Prescription Utilization by Multiple Sclerosis Patients in the United States

ANNA A. THEODOROU, RPH, MBA; KELLY M. JOHNSON, MBA; STACEY RUF, PHD; AND JOHN A. SZYCHOWSKI, AAS, BS

Multiple sclerosis (MS) is a chronic, unpredictable disease of the central nervous system. It is thought to be an autoimmune disease in which the body's immune system attacks the myelin sheath (material that surrounds and protects nerve cells), causing brain signals to be interrupted.[1] Symptoms commonly include numbness in the limbs, muscle weakness, paralysis, and/or vision distortion or impairment. The exact cause of MS is unknown, and symptoms vary greatly from one person to another and for any one person over time. Most people afflicted with MS have a normal or near-normal life expectancy, and the majority of people with the disease do not become severely disabled.

Although there is still no cure for MS, various strategies are available to modify the disease course, treat exacerbations (also known as relapses, attacks, or flare-ups), manage symptoms, and improve physical function and safety. In combination, these treatments are designed to enhance the quality of life for people living with MS. An individual's treatment needs are best identified in an ongoing collaboration between a knowledgeable physician and other members of the treatment team.[2]

Of the approximately 400,000 Americans who have MS[1]:

- Most are diagnosed between the ages of 20 and 50 years.
- Roughly 5% are diagnosed before age 21 years (early onset).
- Approximately 9.4% are diagnosed after age 50 years (late onset).
- An estimated 2 to 3 times as many women as men have MS.

Until recently, all MS-specific drug treatments were administered subcutaneously or intravenously. But in January 2010, Ampyra (dalfampridine) received US Food and Drug Administration (FDA) approval as the first orally administered MS drug indicated to improve patient ambulation.[3] The trend toward less intrusive administration methods has prompted development of several oral drugs in this space.

MS drug utilization had a significant impact on trend in the last few years, as discussed in previously published articles including the generational trend research and the recent Alzheimer's utilization trend research.[4,5] However, future class costs are projected to outpace those of prior years because of the expected March 2010 launch of Ampyra and because of double-digit growth in utilization for existing market drugs. In this article we discuss the impact of MS therapy (MST) on trend and MST utilizers' contributions to total annual drug expenditures compared with contributions of the overall commercial population.

METHODS

This retrospective analysis was conducted using 241.9 million prescription claims from CVS Caremark's computerized database. The population identified for the study consisted of 23.2 million members across funded benefit prescription plans administered by CVS Caremark. The plan sponsors included Medicaid, national and local employers, health plans, managed care organizations, insurance companies, unions, and government agencies located throughout the United States with prescription claims for all months between January 1, 2008, and December 31, 2009.

The members had claims in 2008 and 2009, categorized by generation: GI Generation (age ≥83 years), Silent Generation (age 63-82 years), Baby Boomers (age 44-62 years), Generation X (age 30-43 years), Generation Y (age 18-29 years), and Generation Z (age ≤17 years).[4] In addition to categorizing utilizers by age band, we also separated metrics by sex (**Table 1**).

The utilization trend was based on average days supply and gross cost (which includes both plan sponsor and member contributions), reported on a per member per month basis. Medicare Part D plans were excluded. The plan sponsors had average eligibility changes limited to within ±15% period over period.

Patients on MST were identified by using the product indicator for approved MS treatments, which includes all strengths and dosage forms of the following: Avonex (interferon beta-1a), Betaseron (interferon beta-1b), Copaxone (glatiramer acetate), Rebif (interferon beta-1a),

Table 1. Comparison of Study Cohort With US Population

Generation (Age Band in 2009)	Average No. of Eligible Commercial Members	2009 Percentage of Commercial Members	MST Utilizers		
			Per 10,000 Eligibles	% Female	% Male
Generation Z (≤17 y)	5,758,561	25.4	0.1	59	41
Generation Y (18-29 y)	2,779,736	12.2	5.4	75	25
Generation X (30-43 y)	4,013,077	17.7	18.7	75	25
Baby Boomer (44-62 y)	6,712,898	29.6	21.0	77	23
Silent (63-82 y)	2,861,113	12.6	6.4	78	22
GI (≥83 y)	574,689	2.5	0.2	82	18
Total	**22,700,075**		**11.0**	**76**	**24**

MST indicates multiple sclerosis therapy.
Source: CVS Caremark Industry Analytics multiple sclerosis cohort, January 2008-December 2009.

