insurance coverage, respondents' most common replies included the following:

- Low co-pays for expensive injectable drug therapies
- 100% coverage of medical tests
- Ability to choose one's physicians
- Coverage of all — or nearly all — necessary drugs
- Availability of a disease management program
- Few or no claim problems
- Comprehensiveness
- Flexibility
- Coverage of home healthcare items
- Inexpensive premiums

Asked to identify the one least satisfactory aspect of insurance coverage, respondents' most common responses included the following:

- High deductibles and/or co-pays
- Denial of drug coverage
- Mandatory preauthorization and referrals for a chronic condition
- Claim denials
- Limited choice of physicians
- Denial of coverage for alternative therapies
- Annoying or extensive paperwork
- Denial of drugs without which patients experience debilitating symptoms, such as fatigue
- Billing confusion
- Dealing with managed care bureaucracy

- Ability to obtain only a one-month supply of MS injectable therapies at a time
- Changes in formularies and specialty pharmacies
- Constant changes and constant cost increases
- Denial of coverage for physical therapy
- No home healthcare coverage
- MS patients' impression that managed care is more concerned with saving money than with the overall long-term health of its MS patients.

CONCLUSION

More than two-thirds (68%) of respondents rated their insurance coverage a 7 or above on a scale of 1 to 10, with 10 indicating the highest level of satisfaction. Many respondents cited low co-pays for expensive MS drug therapies, comprehensive coverage, and overall affordability as the major reasons for their satisfaction with their coverage.

MS patients would welcome the development of a disease management program, as one-quarter of respondents clearly appreciate the benefits of such programs. In fact, MS patients cited the availability of a disease management program as a reason for satisfaction with current insurers.

Patients whose MCOs place a lifetime cap on their immunomodulatory drug benefit to treat MS are also less satisfied with their insurer. "I soon will exhaust the retiree lifetime drug coverage limit," said one survey respondent, adding that "drugs are ridiculously expensive!"

Patients voiced their frustration with other insurer actions as well. Insurers "don't understand the whole problem; they only look at each claim," remarked one respondent. "They put profit above patient care," said another. "They question my need for drugs," stated another.

Among the 63% of respondents currently prescribed immunomodulatory drug therapy, more than 21% reported problems with reimbursement for these treatments. The necessity for frequent referrals and prior authorizations puzzles patients who suffer from

a disease that requires regular periodic visits to neurologists, periodic MRIs, and in many cases regular visits to other medical practitioners such as physical therapists and urologists. “I hate the referrals I need for my neurologist. I have MS that won’t go away, so why do I need a referral every few months?” asked one respondent.

Among the 7% of respondents who are prescribed infused disease-modifying agents, more than one-fifth (21%) reported difficulties in obtaining reimbursement. Respondents are frustrated that insurers do not cover all treatments, both pharmaceutical and alternative, that are used in treating MS, and that “they don’t understand all the ways to treat MS symptoms.”

The progressive effects and costs for a particular segment of respondents underscore the need to

treat MS patients early rather than late. Twelve percent of respondents have experienced a major negative impact in regard to their employment; 43% of respondents to the survey can no longer work, on account of their MS. Twenty-two percent of respondents said they require home healthcare. The withdrawal from the workforce, and the concomitant costs of healthcare over years and even decades, both in and out of the home, for patients who can no longer sustain a job or who are working at reduced capacity, indicate a significant drain on individual and family resources. The costs of MS, both obvious and less apparent, seem to accrue more quickly and to greater effect the longer that treatment is delayed.



*The Comments of Randall T. Schapiro, MD
Director, Schapiro Center for Multiple Sclerosis
at the Minneapolis Clinic of Neurology
Clinical Professor of Neurology
University of Minnesota*

Multiple sclerosis can be a very complex disease with an interaction that involves the immune system, the nervous system, and numerous other body systems. This encompasses multiple symptoms and has emotional/psychological issues at every turn. For those many who have these complexities, a team of skilled professionals is necessary for appropriate and efficient management. MS centers have evolved to fill that large gap. In general, these centers not only have physicians and nurses, but other professionals as well, such as physical, occupational, and speech therapists, social workers, psychologists, and other specialties, depending on the particular center. Patients should have confidence that their providers have knowledge and can treat with modern methods, and MS centers address that need. Consider MS centers as gap fillers, and they make the management of MS modern and efficient! While many MS centers exist in the United States, there are not enough at present to fulfill the need. However, new ones are getting started in several areas of the country that up to now were underserved.



Cheryl and Len Chatman

SHINING A LIGHT ON MS

Cheryl Chatman

When I suddenly began losing vision in both eyes at age 25, I was scared and confused. No. I was terrified.

The military physician I was required to see — because my husband, Len, was on active duty — told me the problem was “all in my head.”

After paying for a host of diagnostic tests out-of-pocket, we sought a second opinion a few weeks later from a civilian neurologist, who provided the shocking explanation for my loss of vision: multiple sclerosis.

Now I was more scared. I asked the neurologist if I was going to die. When he hesitated to respond, I knew what I had to do. That day, I took my life into my own hands.

I had two small children at home. I would have to cope with the demands of motherhood, a husband on active duty, the inability to drive, and barely enough vision to see my children clearly on the playground.

To begin with, I decided the extra hundred pounds I'd been toting had to go. Over the next year I walked as much as 10 miles a day — and I haven't stopped walking yet.

Len and I educated ourselves about this strange disease and attempted every affordable treatment to restore my sight. Seventeen years later, my vision has not returned. I remain more than 85% blind, able to see only shadows and silhouettes.

From the start of dealing with MS, though, I learned it is impossible to be pitiful and powerful at the same time. In 1993 I began treatment with Betaseron®, the first available injectable interferon disease-modifying agent designed to slow the progression of MS. My honeymoon with Betaseron ended prematurely, when I developed consistent flu-like symptoms as a side effect and began to spend more time in bed than out. I reluctantly gave up this treatment after four months.

I elected to stay off the other injectable immunomodulatory drug, Avonex®, when it became available a year later. I didn't want to relive the disabling side effects I'd experienced with Betaseron.

Over the next few years my disease remained fairly stable, but trouble with vertigo — a major MS symptom — prevented me from working out and, in turn, only worsened my MS-related fatigue.

When Copaxone® received FDA approval in 1997, Len and I began to research it. In 2001 we decided together that I would give it a try. Six years later my vertigo has nearly disappeared and I have resumed my exercise, which helps reduce my fatigue. I have some residual numbness in my hands and feet; I've had this symptom since age 19 and I now know it is MS-related. But I am still going strong. Despite my loss of vision and other effects of MS, I travel all over the country, and I am thankful.

Len and I teamed up my MS neurologist, nurse practitioner, and family doctor so I can get the best healthcare available. It is empowering to know that my doctors consult together on any health issues that arise. I continue to learn as much as I can about MS and its treatment, and as a result, I can communicate effectively with my physicians and other practitioners. We experienced many difficulties with insurance during the early years. However, I have nothing but praise for my current managed care insurer.

