Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system in which immune cells attack the myelin sheath surrounding the nerve fibers causing demyelination and axonal degeneration. The symptoms and signs of MS can vary depending on the affected neurons. Some of the most common clinical features of MS are optic neuritis, Lhermitte’s sign (an electrical sensation that extends from the neck down to the spine), depression, sexual dysfunction, gait changes, and neurogenic bladder.1

The prevalence of MS in the United States has been increasing over time from 727,344 cases in 2010 to nearly 913,925 in 2017, with female patients having a higher incidence rate than male patients.2 Although MS is classified as a rare disease,3 it carries a substantial economic burden, with an estimated annual direct healthcare cost of $18.94 billion in the United States.4 The high financial burden of MS can be attributed to multiple factors. First, MS is a progressive disabling disorder that predominantly affects younger adults at their most productive years, between age 20 and 50 years.5 As a result, the disease is associated with loss of work productivity, absenteeism costs, and a high burden on

BACKGROUND: Multiple sclerosis (MS) is a rare, long-standing, and disabling disease that affects the central nervous system and causes several clinical manifestations. As a result, this disease is associated with a high societal economic burden.

OBJECTIVE: To analyze the trends in drug expenditure, utilization, and cost of specialty drugs for the treatment of patients with MS in the US Medicaid program.

METHODS: In this retrospective drug utilization research analysis, we obtained prescription data and reimbursement of disease-modifying therapies for MS from the Centers for Medicare & Medicaid Services Medicaid State Drug Utilization Data between January 2008 and December 2018. The specialty drugs considered in our analysis included dimethyl fumarate, fingolimod, teriflunomide, cladribine, siponimod, alemtuzumab, natalizumab, ocrelizumab, daclizumab, glatiramer acetate, peginterferon beta-1a, interferon beta-1b, and interferon beta-1b. The annual trends of the number of prescriptions, reimbursement expenditures, and costs were calculated. The average reimbursement per prescription was calculated as an estimate of the drug cost.

RESULTS: The annual MS drug utilization increased from 85,209 prescriptions in 2008 to 223,604 in 2016, and then decreased to 194,877 in 2018. The annual reimbursement surged by 633% in the 10-year study period between 2008 and 2018, from almost $172 million in 2008 to more than $1.4 billion in 2017, and then to approximately $1.26 billion in 2018. The cost per prescription increased over time for most MS brand-name drugs (eg, from $2033 in 2008 to $5114 in 2018 for natalizumab, and from $19,138 in 2016 to $23,588 in 2018 for alemtuzumab). In 2008, self-injectable drugs dominated the market. In recent years, a shift has occurred in the utilization and reimbursement of MS drugs, with oral medications becoming predominant.

CONCLUSION: The study findings indicate intermarket and interbrand competition among the MS specialty drugs. The growing utilization and spending trends for specialty MS medications are significant and sizable in the US Medicaid programs. Medicaid cost-containment strategy is warranted to control the economic burden of state budgets across the country.

KEY WORDS: cost burden, disease-modifying therapies, drug utilization, Medicaid program, multiple sclerosis, reimbursement, specialty drugs

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Multiple sclerosis (MS), a progressive disabling disorder, is becoming more prevalent each year and is associated with a high economic burden.

This retrospective study analyzed expenditure, utilization, and cost trends of specialty drugs for the treatment of US Medicaid-enrolled patients with MS.

The annual utilization of MS drugs increased from 85,209 in 2008 to 194,877 in 2018.

The annual reimbursement for MS drugs increased by 633% from 2008 to 2018, from almost $172 million to approximately $1.26 billion.

The per-prescription cost for most MS brand-name drugs increased significantly from 2008 to 2018.

From 2008 to 2018, the predominance of disease-modifying therapies for MS shifted from self-injectable drugs to oral medications.

A cost-containment strategy is needed to control the burden of MS specialty drug costs on Medicaid state budgets.

Policymakers need to control spending on specialty drugs for MS, and providers should consider the affordability of these drugs for patients with commercial insurance.

A systematic review showed that productivity loss and informal care in patients with MS account for 17% to 67% of total costs in patients with high disease severity.