Extavia (interferon beta-1b), and Tysabri (natalizumab). Novantrone (mitoxantrone) was not included in the analysis because of its approval and use as a cancer treatment.

THERAPEUTIC CLASS BACKGROUND

Indications

Three primary types of injectable MS drugs are available: glatiramer acetate, interferon beta, and natalizumab (**Table 2**). Each type of drug commonly has a different effect on individual patients. As a result, some product switching may be necessary to find the drug with greatest efficacy.

Current Therapies

Currently several disease-modifying medications are approved by the FDA for use in relapsing forms of MS (including secondary-progressive MS for those people who still are experiencing relapses). These drugs work to slow down the natural course of the disease and prevent recurring symptoms. More specifically, the medications reduce the number of days a person might be actively ill with an attack of symptoms; they reduce or even eliminate the accumulation of lesions, or damaged areas, within the central nervous system; and they appear to slow down the accumulation of disabilities. All class drugs have proven records of partial to substantial success. Unfortunately, none of the currently available disease-modifying drugs are approved for treating primary-progressive MS.

Side effects are common when taking any of the disease-modifying drugs for the treatment of MS, although these vary in nature and severity. As a result, compliance rates can vary, and discontinuation of therapy is not uncommon.[6]

Ampyra, approved in January 2010, is a (non–disease-modifying) potassium channel blocker used to improve ambulation in MS patients and administered orally. It is awaiting market launch, expected in March 2010.

Table 2. The 3 Primary Types of Injectable MS Drugs Available

FDA Indication	Glatiramer Acetate (Copaxone)	Interferons				Natalizumab (Tysabri)
		Beta-1a		Beta-1b		
		Avonex	Rebif	Betaseron	Extavia	
Reduction of the frequency of relapses in relapsing-remitting MS	✓[a]					
Treatment of relapsing forms of MS to reduce clinical exacerbations		✓[a]	✓	✓[a]	✓[a]	✓[b]
Slowing the occurrence of physical disability		✓	✓			✓[b]

FDA indicates US Food and Drug Administration; MS, multiple sclerosis.
[a]Includes patients who have experienced a first clinical episode and have magnetic resonance imaging features consistent with MS.
[b]Generally indicated for patients who cannot tolerate or have not been helped enough by other MS treatments.

Table 3. Study Cohort Demographics

Demographic	Unique MST Utilizers, No. (%)	Average Total Prescription Cost per MST Utilizer per Year, $	Average MST Drug Cost per MST Utilizer per Year, $	Total Drug Cost for MST Drugs, %	Average No. of MS Claims per MST Utilizer per Year
Generation					
Generation Z	74 (0)	20,801.51	19,613.26	94.29	6.68
Generation Y	1511 (6)	20,484.28	18,794.96	91.75	6.14
Generation X	7492 (30)	23,043.08	20,710.73	89.88	6.51
Baby Boomer	14,128 (56)	26,029.45	22,400.67	86.06	6.83
Silent	1843 (7)	25,894.92	21,959.10	84.80	6.68
GI	11 (0)	22,491.02	19,017.64	84.56	6.91
All age female	19,027 (76)	25,069.69	21,811.74	87.00	6.74
All age male	6032 (24)	23,846.93	21,080.87	88.40	6.49
Total	**25,059**	**24,775.36**	**21,635.81**	**87.33**	**6.68**

MST indicates multiple sclerosis therapy.
Source: CVS Caremark Industry Analytics multiple sclerosis cohort, January 2008-December 2009.