The love of Len and our two sons has made it possible for me to face each day. This was especially true in the early years. Right from the start we faced MS as a family, and we still do. With this love, and with the help of my healthcare team and a responsive insurer, the path to living with MS is visible. And as long as all this help is sustained, we will continue to see MS clearly.

WALK A MILE ...

Len Chatman

Ever have a time when your life changed irreversibly? Seventeen years ago, in the middle of my military career, my life changed in an instant with the words “You have MS.”

They were addressed to my 25-year-old wife, Cheryl, in 1990, as I sat beside her. But I too felt overwhelmed with grief and concern. Within a few seconds, the role of caregiver had taken on a radically different meaning. The memory of this defining moment is still with me.

My favorite poet, Langston Hughes, wrote, “Life for me ain’t been no crystal stair” in “Mother to Son.” I can relate. As the primary caregiver for Cheryl, I have faced many challenges, including uncertainty, anxiety, periodic burnout, and depression. But trying to imagine what it’s like for Cheryl to live with MS has been the biggest challenge of all. My respect for her courage and determination is immense.

We informed our two sons little by little about their mother’s MS and, as their understanding of her disability and treatment grew, they realized that she was going to be okay. Living with MS in my role as caregiver has not only brought me closer to Cheryl and our sons, now 19 and 21 years old; it has also afforded me the opportunity to give to so many others who are living with this disease.

MS affects the entire family — emotionally, physically, and financially. Through the losses and the struggles, I discovered that my life has become richer. Our family came together as a team to deal with MS. We’re fortunate that we were able to do so. Many individuals and families deal with MS with varying degrees of success.

One of the lessons I’ve learned from all this experience is that MS cannot be reduced to a cookie cutter set of symptoms or prescriptions. There is no workable one-size-fits-all approach to MS and its symptoms, which range from optic neuritis and numbness to tingling, extreme fatigue, vertigo, bladder and bowel problems, tremors, muscle spasticity, depression, and more. Add ethnicity, gender, cultural differences, frequent bias in the work setting, and the lack of family or social support that many patients face, and it is clear that each MS patient must be helped on his or her own terms if treatment is to succeed.

Individuals who are diagnosed with MS place great trust and confidence in those who manage or oversee their treatment. Families and other caregivers who assist patients must also extend a substantial amount of trust to those who manage treatment. My

experience over the years has convinced me that successful treatment of patients with MS, as well as quality of life for patients and their caregivers, depends on managed care providers making choices that benefit both the company and the patient.

I am certain that most managed care representatives have encountered situations in which the treatment needed or prescribed made all the sense in the world but was not covered by the policy. Items not covered can range from medications to physical therapy to assistive devices such as walkers. This is when MS patients need managed care the most. These are the instances when insurers must fight on behalf of their customers. Remember, you or someone you love could be a patient!

Depression is one side effect of MS that could be reduced if more insurers understood the disease better and had more empathy for patients living with MS. Insurers may not be aware, for example, of how many patients with MS leave the workforce. Forty-seven percent of the patient respondents in this report said they are currently not working owing to their MS, and 43% said they can no longer work on account of their MS. These numbers could be reduced through faster diagnosis and better treatment.

I came by my insight out of necessity. I have witnessed the breaking apart of families who are living with MS because they were unable to advocate effectively for themselves and could not find ways to work in partnership with an insurer and a healthcare team.

Caregivers who are strong advocates bring an important resource to managing treatment for patients with MS. When caregivers are absent or lack resources, whether emotional or financial or physical, the challenges of managing treatment escalate. Decisions made by managed care on behalf of patients with MS can never be overestimated in their importance, and this is even more the case when care giving is less than optimal.

LET ME TELL YOU ... ABOUT LIVING WITH MS FOR 40 YEARS



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I was 14 years old when I hurried off the tennis court and found my mother. I complained that I was seeing two tennis balls coming at me, and my mother just looked perplexed. “But you can see that there is only one tennis ball.” I shook my head in something of a panic and said, “I know, but I’m seeing two.” And sometimes, when I looked up to serve the tennis ball in the evenings, there would appear to be two sets of stadium lights.

I started playing tennis when I was 11 years old and thought that I would play the game all of my life. I grew up in Orlando, Florida, where the tennis was great. But all during my junior competitive years, weird things kept occurring. One time when I looked at the lawn around the courts, the blades of grass looked painted together almost as if they were on an artist’s canvas. It wasn’t just my vision. Frequently when I would retrieve the ball to my right, my knee would just give out.

I seemed to do very well playing tennis in cooler weather during my undergraduate years at Frostburg State University. A lot cooler. Sometimes the team even played when there were snow flurries. It never bothered me. But indoors when we had to do our workouts in the gymnasium, I fatigued very quickly.

I fell in love during my sophomore year in college. I graduated early, and earned a master's degree at Ball State University before marrying in 1973. I was anxious to get back to tennis, and I competed in a few national tennis tournaments.

My husband was an officer in the Marine Corps. We were stationed in Camp Pendleton, California, where there was wonderful tennis weather. I continued to play and didn't seem to have many of the crazy things or weird sensations anymore. I would just get so tired doing the simplest things. Fatigue would come over me for no reason. I knew something was wrong.

By 1977, my foot was dropping every time I tried to take a step with my right leg. I would trip going up steps. I kept getting weaker until August of that year, when I barely got to a hospital emergency room before I collapsed. After a series of tests, I was diagnosed with MS.

I don't believe that anyone thought I could have something like MS because I was so healthy and such a good tennis player. Matters became more complicated. My husband filed for divorce. I knew that whatever the future held, I had to get back on my feet and get going again. I had to do it on my own. I was lucky to finish my doctorate.

But in my early forties things changed again. I had been hired in a tenure-track position back at Frostburg. But my students kept evaluating me as an alcoholic at the end of the semester. One student wrote that I was constantly holding onto the blackboard and it was clear that I had a hangover when I was in class. Finally, I told everyone I had MS.

These days I am the senior full professor in the Department of Mass Communication at Frostburg State University. I use an electric scooter. My reputation is widely known. A student in the back of the classroom raised his hand during an examination to ask a question. While I walked to the student with ease, as I came back up the aisle I lost my balance. If you have ever started to fall, you know that you start to grab anything you can. In this case my hand went out in midair but found its way under the top of the desk and into a student's groin. It was a male student who played football, and the entire class during this quiet exam listened to the universal male call: "Uggggghhhh!" But everyone understood.

I started doing a disease-modifying drug as soon as they were available and I hope that, if nothing else, my condition is on hold. One thing is for sure in my present career: no male students ever sit in the front row!

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NO SMALL THING



Sheri Horn Hasan

Freelance Journalist and Patient Advocate

Marketing Manager, Easter Seals New Jersey

East Brunswick, NJ

Numb from the waist down and having difficulty walking — that was my condition when I first heard the words “multiple sclerosis.”