Furthermore, different conditions and diseases arise as sequelae of MS, requiring more expenses for the treatment of these conditions (ie, depression, malaise, fatigue, and convulsions). However, the most significant cost driver in the management of MS is spending on prescription drugs. It is estimated that prescription drugs represent 29% to 82% of all healthcare costs for patients with MS who have low disease severity.

Moreover, in a retrospective study of patients with MS, increased spending on prescription medications totaled 76% of the incremental total MS-related healthcare expenses from 2010 to 2015.

To date, there is no cure for MS; therefore, treatment is based on the use of disease-modifying therapies to stop the progression of disease and to prevent future relapses. Currently, there are 18 disease-modifying therapies approved by the US Food and Drug Administration (FDA) for the treatment of MS (Table 1). Only 1 medication, daclizumab (Zinbryta), has been withdrawn from the market (in 2018) because of safety issues.

Most disease-modifying therapies are classified as specialty drugs because they meet the criteria set by the Pharmaceutical Care Management Association.

Some of the characteristics of these drugs are that they have a high monthly cost, require special storage and transportation conditions, are usually indicated for patients with complex conditions, need considerable patient education, and are available through specialty pharmacies rather than retail pharmacies. In a 2018 report, spending on specialty drugs constituted 44.7% of the total drug expenditure, and this spending is projected to increase in

### Table 1 FDA-Approved Disease-Modifying Therapies for Multiple Sclerosis

<table>
<thead>
<tr>
<th>Generic drug name</th>
<th>Brand name</th>
<th>Approval date</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glatiramer acetate</td>
<td>Copaxone 20 mg</td>
<td>December 1996</td>
<td>Teva Pharmaceuticals</td>
</tr>
<tr>
<td></td>
<td>Copaxone 40 mg</td>
<td>January 2014</td>
<td>Teva Pharmaceuticals</td>
</tr>
<tr>
<td></td>
<td>Glatopa 20 mg</td>
<td>April 2015</td>
<td>Sandoz</td>
</tr>
<tr>
<td></td>
<td>Glatopa 40 mg</td>
<td>February 2018</td>
<td>Sandoz</td>
</tr>
<tr>
<td></td>
<td>Glatiramer acetate 20 mg, 40 mg</td>
<td>October 2017</td>
<td>Mylan</td>
</tr>
<tr>
<td>Interferon beta-1a (Intramuscular)</td>
<td>Avonex</td>
<td>May 1996</td>
<td>Biogen</td>
</tr>
<tr>
<td>Interferon beta-1a (Subcutaneous)</td>
<td>Reblif</td>
<td>March 2002</td>
<td>EMD Serono</td>
</tr>
<tr>
<td>Interferon beta-1b (Subcutaneous)</td>
<td>Betaseron</td>
<td>July 1993</td>
<td>Bayer Healthcare</td>
</tr>
<tr>
<td>Extavia</td>
<td>August 2009</td>
<td>Novartis</td>
<td></td>
</tr>
<tr>
<td>Peginterferon beta-1a</td>
<td>Pegasys</td>
<td>August 2009</td>
<td>Biogen Idc</td>
</tr>
<tr>
<td>Dimethyl fumarate</td>
<td>Tecfidera</td>
<td>March 2013</td>
<td>Biogen Idc</td>
</tr>
<tr>
<td>fingolimod hydrochloride</td>
<td>Gilenya</td>
<td>September 2010</td>
<td>Novartis</td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>Aubagio</td>
<td>September 2012</td>
<td>Sanofi Aventis</td>
</tr>
<tr>
<td>Cladribine</td>
<td>Mavenclad</td>
<td>March 2019</td>
<td>EMD Serono</td>
</tr>
<tr>
<td>Siponimod</td>
<td>Mayzent</td>
<td>March 2019</td>
<td>Novartis</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Lemtrada</td>
<td>November 2014</td>
<td>Genzyme</td>
</tr>
<tr>
<td>Mitoxantrone hydrochloride</td>
<td>Novantrone</td>
<td>October 2000</td>
<td>Immunex, then sold to EMD Serono</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>Tysabri</td>
<td>November 2004</td>
<td>Biogen Idc</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>Ocrevus</td>
<td>March 2017</td>
<td>Genentech</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>Zinbryta</td>
<td>May 2016</td>
<td>Biogen</td>
</tr>
<tr>
<td>Droxemel fumarate</td>
<td>Vumerity</td>
<td>October 2019</td>
<td>Biogen</td>
</tr>
</tbody>
</table>