IMPACT BY GENERATION

In 2009, 25,059 unique MST utilizers were identified based on prescription claim data, representing approximately 0.11% of the overall cohort population studied. More than 75% of utilizers were female and the majority were Baby Boomers, although Generation X represented 30% of the MST utilizers (**Table 3**).

The average age of the study commercial group was compared with 2005 US Census population estimates by age bands. According to the Census estimate, those aged 20 to 49 years comprised 42.8% of the population. The same population in the study cohort made up 41.3%.

MARKET SHARE

Four disease-modifying injectable drugs dominate the MS treatment landscape: the complex nonbiologic Copaxone and 3 biologic derivative interferon-beta drugs (Avonex, Rebif, and Betaseron). The **Figure** indicates market share by days supply in 2009. Copaxone was the leader with a 37.5% market share. Avonex, the number 2 player, lost 2.2% share year-over-year, while Copaxone gained 2.3%. Despite a significant year-over-year increase in claims, Tysabri only gained 0.2% share due to low volumes.

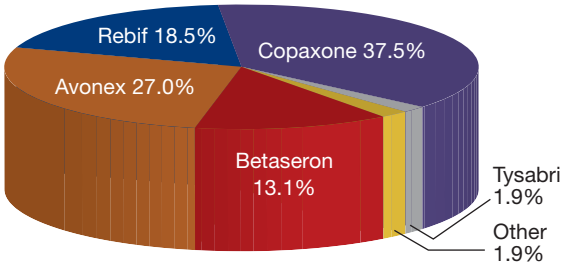
Tysabri is commonly prescribed when other drugs fail to satisfy the patient's needs, but the drug can lead to progressive multifocal leukoencephalopathy, a rare brain infection that usually causes death or severe disability. Therefore, Tysabri market penetration is likely to remain low.

COST TRENDS

The average cost per prescription for an MST drug was $3434.63. However, the average cost per day provides a better comparison, as the figure increased from $67.52 in 2008 to $81.15 (20.2%) in 2009. **Table 4** provides the average gross cost per day for MST drugs.

Table 5 shows the top non-MST drugs by gross cost, the percentage of MST utilizers, and the ranking by gross cost, claims, and utilizers. Approximately 41.3% of MST utilizers also were on antidepressants (selective norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, and miscellaneous), 31.7% were on a central muscle relaxant, and 27.4% were on an anticonvulsant. Although concomitant corticotropin utilization was very low (0.2%), this class was ranked number 2 in gross costs due to a gross cost per day of $2039.74.

Figure. Market Share by Days Supply—Period Ending December 2009



Source: CVS Caremark Industry Analytics multiple sclerosis cohort, January 2008-December 2009.

Table 4. Cost Trends for Multiple Sclerosis Agents

Drug Ranking by Percentage of Total Gross Cost	Annual Gross Cost per Day		
	2009, $	2008, $	Change, %
Copaxone	80.46	64.50	24.7
Avonex	81.21	68.14	19.2
Rebif	81.32	70.40	15.5
Betaseron	82.15	65.47	20.3
Avonex Administration Pack	79.43	67.09	18.4
Tysabri	87.14	83.19	4.7

Source: CVS Caremark Industry Analytics multiple sclerosis cohort, January 2008-December 2009.

DISCUSSION

According to the recent generational analysis, the gross cost for MST was ranked 5th for Generation X and 8th for Baby Boomers.[4,7] The current study population had a 0.11% prevalence of members using MST compared with the reported 0.13% estimated in the US population. A recent study indicated that direct MST spending combined with concurrent drug utilization, on a per-patient basis, is estimated to be an average of $24,775 per year.[7]

Recent, significant developments in the MS drug treatment market include:

- Another year of double-digit cost increases in 2009 for all 4 of the major MS drugs.[8]
- Regulatory filings with the FDA seeking marketing approval of the first oral MS drugs.[7]
- Approval of the first drug indicated solely to improve mobility in MS patients.[9]

All 4 of the leading MS drugs have had ongoing double-digit price increases well in excess of the inflation rate. In the CVS Caremark overall Book of Business data (a different cohort group than the underlying secular trend cohort), an analysis showed the overall average gross cost per day of therapy for MS drugs in December 2009 was $82.17. This increase followed a 21.28% price increase in December 2008 to $75.18 from $61.99 in December 2007.[10] As the price hikes are greater than the number of new MS patients seeking treatment each year, they are the most significant source of sales growth for the class.