I was told I had a back tumor, or some form of general encephalitis, or MS. My back MRIs showed no tumor, so ... a weekend in the hospital receiving methylprednisolone infusions and one spinal tap later, the diagnosis was conclusive.

Now what? Go home, learn all I can, and pray I don't end up in a wheelchair in ten years?

And, while I lived in absolute terror of the prediction by not one, but two well-respected MS neurologists that I might relapse within three to four months of my initial diagnosis — and I'd be a liar if I said I don't feel fear and panic occasionally when I let myself project too far into the future — I know now that I defied the odds.

Not only did I not experience a relapse within the months following my diagnosis; I have been relapse-free for seven years — ever since I first heard the dreaded words “multiple sclerosis” in March 2000.

Since then, I attribute my “positive” experience with this incurable disease to immunomodulatory drug therapy, my decision to be proactive, and a positive mindset — which doesn't mean I escaped such symptoms as overwhelming fatigue, vertigo, tingling, numbness, and bouts of optic neuritis and fuzzy-headedness during the first two years or so after my diagnosis, or that it did not take nearly three full years for the burning in my right leg to subside slowly before it all but disappeared.

Although the realities of the disease were tough at first to digest, and it was even tougher to believe that I would at some point fully recover the feeling in my lower body and be able to walk normally and take care of my then almost-five-year-old son without succumbing to total exhaustion, I resolved early on to become my own advocate and to act as decisively as possible.

Concerned that my brain MRI indicated I might relapse quickly, my diagnosing neurologist suggested a particular disease-modifying agent. After doing my own research on MS drugs and soliciting the opinion of another MS specialist, who confirmed my diagnosis and the possibility of a quick relapse, I chose a different MS drug than the one originally recommended by the doctor who diagnosed me. Terrified at the prospect of a relapse, I realized that I had to become an active participant in decisions concerning

my treatment. Claiming the choice to determine which drug to take turned out to be instrumental in my ability to maintain control of my life and to face the threat posed by this unpredictable disease.

At the time of my diagnosis, the National MS Society had already released its 1998 statement that anyone diagnosed with relapsing-remitting MS should initiate drug therapy as soon as possible because medical research had proven that MS progresses regardless of the manifestation of symptoms.

I initially equated my MS diagnosis with inevitable disability and a drastic reduction in quality of life. But with even more disease-modifying drugs on the market today and several more agents in the pipeline, MS neurologists and patients stand a much better chance of improving quality of life for those like me.

These drugs — and patients' freedom to choose their course of treatment, with the guidance of their doctors — have given MS patients the opportunity to stop an awful, potentially debilitating disease from ravaging them as badly as it might.

I am strongly of the opinion that I represent a new generation of MS patients. I credit my choice of drug therapy and my life decisions with allowing me to lead a normal life, nowhere near as badly affected by my MS as my original MRI suggested.

For example, since my diagnosis, I decided it would be healthier for me to leave an unhappy marriage; I decided it would be more fulfilling to go back to full-time employment; I decided to keep myself as healthy as possible through diet and exercise. These things are not beyond my control, and I am certain that acting as my own patient advocate by educating myself about MS and maintaining a positive attitude has contributed to lower costs for managed care.

While I pray for a cure for MS, I also count my blessings — which include coverage, by my insurer, of my drug of choice at a reasonable co-pay, and the benefit, at times (depending on my insurer), of an MS wellness and education program.

In addition, ongoing MS research gives me the greatest hope, when I picture my future, that it does not contain a wheelchair.

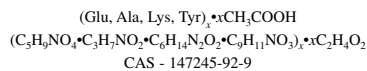
And believe me — that is no small thing.

COPAXONE® (glatiramer acetate injection)

DESCRIPTION

COPAXONE® is the brand name for glatiramer acetate (formerly known as copolymer-1). Glatiramer acetate, the active ingredient of COPAXONE®, consists of the acetate salts of synthetic polypeptides, containing four naturally occurring amino acids: L-glutamic acid, L-alanine, L-tyrosine, and L-lysine with an average molar fraction of 0.141, 0.427, 0.095, and 0.338, respectively. The average molecular weight of glatiramer acetate is 5,000–9,000 daltons. Glatiramer acetate is identified by specific antibodies.

Chemically, glatiramer acetate is designated L-glutamic acid polymer with L-alanine, L-lysine and L-tyrosine, acetate (salt). Its structural formula is:



COPAXONE® Injection is a clear, colorless to slightly yellow, sterile, non-pyrogenic solution for subcutaneous injection. Each 1.0 mL of solution contains 20 mg of glatiramer acetate and 40 mg of mannitol, USP. The pH range of the solution is approximately 5.5 to 7.0. The biological activity of COPAXONE® is determined by its ability to block the induction of EAE in mice.

CLINICAL PHARMACOLOGY

Mechanism of Action

The mechanism(s) by which glatiramer acetate exerts its effects in patients with Multiple Sclerosis (MS) is (are) not fully elucidated. However, it is thought to act by modifying immune processes that are currently believed to be responsible for the pathogenesis of MS. This hypothesis is supported by findings of studies that have been carried out to explore the pathogenesis of experimental allergic encephalomyelitis (EAE), a condition induced in several animal species through immunization against central nervous system derived material containing myelin and often used as an experimental animal model of MS. Studies in animals and *in vitro* systems suggest that upon its administration, glatiramer acetate-specific suppressor T-cells are induced and activated in the periphery.

Because glatiramer acetate can modify immune functions, concerns exist about its potential to alter naturally occurring immune responses. Results of a limited battery of tests designed to evaluate this risk produced no finding of concern; nevertheless, there is no logical way to absolutely exclude this possibility (see **PRECAUTIONS**).

Pharmacokinetics

Results obtained in pharmacokinetic studies performed in humans (healthy volunteers) and animals support the assumption that a substantial fraction of the therapeutic dose delivered to patients subcutaneously is hydrolyzed locally. Nevertheless, larger fragments of glatiramer acetate can be recognized by glatiramer acetate-reactive antibodies. Some fraction of the injected material, either intact or partially hydrolyzed, is presumed to enter the lymphatic circulation, enabling it to reach regional lymph nodes, and some may enter the systemic circulation intact.

Clinical Trials

Evidence supporting the effectiveness of glatiramer acetate in decreasing the frequency of relapses in patients with Relapsing-Remitting Multiple Sclerosis (RR MS) derives from two placebo-controlled trials, both of which used a glatiramer acetate dose of 20 mg/day. (No other dose or dosing regimen has been studied in placebo-controlled trials of RR MS.)

One trial was performed at a single center. It enrolled 50 patients who were randomized to receive daily doses of either glatiramer acetate, 20 mg subcutaneously, or placebo (glatiramer acetate, n=25; placebo, n=25). Patients were diagnosed with RR MS by standard criteria, and had had at least 2 exacerbations during the 2 years immediately preceding enrollment. Patients were ambulatory, as evidenced by a score of no more than 6 on the Kurtzke Disability Scale Score (DSS), a standard scale ranging from 0–Normal to 10–Death due to MS. A score of 6 is defined as one at which a patient is still ambulatory with assistance; a score of 7 means the patient must use a wheelchair.