*Mylan only has generic drugs.
*Has a black box warning.
*Requires careful monitoring.
*Discontinued; removed from the market in March 2018.
*FDA indicates US Food and Drug Administration.

future years. The annual cost of disease-modifying therapies per patient with MS in a commercial population increased by an annual rate of 13% from 2011 to 2015. A research reported by Hartung and colleagues revealed that from 1993 to 2013, the annual inflation rate of disease-modifying therapy costs in the United States skyrocketed 5 to 7 times more than the inflation rate of other prescription drugs. Furthermore, newer disease-modifying therapies were launched with a 25% to 60% greater cost than the already-available disease-modifying therapies, with an annual cost averaging of approximately $60,000 in 2015.

Studies have concluded that more than 90% of patients with MS had health insurance coverage. Nonetheless, patients’ accessibility to drugs may be compromised because of higher out-of-pocket payments required by the insurance industry to combat the soaring cost of disease-modifying therapies. In 2018, disease-modifying therapies for MS were ranked among the top 15 therapy classes based on the total per-member per-year drug spending for commercial health plans, for Medicare, and for Medicaid.

Several studies investigated the utilization and cost patterns of disease-modifying therapies in commercially insured and in Medicare populations. To our knowledge, this is the first study to calculate these trends in the Medicaid-covered population. Medicaid is targeted mainly toward patients with low incomes and is sponsored by federal and state governments. Medicaid eligibility requirements and coverage may differ from one state to another, making it difficult to obtain accurate information about Medicaid-covered patients with MS.

The objective of this study was to analyze the trends in drug expenditure, utilization, and cost of specialty drugs for the treatment of patients with MS who were enrolled in Medicaid between 2008 and 2018. By studying these patterns, we aim to elucidate the MS drug market and to guide policymakers to adapt the best strategies to allocate resources for this patient population.

### Methods

In this retrospective study, we analyzed the National Pharmacy Summary Files for the Medicaid State Drug Utilization Data from the first quarter of 2008 to the fourth quarter of 2018. The Medicaid State Drug Utilization Data are provided by the Centers for Medicare & Medicaid Services (CMS) and are freely available to the public. The files were combined by pooling the state files, which contain information about outpatient drug utilization for drugs that are paid for by state Medicaid agencies. The database’s records include the state, drug name, National Drug Code (NDC), number of prescriptions, and the amount of dollars reimbursed. We searched each of the drugs listed in Table 1 using NDC codes. All drugs for the treatment of MS were included in our study.

### Table 3: Total Annual Utilization, Spending of Disease-Modifying Drugs for MS in Medicaid, 2008-2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Total annual utilization (prescription count, N)</th>
<th>Increase, %</th>
<th>Total annual reimbursement &amp; spending, $</th>
<th>Increase, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>85,209</td>
<td>0.64</td>
<td>171,933,894</td>
<td>23.44</td>
</tr>
<tr>
<td>2009</td>
<td>86,479</td>
<td>3.84</td>
<td>212,253,962</td>
<td>23.44</td>
</tr>
<tr>
<td>2010</td>
<td>93,754</td>
<td>7.36</td>
<td>248,577,975</td>
<td>16.49</td>
</tr>
<tr>
<td>2011</td>
<td>141,770</td>
<td>51.21</td>
<td>448,562,596</td>
<td>81.42</td>
</tr>
<tr>
<td>2012</td>
<td>149,923</td>
<td>5.75</td>
<td>552,919,466</td>
<td>23.26</td>
</tr>
<tr>
<td>2014</td>
<td>168,647</td>
<td>–14.98</td>
<td>794,688,700</td>
<td>28.06</td>
</tr>
<tr>
<td>2015</td>
<td>186,917</td>
<td>17.95</td>
<td>1,044,605,630</td>
<td>31.45</td>
</tr>
<tr>
<td>2016</td>
<td>223,604</td>
<td>12.41</td>
<td>1,276,618,988</td>
<td>22.21</td>
</tr>
<tr>
<td>2017</td>
<td>219,961</td>
<td>–1.63</td>
<td>1,465,949,876</td>
<td>10.13</td>
</tr>
<tr>
<td>2018</td>
<td>194,877</td>
<td>–11.40</td>
<td>1,259,861,796</td>
<td>–10.39</td>
</tr>
</tbody>
</table>