Teva, the Copaxone manufacturer, announced in August 2009 that the average copayment (at that time) for the drug was $26, and that more than half of the patients on the drug paid nothing at all.[11] This phenomenon helps to promote therapy adherence despite very high drug costs.

In late 2009, new drug applications were filed with the FDA for the first oral MSTs. Neither of the 2 filings were for biologic drugs. Merck Serono's candidate, cladribine, was submitted in September 2009, but the FDA refused

Table 5. Top Non-MST Drugs

Drug Name	Therapeutic Class	Percent		Rank		
		MST Utilizers	Total Annual Drug Cost	Gross Cost	Claims	Utilizers
Provigil	Stimulants, miscellaneous	11.54	1.24	1	4	7
H.P. Acthar	Corticotropin	0.24	0.49	2	650	461
Cymbalta	Serotonin and norepinephrine reuptake inhibitors	7.45	0.37	3	7	15
Gabapentin	Anticonvulsants, miscellaneous	15.50	0.28	4	3	4
Effexor XR	Serotonin and norepinephrine reuptake inhibitors	4.10	0.25	5	20	52
Nexium	Proton pump inhibitors	5.25	0.25	6	26	37
Lexapro	Selective serotonin reuptake inhibitors	8.45	0.23	7	5	12
Detrol LA	Urinary antispasmodics	5.96	0.23	8	15	30
Lipitor	HMG-CoA reductase inhibitors (statins)	6.34	0.22	9	13	29
Lyrica	Anticonvulsants, miscellaneous	5.45	0.21	10	21	35

HMG-CoA indicates 3-hydroxy-3-methylglutaryl-coenzyme A; MST, multiple sclerosis therapy.
Source: CVS Caremark Industry Analytics multiple sclerosis cohort, January 2008-December 2009.

the application 2 months later, which suggests that it was incomplete. Merck has said that it would meet with the agency in an effort to understand the deficiency and outline any next steps that might be necessary. The other oral drug, fingolimod, was submitted for approval by Novartis at the end of December 2009.[7]

Oral therapies would be more convenient for the MS patient than the current regimen of injectables and would represent another treatment option for physicians. Still, it's not clear that either cladribine or fingolimod will be approved, or if they are approved, that it will be on the first review cycle at the FDA. Furthermore, there are potential safety concerns, as there are with the injectable disease-modifying drugs. Oral therapies have been characterized as generally being more toxic and likely to have a more problematic side-effect profile than the injectables.[11] Finally, given the many years of experience patients and physicians have with the existing drugs, it may be difficult initially for new oral therapies to gain widespread acceptance in the first-line treatment setting.

CONCLUSION

Using 2009 prescription data to determine MST utilization, 0.11% of commercial utilizers received an MS agent. The study results indicated that the average member on MST had an average annual prescription cost of $24,775. Of that amount, 87% ($21,635) was spent on MST.

According to the National Multiple Sclerosis Society, even a modest improvement in walking ability could mean that thousands of people might benefit from taking Ampyra.[12] Ampyra's manufacturer, Acorda, has set a price of $12,850 a year for the drug.[13] Furthermore, the company added, the add-on therapy may be utilized by as many as 180,000 patients or approximately 40% of Americans with MS. If so, the class will experience a substantially higher trend in 2010.

Author Affiliations: From the Division of Industry Analytics & Outcomes (AAT, KMJ, SR, JAS), CVS Caremark, Scottsdale, AZ.

Address correspondence to: Anna A. Theodorou, RPh, MBA, Director, Industry Analytics & Outcomes, CVS Caremark, 9501 East Shea Blvd, Mail Code #097, Scottsdale, AZ 85260. E-mail: anna.theodorou@caremark.com.

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