Patients were examined every 3 months for 2 years, as well as within several days of a presumed exacerbation. To confirm an exacerbation, a blinded neurologist had to document objective neurologic signs, as well as document the existence of other criteria (e.g., the persistence of the neurological signs for at least 48 hours).

The protocol-specified primary outcome measure was the proportion of patients in each treatment group who remained exacerbation free for the 2 years of the trial, but two other important outcomes were also specified as endpoints: 1) the frequency of attacks during the trial, and 2) the change in the number of attacks compared with the number which occurred during the previous 2 years.

Table 1 presents the values of the three outcomes described above, as well as several protocol specified secondary measures. These values are based on the intent-to-treat population (i.e., all patients who received at least 1 dose of treatment and who had at least 1 on-treatment assessment):

Table 1: Study 1 Efficacy Results

Outcome	Glatiramer Acetate (N=25)	Placebo (N=25)	P-Value
% Relapse-Free Patients	14/25 (56%)	7/25 (28%)	0.085
Mean Relapse Frequency	0.6/2 years	2.4/2 years	0.005
Reduction in Relapse Rate Compared to Pre-Study	3.2	1.6	0.025
Median Time to First Relapse (days)	>700	150	0.03
% of Progression-Free* Patients	20/25 (80%)	13/25 (52%)	0.07

*Progression was defined as an increase of at least 1 point on the DSS, persisting for at least 3 consecutive months.

The second trial was a multicenter trial of similar design which was performed in 11 US centers. A total of 251 patients (glatiramer acetate, 125; placebo, 126) were enrolled. The primary outcome measure was the Mean 2-Year Relapse Rate. The table below presents the values of this outcome for the intent-to-treat population, as well as several secondary measures:

Table 2: Study 2 Efficacy Results

Outcome	Glatiramer Acetate (N=125)	Placebo (N=126)	P-Value
Mean No. of Relapses	1.19/2 years	1.68/2 years	0.055
% Relapse-Free Patients	42/125 (34%)	34/126 (27%)	0.25
Median Time to First Relapse (days)	287	198	0.23
% of Progression-Free Patients	98/125 (78%)	95/126 (75%)	0.48
Mean Change in DSS	-0.05	+0.21	0.023

In both studies glatiramer acetate exhibited a clear beneficial effect on relapse rate, and it is based on this evidence that glatiramer acetate is considered effective.

A third study was a multi-national study in which MRI parameters were used both as primary and secondary endpoints. A total of 239 patients with RR MS (119 on glatiramer acetate and 120 on placebo) were randomized. Inclusion criteria were similar to those in the second study with the additional criterion that patients had to have at least one Gd-enhancing lesion on the screening MRI. The patients were treated in a double-blind manner for nine months, during which they underwent monthly MRI scanning. The primary

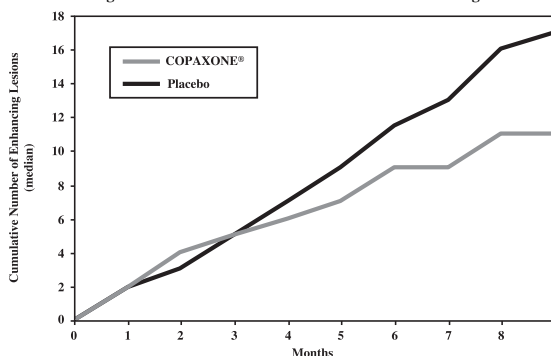
endpoint for the double-blind phase was the total cumulative number of T1 Gd-enhancing lesions over the nine months. Table 3 summarizes the results for the primary outcome measure monitored during the trial for the intent-to-treat cohort.

Table 3: Study 3 MRI Results

Outcome	Glatiramer Acetate (N=119)	Placebo (N=120)	P-Value
Medians of the Cumulative Number of T1 Gd-Enhancing Lesions	11	17	0.0030

The following figure displays the results of the primary outcome on a monthly basis.

Figure 1: Median Cumulative Number of Gd-Enhancing Lesions



p=0.0030 for the difference between the placebo-treated (n=120) and glatiramer acetate-treated (n=119) groups

INDICATIONS AND USAGE

COPAXONE® Injection is indicated for reduction of the frequency of relapses in patients with Relapsing-Remitting Multiple Sclerosis.

CONTRAINDICATIONS

COPAXONE® Injection is contraindicated in patients with known hypersensitivity to glatiramer acetate or mannitol.

WARNINGS

The only recommended route of administration of COPAXONE® Injection is the subcutaneous route. COPAXONE® Injection should not be administered by the intravenous route.

PRECAUTIONS

General

Patients should be instructed in self-injection techniques to assure the safe administration of COPAXONE® Injection (see **PRECAUTIONS: Information for Patients and the COPAXONE® INJECTION PATIENT INFORMATION Leaflet**). Current data indicate that no special caution is required for patients operating an automobile or using complex machinery.

Considerations Regarding the Use of a Product Capable of Modifying Immune Responses

Because glatiramer acetate can modify immune response, it could possibly interfere with useful immune functions. For example, treatment with glatiramer acetate might, in theory, interfere with the recognition of foreign antigens in a way that would undermine the body's tumor surveillance and its defenses against infection. There is no evidence that glatiramer acetate does this, but there has as yet been no systematic evaluation of this risk. Because glatiramer acetate is an antigenic material, it is possible that its use may lead to the induction of host responses that are untoward, but systematic surveillance for these effects has not been undertaken.

Although glatiramer acetate is intended to minimize the autoimmune response to myelin, there is the possibility that continued alteration of cellular immunity due to chronic treatment with glatiramer acetate might result in untoward effects.

Glatiramer acetate-reactive antibodies are formed in practically all patients exposed to daily treatment with the recommended dose. Studies in both the rat and monkey have suggested that immune complexes are deposited in the renal glomeruli. Furthermore, in a controlled trial of 125 RR MS patients given glatiramer acetate, 20 mg, subcutaneously every day for 2 years, serum IgG levels reached at least 3 times baseline values in 80% of patients by 3 months of initiation of treatment. By 12 months of treatment, however, 30% of patients still had IgG levels at least 3 times baseline values, and 90% had levels above baseline by 12 months. The antibodies are exclusively of the IgG subtype and predominantly of the IgG-1 subtype. No IgE type antibodies could be detected in any of the 94 sera tested; nevertheless, anaphylaxis can be associated with the administration of most any foreign substance, and therefore, this risk cannot be excluded.

Information for Patients

To assure safe and effective use of COPAXONE® Injection, the following information and instructions should be given to patients:

1. Inform your physician if you are pregnant, if you are planning to have a child, or if you become pregnant while taking this medication.
2. Inform your physician if you are nursing.
3. Do not change the dose or dosing schedule without consulting your physician.
4. Do not stop taking the drug without consulting your physician.