*Percent increases in total annual utilization and total annual reimbursement have been rounded to 2 decimal places. *Total annual reimbursement and spending in US dollars has been approximated to nearest integer. MS indicates multiple sclerosis.
except for cladribine (Mavenclad), siponimod (Mayzent), and diroximel fumarate (Vumerity), because they were approved for the treatment of MS in 2019, after our study period.

The annual number of prescriptions and the annual reimbursement amount were calculated for each drug separately, and then the annual total was aggregated. In addition, we estimated the annual cost per prescription for each of the drugs, by dividing the reimbursement amount by the prescription counts. This cost may not represent the real per-prescription amount exactly, because information about state rebates from pharmaceutical companies is not publicly available and therefore was not included in this analysis.

Moreover, the market share in the Medicaid program for the various disease-modifying therapy classes was computed as a percentage of the total prescription count and as a percentage of the total reimbursement amount. The disease-modifying therapy classes were categorized according to the drugs’ route of administration (ie, injectable, oral, or infusion; Table 2). Descriptive statistics were used to analyze the trends in the prescription counts, the total reimbursement amount, and the cost per prescription over the 10-year study period.

**Results**

**Total Annual Utilization and Reimbursement of All Study Drugs**

The total MS disease-modifying therapies prescription counts, as well as the total spending over time, are shown in Table 3. In general, the number of prescriptions increased by 128.7% from 85,209 in 2008 to 194,877 in 2018. When comparing the annual change by year, the greatest percent increase was observed in 2011 when the number of prescriptions increased by approximately 51% compared with 2010. The prescription count declined in 2017 and 2018, by 1.63% in 2017 and by 11.4% in 2018.

The total annual spending increased by almost 633% from $171,953,894 in 2008 to $1,259,861,796 in 2018. As with the total prescription utilization pattern, the greatest percent increase in spending (ie, 81.42%) was in 2011. The only year in which spending decreased was 2018, by 10.39%.

**Total Annual Utilization of Each Drug**

(To avoid confusion, brand names are used in the following sections for drugs that have more than 1 brand name drug). The total prescription counts for each disease-modifying therapy by year are listed in Appendix Table 1 (available at www.AHDBonline.com) and Figure 1.

From 2008 through 2012, glatiramer acetate (Copaxone) 20 mg was dominating the MS market, and its
prescription count reached a peak of 51,147 in 2012. Intramuscular interferon beta-1a (Avonex), subcutaneous interferon beta-1a (Rebif), and subcutaneous interferon beta-1b (Betaseron) showed a similar utilization pattern to Copaxone 20 mg, but with lower prescription counts. The use of natalizumab (Tysabri) increased by 384.5% from only 2992 prescriptions in 2008 to 14,499 prescriptions in 2012. Fingolimod (Gilenya), the first oral disease-modifying therapy for MS, was introduced in 2010, and its utilization increased rapidly from a prescription count of 29 in 2010 to 9032 prescriptions in 2012.

Subsequently, the use of Copaxone 20 mg significantly declined from 46,203 prescriptions in 2013 to 8165 prescriptions in 2018, and the drug no longer dominated the MS market. From 2013 to 2018, the use of intramuscular interferon beta-1a, subcutaneous interferon beta-1a, and interferon beta-1a (Betaseron) significantly decreased as well. From 2014 to 2016, the prescription counts of Copaxone 40 mg increased and the counts for the 20 mg decreased; in 2017, these trends reversed. In 2018, the use of Copaxone 20 mg and 40 mg decreased from the previous year. By contrast, in 2017 and 2018, there were substantial increases in the prescription counts of generic glatiramer acetate 20 mg and 40 mg.

The utilization of oral MS medications increased from 2013 to 2018, except for dimethyl fumarate (Tecfidera), which had a decline in its prescription count in 2016. Nevertheless, from the year 2015, dimethyl fumarate was the drug with the highest prescription count, with a market share of 22.2% in 2018. As for infusion drugs, the utilization of natalizumab started to decrease in 2016. The use of alemtuzumab (Lemtrada) increased during its first year (2016-2017), but its use decreased in 2018. The use of ocrelizumab (Ocrevus) has been increasing since its entry into the market in 2017.

**Total Annual Reimbursement of All Study Drugs**

The patterns of reimbursement and spending on disease-modifying therapies are similar to those of utilization, as shown in Figure 2 and Appendix Table 2 (www.AHDBonline.com). Until 2013, Copaxone 20 mg was the medication with the highest total reimbursement amount, reaching $211,813,564. After 2013, among injectable drugs, spending on Copaxone 40 mg declined, but in 2017, spending on brand-name Copaxone 40 mg and generic glatiramer acetate 20 mg and 40 mg increased.

Since the entry of oral drugs to the market, their reimbursement amount has been increasing sharply. Dimethyl fumarate had the greatest increase in reimbursement, which saw a slight decline in 2018, when the reimbursement amount reached $297,683,988. For the infusion drugs natalizumab and alemtuzumab, spending...
increased until 2017, then decreased. Spending on ocrelixumab, however, increased by 854% in only 2 years (ie, 2017 and 2018).

Annual Cost per Prescription of Each Study Drug
The cost of prescriptions of most disease-modifying therapies for MS has been increasing between 2008 and 2018 at high rates (Figure 3 and Appendix Table 3 [www.AHDBonline.com]). For example, the cost of Copaxone 20 mg has increased by 307% from $2030 in 2008 to a high of $8268 in 2017. However, in 2018, the cost of the generic drugs glatiramer acetate 20 mg (Glatopa); glatiramer acetate 20 mg and 40 mg; Copaxone 20 mg and 40 mg; and natalizumab declined. The exception to this trend included mitoxantrone hydrochloride (Novantrone), whose cost showed an overall decrease during our study period.

Market Share
In 2008, based on the annual reimbursement data, injectables drugs were the predominant medications on the MS market (Figure 4). However, the market share percentage for injectable drugs decreased significantly, from 96% in 2008 to 37% in 2018. By comparison, the market share for infusion drugs and oral drugs has been increasing. In 2008, the share of infusion drugs was 4%, and no oral medications had launched in the market. In 2011, oral drugs had a market share of 4%. Between 2017 and 2018, the market share for injectable drugs and oral drugs flipped, and the share of oral medications reached 46% in 2018.

The annual market share for each disease-modifying therapy is shown in the Appendix Table 4 (www.AHDBonline.com).

Discussion
Overall, the utilization of MS drugs increased by approximately 128.7% from 2008 to 2018. Many reasons could have accounted for this growth. First, the number of available medications for the treatment of MS increased from 6 drugs in 2008 to 16 drugs in 2018, with each drug having several doses and dosage forms approved by the FDA. Advancements in medical technology and the introduction of the Orphan Drug Act (ODA) of 1983 could have caused this increase; the ODA incentivized pharmaceutical companies to develop drugs for rare diseases.25

Second, as a result of the increases in disease prevalence and the life expectancy of patients with MS, there is more demand for drugs, which leads to an increase in the volume of drug purchases.2,26 Another contributing factor to these increases could be the growth in Medicaid beneficiaries and enrollment, which likely results from the Medicaid expansion endorsed by several states after

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Vol 13, No 2 | May 2020 www.AHDBonline.com | American Health & Drug Benefits | 79
the Affordable Care Act in 2010. Between 2013 and 2019, Medicaid enrollment increased by 14.7 million across 49 states. Despite this rise in the utilization of drugs for MS, prescription counts for disease-modifying therapies for MS in 2018 declined by 11.4% compared with 2017; this trend has also been observed in commercial health plans.