Patients should be instructed in the use of aseptic techniques when administering COPAXONE® Injection. Appropriate instructions for the self-injection of COPAXONE® Injection should be given, including a careful review of the **COPAXONE® INJECTION PATIENT INFORMATION Leaflet**. The first injection should be performed under the supervision of an appropriately qualified health care professional. Patient understanding and use of aseptic self-injection techniques and procedures should be periodically reevaluated. Patients should be cautioned against the reuse of needles or syringes and instructed in safe disposal procedures. They should use a puncture-resistant container for disposal of used needles and syringes. Patients should be instructed on the safe disposal of full containers according to local laws.

Awareness of Adverse Reactions: Physicians are advised to counsel patients about adverse reactions associated with the use of COPAXONE® Injection (see **ADVERSE REACTIONS** section). In addition, patients should be advised to read the **COPAXONE® INJECTION PATIENT INFORMATION Leaflet** and resolve any questions regarding it prior to beginning COPAXONE® Injection therapy.

Laboratory Tests

Data collected during premarketing development do not suggest the need for routine laboratory monitoring.

Drug Interactions

Interactions between COPAXONE® Injection and other drugs have not been fully evaluated. Results from existing clinical trials do not suggest any significant interactions of COPAXONE® Injection with therapies commonly used in MS patients, including the concurrent use of corticosteroids for up to 28 days. COPAXONE® Injection has not been formally evaluated in combination with Interferon beta.

Drug/Laboratory Test Interactions

None are known.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In a two-year carcinogenicity study, mice were administered up to 60 mg/kg/day glatiramer acetate by subcutaneous injection (up to 15 times the human therapeutic dose on a mg/m² basis). No increase in systemic neoplasms was observed. In males of the high dose group (60 mg/kg/day), but not in females, there was an

increased incidence of fibrosarcomas at the injection sites. These sarcomas were associated with skin damage precipitated by repetitive injections of an irritant over a limited skin area.

In a two-year carcinogenicity study, rats were administered up to 30 mg/kg/day glatiramer acetate by subcutaneous injection (up to 15 times the human therapeutic dose on a mg/m² basis). No increase in systemic neoplasms was observed.

Mutagenesis

Glatiramer acetate was not mutagenic in four strains of *Salmonella typhimurium* and two strains of *Escherichia coli* (Ames test) or in the *in vitro* mouse lymphoma assay in L5178Y cells. Glatiramer acetate was clastogenic in two separate *in vitro* chromosomal aberration assays in cultured human lymphocytes; it was not clastogenic in an *in vivo* mouse bone marrow micronucleus assay.

Impairment of Fertility

In a multigeneration reproduction and fertility study in rats, glatiramer acetate at subcutaneous doses of up to 36 mg/kg (18 times the human therapeutic dose on a mg/m² basis) had no adverse effects on reproductive parameters.

Pregnancy

Pregnancy Category B. No adverse effects on embryofetal development occurred in reproduction studies in rats and rabbits receiving subcutaneous doses of up to 37.5 mg/kg of glatiramer acetate during the period of organogenesis (18 and 36 times the therapeutic human dose on a mg/m² basis, respectively). In a prenatal and postnatal study in which rats received subcutaneous glatiramer acetate at doses of up to 36 mg/kg from day 15 of pregnancy throughout lactation, no significant effects on delivery or on offspring growth and development were observed.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, glatiramer acetate should be used during pregnancy only if clearly needed.

Labor and Delivery

In a prenatal and postnatal study, in which rats received subcutaneous glatiramer acetate at doses of up to 36 mg/kg from day 15 of pregnancy throughout lactation, no significant effects on delivery were observed. The relevance of these findings to humans is unknown.

Nursing Mothers

It is not known whether glatiramer acetate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when COPAXONE[®] is administered to a nursing woman.

Pediatric Use

The safety and efficacy of COPAXONE[®] Injection have not been established in individuals under 18 years of age.

Use in the Elderly

COPAXONE[®] Injection has not been studied specifically in elderly patients.

Use in Patients with Impaired Renal Function

The pharmacokinetics of glatiramer acetate in patients with impaired renal function have not been determined.

ADVERSE REACTIONS

During premarketing clinical trials approximately 900 individuals received at least one dose of glatiramer acetate.

In controlled clinical trials the most commonly observed adverse experiences associated with the use of glatiramer acetate and not seen at an equivalent frequency among placebo-treated patients were: injection site reactions, vasodilatation, chest pain, asthenia, infection, pain, nausea, arthralgia, anxiety, and hypertonia.

Approximately 8% of the 893 subjects receiving glatiramer acetate discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: injection site reaction (6.5%), vasodilatation, unintended pregnancy, depression, dyspnea, urticaria, tachycardia, dizziness, and tremor.

Immediate Post-Injection Reaction

Approximately 10% of MS patients exposed to glatiramer acetate in premarketing studies experienced a constellation of symptoms immediately after injection that included flushing, chest pain, palpitations, anxiety, dyspnea, constriction of the throat, and urticaria. In clinical trials, the symptoms were generally transient and self-limited and did not require specific treatment. In general, these symptoms have their onset several months after the initiation of treatment, although they may occur earlier, and a given patient may experience one or several episodes of these symptoms. Whether or not any of these symptoms actually represent a specific syndrome is uncertain. During the postmarketing period, there have been reports of patients with similar symptoms who received emergency medical care.

Whether an immunologic or non-immunologic mechanism mediates these episodes, or whether several similar episodes seen in a given patient have identical mechanisms, is unknown.

Chest Pain

Approximately 21% of glatiramer acetate patients in the pre-marketing controlled studies (compared to 11% of placebo patients) experienced at least one episode of what was described as transient chest pain. While some of these episodes occurred in the context of the Immediate Post-Injection Reaction described above, many did not. The temporal relationship of this chest pain to an injection of glatiramer acetate was not always known. The pain was transient (usually lasting only a few minutes), often unassociated with other symptoms, and appeared to have no important clinical sequelae. There has been only one episode of chest pain during which a full EKG was performed; that EKG showed no evidence of ischemia. Some patients experienced more than one such episode, and episodes usually began at least 1 month after the initiation of treatment. The pathogenesis of this symptom is unknown.

Incidence in Controlled Clinical Studies: The following table lists treatment-emergent signs and symptoms that occurred in at least 2% of MS patients treated with glatiramer acetate in the pre-marketing placebo-controlled trials. These signs and symptoms were numerically more common in patients treated with glatiramer acetate than in patients treated with placebo. These trials include the first two controlled trials in RR MS patients and a controlled trial in patients with Chronic-Progressive MS. Adverse reactions were usually mild in intensity.

The prescriber should be aware that these figures cannot be used to predict the frequency of adverse experiences in the course of usual medical practice where patient characteristics and other factors may differ from those prevailing during clinical studies. Similarly, the cited frequencies cannot be directly compared with figures obtained from other clinical investigations involving different treatments, uses, or investigators. An inspection of these frequencies, however, does provide the prescriber with one basis on which to estimate the relative contribution of drug and nondrug factors to the adverse reaction incidences in the population studied.