The market shift from treatment with dimethyl fumarate to ocrelizumab may have contributed to this trend. Dimethyl fumarate is a twice-daily oral regimen, whereas ocrelizumab is a twice-annual infusion. Shifting from dimethyl fumarate to ocrelizumab may have resulted in less prescription purchases because ocrelizumab may be more convenient to take for some patients. Moreover, ocrelizumab has a safety profile comparable to and similar or superior efficacy to other disease-modifying therapies, which may have led physicians to prefer one drug over the other.²⁸,²⁹

Our analysis also shows strong competition between disease-modifying therapies in the healthcare market. There is intermarket competition between the different classes. Self-injectable drugs dominated the market when they were introduced; however, in 2018, the market share was almost split between self-injectable and oral medications. As noted, intermarket competition was also evident between certain drugs of different classes, such as dimethyl fumarate and ocrelizumab. Competition also exists within each class; there was interbrand competition in oral drugs between fingolimod and teriflunomide (Aubagio). Although fingolimod was launched in 2010, 2 years before teriflunomide and had more market share than teriflunomide, by 2018 the 2 drugs had a comparable market share.

There was also competition between natalizumab and ocrelizumab. Natalizumab has a black box warning for progressive multifocal leukoencephalopathy, and physicians likely preferred prescribing ocrelizumab for its better safety profile.²⁹,³⁰ The influence of brand name–generic drug competition is still not very clear in the MS drug market. Despite Teva Pharmaceuticals’ efforts of evergreening with the launch of Copaxone 40 mg in 2014 (taken 3 times weekly) to extend Copaxone patent, generic equivalents for Copaxone 20 mg (taken once daily) and Copaxone 40 mg are now available.³¹,³²

The impact of Glatopa 40 mg was not found in our study, because the drug was approved in 2018; however, in 2016, the utilization of Glatopa 20 mg increased, with a corresponding decrease in the use of Copaxone 20 mg. There was brand-name drug versus generic drug competition between glatiramer acetate 40 mg and Copaxone 20 mg and 40 mg. Before the market entry of glatiramer acetate 40 mg, the market share of Copaxone 20 mg was 6.16% and that of Copaxone 40 mg was 16.62%; in 2018, the market share decreased to 4.2% and 9.03%, respectively, in contrast to glatiramer acetate 40 mg, which reached 7.6% that year. By contrast, the utilization of glatiramer acetate 20 mg increased only slightly in market share since its entry into the market.

In general, the total Medicaid expenditures on MS drugs increased from 2008 to 2018. The reasons for the increased spending resemble the causes for the increased

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Figure 4 Annual Market Share of Each Drug Category, Represented as Percentage, 2008-2018

A. Market share percent based on utilization data

B. Market share percent based on reimbursement data

**NOTES:** Figure 4A represents the annual market share percentage of MS disease-modifying therapy drug classes calculated based on utilization data; Figure 4B also represents the annual market share percentage of MS disease-modifying therapy classes but calculated based on reimbursement. MS indicates multiple sclerosis.
utilization of MS drugs and the inflated medication costs. As noted earlier, most medications for the treatment of MS are specialty drugs that have higher costs than many other medications on the market. A report from the AARP Public Policy Institute lists 101 specialty drugs frequently used by older Americans. A total of 12 of these specialty drugs are indicated for the treatment of MS; 7 of the MS drugs were ranked among the 30 top-selling specialty drugs. The 7 MS drugs include Copaxone 20 mg and 40 mg, dimethyl fumarate, intramuscular interferon beta-1a autoinjection and prefilled syringes, subcutaneous interferon beta-1a, and interferon beta-1b (Betaseron).

In 2018, a decrease in overall spending was observed, which could have resulted from the decreased overall prescription purchases during that year and/or a market shift from brand-name Copaxone to less-costly generic glatiramer acetate. Market share and competition among MS drugs calculated based on the total reimbursement data yielded similar results to those calculated based on utilization data. The only difference found was that the market share for oral drugs in the reimbursement data surpassed that of injectable therapies.