**Controlled Trials in Patients with Multiple Sclerosis:
Incidence of Glatiramer Acetate Adverse Reactions $\geq 2\%$
and More Frequent than Placebo**

Preferred Term	Glatiramer Acetate (N = 201)		Placebo (N = 206)	
	N	%	N	%
Body as a Whole				
Asthenia	83	41	78	38
Back Pain	33	16	30	15
Bacterial Infection	11	5	9	4
Chest Pain	43	21	22	11
Chills	8	4	2	1
Cyst	5	2	1	0
Face Edema	12	6	2	1
Fever	17	8	15	7
Flu Syndrome	38	19	35	17
Infection	101	50	99	48
Injection Site Erythema	132	66	40	19
Injection Site Hemorrhage	11	5	6	3
Injection Site Induration	26	13	1	0

Preferred Term (continued)	Glatiramer Acetate (N = 201)		Placebo (N = 206)	
	N	%	N	%
Injection Site Inflammation	98	49	22	11
Injection Site Mass	54	27	21	10
Injection Site Pain	147	73	78	38
Injection Site Pruritus	80	40	12	6
Injection Site Urticaria	10	5	0	0
Injection Site Welt	22	11	5	2
Neck Pain	16	8	9	4
Pain	56	28	52	25
Cardiovascular System				
Migraine	10	5	5	2
Palpitations	35	17	16	8
Syncope	10	5	5	2
Tachycardia	11	5	8	4
Vasodilatation	55	27	21	10
Digestive System				
Anorexia	17	8	15	7
Diarrhea	25	12	23	11
Gastroenteritis	6	3	2	1
Gastrointestinal Disorder	10	5	8	4
Nausea	44	22	34	17
Vomiting	13	6	8	4
Hemic and Lymphatic System				
Ecchymosis	16	8	13	6
Lymphadenopathy	25	12	12	6
Metabolic and Nutritional				
Edema	5	3	1	0
Peripheral Edema	14	7	8	4
Weight Gain	7	3	0	0
Musculoskeletal System				
Arthralgia	49	24	39	19
Nervous System				
Agitation	8	4	4	2
Anxiety	46	23	40	19
Confusion	5	2	1	0
Foot Drop	6	3	4	2
Hypertonia	44	22	37	18
Nervousness	4	2	2	1
Nystagmus	5	2	2	1
Speech Disorder	5	2	3	1
Tremor	14	7	7	3
Vertigo	12	6	11	5
Respiratory System				
Bronchitis	18	9	12	6
Dyspnea	38	19	15	7
Laryngismus	10	5	7	3
Rhinitis	29	14	27	13
Skin and Appendages				
Erythema	8	4	4	2
Herpes Simplex	8	4	6	3
Pruritus	36	18	26	13
Rash	37	18	30	15
Skin Nodule	4	2	1	0
Sweating	31	15	21	10
Urticaria	9	4	5	2
Special Senses				
Ear Pain	15	7	12	6
Eye Disorder	8	4	1	0
Urogenital System				
Dysmenorrhea	12	6	10	5
Urinary Urgency	20	10	17	8
Vaginal Moniliasis	16	8	9	4

Other events which occurred in at least 2% of glatiramer acetate patients but were present at equal or greater rates in the placebo group included:

Body as a Whole: Headache, injection site ecchymosis, accidental injury, abdominal pain, allergic rhinitis, neck rigidity, and malaise.

Digestive System: Dyspepsia, constipation, dysphagia, fecal incontinence, flatulence, nausea and vomiting, gastritis, gingivitis, periodontal abscess, and dry mouth.

Musculoskeletal: Myasthenia and myalgia.

Nervous System: Dizziness, hypesthesia, paresthesia, insomnia, depression, dysesthesia, incoordination, somnolence, abnormal gait, amnesia, emotional lability, Lhermitte's sign, abnormal thinking, twitching, euphoria, and sleep disorder.

Respiratory System: Pharyngitis, sinusitis, increased cough, and laryngitis.

Skin and Appendages: Acne, alopecia, and nail disorder.

Special Senses: Abnormal vision, diplopia, amblyopia, eye pain, conjunctivitis, tinnitus, taste perversion, and deafness.

Urogenital System: Urinary tract infection, urinary frequency, urinary incontinence, urinary retention, dysuria, cystitis, metrorrhagia, breast pain, and vaginitis.

Data on adverse reactions occurring in the controlled clinical trials were analyzed to evaluate differences based on sex. No clinically significant differences were identified. Ninety-two percent of patients in these clinical trials were Caucasian. This percentage reflects the racial composition of the MS population. In addition, the vast majority of patients treated with COPAXONE[®] were between the ages of 18 and 45. Consequently, data are inadequate to perform an analysis of the adverse reaction incidence related to clinically relevant age subgroups.

Laboratory analyses were performed on all patients participating in the clinical program for glatiramer acetate. Clinically significant laboratory values for hematology, chemistry, and urinalysis were similar for both glatiramer acetate and placebo groups in blinded clinical trials. No patient receiving glatiramer acetate withdrew from any trial because of abnormal laboratory findings.

Other Adverse Events Observed During Clinical Trials

Glatiramer acetate was administered to 979 individuals during premarketing clinical trials, only some of which were placebo-controlled. During these trials, all adverse events were recorded by the clinical investigators,

using terminology of their own choosing. To provide a meaningful estimate of the proportion of individuals having adverse events, similar types of events were grouped into standardized categories using COSTART dictionary terminology. All reported events occurring at least twice and potentially important events occurring once are listed below, except those already listed in the previous table, those too general to be informative, trivial events, and other reactions which occurred in at least 2% of treated patients and were present at equal or greater rates in the placebo group. Additional adverse reactions reported during the post-marketing period are included.

Events are further classified within body system categories and listed in order of decreasing frequency using the following definitions: *Frequent* adverse events are defined as those occurring in at least 1/100 patients; *Infrequent* adverse events are those occurring in 1/100 to 1/1000 patients; *Rare* adverse events are those occurring in less than 1/1000 patients.

Body as a Whole:

- ◆ *Frequent:* Injection site edema, injection site atrophy, abscess, injection site hypersensitivity.
- ◆ *Infrequent:* Injection site hematoma, injection site fibrosis, moon face, cellulitis, generalized edema, hernia, injection site abscess, serum sickness, suicide attempt, injection site hypertrophy, injection site melanosis, lipoma, and photosensitivity reaction.

Cardiovascular:

- ◆ *Frequent:* Hypertension.
- ◆ *Infrequent:* Hypotension, midsystolic click, systolic murmur, atrial fibrillation, bradycardia, fourth heart sound, postural hypotension, and varicose veins.

Digestive:

- ◆ *Infrequent:* Dry mouth, stomatitis, burning sensation on tongue, cholecystitis, colitis, esophageal ulcer, esophagitis, gastrointestinal carcinoma, gum hemorrhage, hepatomegaly, increased appetite, melena, mouth ulceration, pancreas disorder, pancreatitis, rectal hemorrhage, tenesmus, tongue discoloration, and duodenal ulcer.

Endocrine:

- ◆ *Infrequent:* Goiter, hyperthyroidism, and hypothyroidism.

Gastrointestinal:

- ◆ *Frequent:* Bowel urgency, oral moniliasis, salivary gland enlargement, tooth caries, and ulcerative stomatitis.

Hemic and Lymphatic:

- ◆ *Infrequent:* Leukopenia, anemia, cyanosis, eosinophilia, hematemesis, lymphedema, pancytopenia, and splenomegaly.

Metabolic and Nutritional:

- ◆ *Infrequent:* Weight loss, alcohol intolerance, Cushing's syndrome, gout, abnormal healing, and xanthoma.

Musculoskeletal:

- ◆ *Infrequent:* Arthritis, muscle atrophy, bone pain, bursitis, kidney pain, muscle disorder, myopathy, osteomyelitis, tendon pain, and tenosynovitis.

Nervous:

- ◆ *Frequent:* Abnormal dreams, emotional lability, and stupor.
- ◆ *Infrequent:* Aphasia, ataxia, convulsion, circumoral paresthesia, depersonalization, hallucinations, hostility, hypokinesia, coma, concentration disorder, facial paralysis, decreased libido, manic reaction, memory impairment, myoclonus, neuralgia, paranoid reaction, paraplegia, psychotic depression, and transient stupor.

Respiratory:

- ◆ *Frequent:* Hyperventilation, hay-fever.
- ◆ *Infrequent:* Asthma, pneumonia, epistaxis, hypoventilation, and voice alteration.

Skin and Appendages:

- ◆ *Frequent:* Eczema, herpes zoster, pustular rash, skin atrophy, and warts.
- ◆ *Infrequent:* Dry skin, skin hypertrophy, dermatitis, furunculosis, psoriasis, angioedema, contact dermatitis, erythema nodosum, fungal dermatitis, maculopapular rash, pigmentation, benign skin neoplasm, skin carcinoma, skin striae, and vesiculobullous rash.

Special Senses:

- ◆ *Frequent:* Visual field defect.
- ◆ *Infrequent:* Dry eyes, otitis externa, ptosis, cataract, corneal ulcer, mydriasis, optic neuritis, photophobia, and taste loss.

Urogenital:

- ◆ *Frequent:* Amenorrhea, hematuria, impotence, menorrhagia, suspicious papnicolaou smear, urinary frequency and vaginal hemorrhage.
- ◆ *Infrequent:* Vaginitis, flank pain (kidney), abortion, breast engorgement, breast enlargement, carcinoma *in situ* cervix, fibrocystic breast, kidney calculus, nocturia, ovarian cyst, priapism, pyelonephritis, abnormal sexual function, and urethritis.

Postmarketing Clinical Experience

Postmarketing experience has shown an adverse event profile similar to that presented above. Reports of adverse reactions occurring under treatment with COPAXONE® (glatiramer acetate for injection) not mentioned above that have been received since market introduction and that may have or not have causal relationship to the drug include the following:

Body as a Whole: sepsis; LE syndrome; hydrocephalus; enlarged abdomen; injection site hypersensitivity; allergic reaction; anaphylactoid reaction

Cardiovascular System: thrombosis; peripheral vascular disease; pericardial effusion; myocardial infarct; deep thrombophlebitis; coronary occlusion; congestive heart failure; cardiomyopathy; cardiomegaly; arrhythmia; angina pectoris

Digestive System: tongue edema; stomach ulcer; hemorrhage; liver function abnormality; liver damage; hepatitis; eructation; cirrhosis of the liver; cholelithiasis

Hemic and Lymphatic System: thrombocytopenia; lymphoma-like reaction; acute leukemia

Metabolic and Nutritional Disorders: hypercholesterolemia

Musculoskeletal System: rheumatoid arthritis; generalized spasm

Nervous System: myelitis; meningitis; CNS neoplasm; cerebrovascular accident; brain edema; abnormal dreams; aphasia; convulsion; neuralgia

Respiratory System: pulmonary embolus; pleural effusion; carcinoma of lung; hay fever

Special Senses: glaucoma; blindness; visual field defect

Urogenital System: urogenital neoplasm; urine abnormality; ovarian carcinoma; nephrosis; kidney failure; breast carcinoma; bladder carcinoma; urinary frequency

Adverse Reactions Associated with Subcutaneous Use

At injection sites, localized lipoatrophy and, rarely, injection site skin necrosis has been reported during the postmarketing experience. Lipoatrophy may occur at various times after treatment onset (sometimes after several months) and is thought to be permanent. There is no known therapy for lipoatrophy. To assist in possibly minimizing these events the patient should be advised to follow proper injection technique and to rotate injection areas and sites on a daily basis. (See PATIENT INFORMATION)

DRUG ABUSE AND DEPENDENCE

No evidence of experience suggests that abuse or dependence occurs with COPAXONE® Injection therapy; however, the risk of dependence has not been systematically evaluated.

DOSAGE AND ADMINISTRATION

The recommended dose of COPAXONE® Injection for the treatment of RR MS is 20 mg/day injected subcutaneously.

Instructions for Use

Remove one blister with the syringe inside from the COPAXONE® Injection Pre-filled syringes package from the refrigerator. For refrigerated product, let the pre-filled syringe package stand at room temperature for

20 minutes to allow the solution to warm up to room temperature. Inspect the product visually and discard or return the product to the pharmacist before use if it contains any particulate matter.

Sites for self-injection include arms, abdomen, hips, and thighs. The pre-filled syringe is suitable for single use only; unused portions should be discarded. (See the COPAXONE® Injection PATIENT INFORMATION Leaflet for INSTRUCTIONS FOR INJECTING COPAXONE®.)

HOW SUPPLIED

COPAXONE® Injection is supplied as a single-use pre-filled syringe containing 1.0 mL of a clear, colorless to slightly yellow, sterile, non-pyrogenic solution containing 20 mg of glatiramer acetate and 40 mg of mannitol, USP in cartons of 30 single-use pre-filled syringes, 33 alcohol preps (wipes) and instructions for use.

The recommended storage condition for the COPAXONE® Injection is refrigeration (2°C to 8°C / 36°F to 46°F). However, excursions from recommended storage conditions to room temperature conditions (15° to 30°C / 59° to 86° F) for up to one month have been shown to have no adverse impact on the product. Exposure to higher temperatures or intense light should be avoided.

COPAXONE® Injection contains no preservative. Do not use if the solution contains any particulate matter.

COPAXONE® Injection is available in packs of 30 single-use Pre-Filled Syringes (NDC 0088-1153-30).

Rx only.

PATIENT INFORMATION

COPAXONE® (glatiramer acetate injection)

Read this information carefully before you use COPAXONE®. Read the information you get when you refill your COPAXONE® prescriptions because there may be new information. This information does not take the place of your doctor's advice. Ask your doctor or pharmacist if you do not understand some of this information or if you want to know more about this medicine.

What is COPAXONE®?

COPAXONE® (co-PAX-own) is a medicine you inject to treat Relapsing-Remitting Multiple Sclerosis. Although COPAXONE® is not a cure, patients treated with COPAXONE® have fewer relapses.

Who should not use COPAXONE®?

- COPAXONE® is not recommended for use in pregnancy. So, tell your doctor if you are pregnant or if you plan to become pregnant while taking this medicine.
- Tell your doctor if you are nursing. It is not known if COPAXONE® is passed through the breast milk to the baby.
- Do not use COPAXONE® if you are allergic to glatiramer acetate or mannitol.

What are the possible side effects of COPAXONE®?

- Call your doctor right away if you develop any of the following symptoms: hives, skin rash with irritation, dizziness, sweating, chest pain, trouble breathing, or severe pain at the injection site. Do not give yourself any more injections until your doctor tells you to begin again.
- The most common side effects of COPAXONE® are redness, pain, swelling, itching, or a lump at the injection site. These reactions are usually mild and seldom require medical care.
- Some patients report a short-term reaction right after injecting COPAXONE®. This reaction can involve flushing (feeling of warmth and/or redness), chest tightness or pain with heart palpitations, anxiety, and trouble breathing. These symptoms generally appear within minutes after an injection, last a few minutes, then go away by themselves without further problems.
- A permanent depression under the skin at the injection site may occur, due to a local destruction of fat tissue.
- If symptoms become severe, call the emergency phone number in your area. Do not give yourself any more injections until your doctor tells you to begin again.

These are not all the possible side effects of COPAXONE®. For a complete list, ask your doctor or pharmacist. Tell your doctor about any side effects you have while taking COPAXONE®.

How should I use COPAXONE®?

- The recommended dose of COPAXONE® for the treatment of Relapsing-Remitting Multiple Sclerosis is 20 mg once a day injected subcutaneously (in the fatty layer under the skin).
- Look at the medicine in the pre-filled syringe. If the medicine is cloudy or has particles in it, do not use it. Instead, call Shared Solutions® at 1-800-887-8100 for assistance.
- Have a friend or relative with you if you need help, especially when you first start giving yourself injections.
- Each pre-filled syringe should be used for only one injection. Do not reuse the pre-filled syringe. After use, throw it away properly.
- Do not change the dose or dosing schedule or stop taking the medicine without talking with your doctor.

How do I inject COPAXONE®?

There are 3 basic steps for injecting COPAXONE® pre-filled syringes:

1. Gather the materials.
2. Choose the injection site.
3. Give yourself the injection.

Step 1: Gather the materials

1. First, place each of the items you will need on a clean, flat surface in a well-lit area:
 - 1 blister pack with COPAXONE® Pre-Filled Syringe
 - Remove only 1 blister pack from the COPAXONE® Pre-Filled Syringe carton. Keep all unused syringes in the Pre-Filled Syringe carton and store them in the refrigerator.
 - Alcohol prep (wipe)
 - Dry cotton ball (not supplied)

2. Let the blister pack with the syringe inside warm up to room temperature for 20 minutes.

3. To prevent infection, wash and dry your hands. Do not touch your hair or skin after washing.
4. There may be small air bubbles in the syringe. To avoid loss of medicine when using COPAXONE® pre-filled syringes, do not expel (or do not attempt to expel) the air bubble from the syringe before injecting the medicine.

Step 2: Choose the injection site

- There are 7 possible injection areas on your body: arms, thighs, hips and lower stomach area (abdomen) (See Figure 1).
- Each day, pick a different injection area from one of the 7 areas. Do not inject in the same area more than once a week.
- Within each injection area there are multiple injection sites. Have a plan for rotating your injection sites. Keep a record of your injection sites, so you know where you have injected.
- There are some sites in your body that may be hard to reach for self-injection (like the back of your arm), and you may need help.
- Do not inject in sites where skin depression has occurred, because further injections in these sites may make the depression deeper.

Step 3: Give yourself the injection

1. Remove the syringe from its protective blister pack by peeling back the paper label. Before use, look at the liquid in the syringe. If it is cloudy or contains any particles, do not use it and call Shared Solutions® at 1-800-887-8100 for assistance. If the liquid is clear, place the syringe on the clean, flat surface.

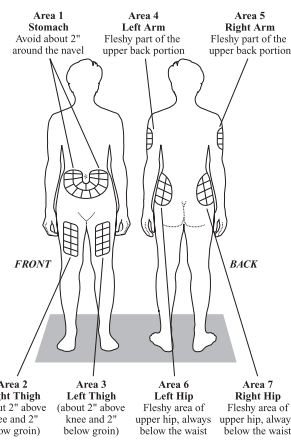


Figure 1

- Choose an injection site on your body. Clean the injection site with a new alcohol prep and let the site air dry to reduce stinging.
- Pick up the syringe as you would a pencil. Remove the needle shield from the needle.



Figure 2

- With your other hand, pinch about a 2-inch fold of skin between your thumb and index finger (See Figure 2).

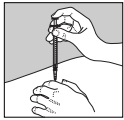


Figure 3

- Insert the needle at a 90-degree angle (straight in), resting the heel of your hand against your body. When the needle is all the way in release the fold of skin (See Figure 3).

- To inject the medicine, hold the syringe steady and push down the plunger.
- When you have injected all of the medicine, pull the needle straight out.
- Press a dry cotton ball on the injection site for a few seconds. **Do not rub the injection site.**
- Throw away the syringe in a safe hard-walled plastic container.

What is the proper use and disposal of Pre-Filled Syringes?

Each Pre-Filled Syringe should be used for only 1 injection. Throw away all used Pre-Filled Syringes in a hard-walled plastic container, such as an empty liquid laundry detergent bottle. Keep the container closed tightly and out of the reach of children. When the container is full, check with your doctor, pharmacist, or nurse about proper disposal, as laws vary from state to state.

How should I store COPAXONE® Pre-Filled Syringes?

Keep the COPAXONE® Pre-Filled Syringe carton in the refrigerator, out of the reach of children.

The COPAXONE® package should be refrigerated at 36-46°F (2-8°C). You can store it at room temperature, 59-86°F (15-30°C), for up to one month. Do not store COPAXONE® at room temperature for longer than one month. **Do not freeze COPAXONE®.** If a COPAXONE® pre-filled syringe freezes, throw it away in a proper container.

COPAXONE® is light sensitive. Protect it from light when not injecting. Do not use the pre-filled syringe if the solution contains particles or is cloudy.

General advice about prescription medicines

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use COPAXONE® for a condition for which it was not prescribed. Do not give COPAXONE® to other people, even if they have the same condition you have. It may harm them.

This leaflet summarizes the most important information about COPAXONE®. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about COPAXONE® that is written for health professionals. Also, you can call Shared Solutions® for any questions about COPAXONE® and its use. The phone number for Shared Solutions® is 1-800-887-8100.



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