In general, the cost per prescription for most of the MS drugs increased from 2008 to 2018. This upsurge in most of the costs of the MS drugs has also been observed in previous studies. Theoretically, when there is a competing drug market, the entry of new brand-name drugs reduces, or at least sustains, the cost of existing older drugs; however, this was not the case in the MS drug market. Instead, our data show that when new brand-name drugs were launched, the cost of already existing disease-modifying therapies was elevated to compete with the new drugs on the same cost level and maximize profit. This finding was supported by Hartung and colleagues, who observed that the phenomenon was only happening in the United States.

Another factor that contributes to the constant rise in MS drug costs is the lack of competition between brand-name biologic drugs (reference drugs) and their biosimilars. Most current therapies for MS are biologic drugs; therefore, pharmaceutical companies have been slow in developing biosimilars, because these drugs require large investments, in accordance with the Biologics Price Competition and Innovation Act of 2009.

Only in 2017 and 2018 did generic Glatopa and glatiramer acetate receive FDA approvals. In general, the advantage of having generic drugs and biosimilars on the market is that they serve as the antidote to skyrocketing prescription costs, as suggested in previous studies conducted in various therapeutic areas.

Paradoxically, when they entered the market, the cost per prescription of Glatopa 20 mg was higher than those of Copaxone 20 mg and 40 mg. Then, the cost of Glatopa 20 mg started declining, which was met by a rise in the cost of the 2 doses of Copaxone to leverage revenues. In 2017, generic glatiramer acetate (20 mg and 40 mg) was introduced, at which time glatiramer acetate 20 mg and Glatopa 20 mg were approximately half the cost of Copaxone 20 mg. In 2018, the cost of both doses of Copaxone, Glatopa 20 mg, and both doses of glatiramer acetate decreased. Furthermore, Glatopa 40 mg was introduced at a cost between Copaxone 40 mg and glatiramer acetate 40 mg. Although it can be argued that the effect of brand-name and generic drug competition was seen in 2018, the impact of this competition on the broader MS drug market remains to be more clearly defined in the future.

Limitations

This study has several limitations. The current findings are limited by the available data on the CMS National Medicaid Pharmacy File. Patient-specific information was not available in the national Medicaid database, so we could not perform multivariate analysis to study the impact of various patient characteristics on spending and utilization of MS drugs. Also, we could not obtain information about the indication of each prescribed medication, and this could have potentially biased our results.

The effect of brand-name versus generic drug competition is constrained by the limited measurement available to calculate competition during the study period. Moreover, prescribing patterns may be influenced by the prescriber’s and the patient’s ability to access a medication. No data about the appropriate use of the drugs or the patient’s adherence are reported.

Finally, this study only focused on the Medicaid population, which encompasses the underserved, low-income population. Consequently, our findings may not be generalizable to other populations, such as patients with Medicare or with commercial insurance.

Conclusion

Our findings indicate the presence of intermarket and interbrand competition among MS specialty drugs between 2008 and 2018. The increased utilization and spending trends for specialty MS medications are significant and sizable for Medicaid beneficiaries. This research provides informative data about the increasing cost trends of MS medications for Medicaid-related policymakers. These findings highlight the need to have a cost-containment strategy to control the economic burden of MS specialty drugs on Medicaid state budgets. This information can allow policymakers to investigate new ways to control spending in this high-cost therapeutic drug class. Our study also allows clinical providers to
consider the affordability of MS drugs for non-Medicaid patients who are enrolled in commercial or private insurance plans with less generous benefit designs.

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Author Disclosure Statement

Ms Elsis, Dr Hincapie, and Dr Guo have no conflicts of interest to report. Dr Guo was a principal or co-investigator on research studies sponsored by Novartis, AstraZeneca, Bristol-Myers Squibb, Janssen Ortho-McNeil, Roche-Genentech, and Eli Lilly, none of which involved specialty drugs for MS.

References

STAKEHOLDER PERSPECTIVE

Utilization Challenges of Drugs for Multiple Sclerosis in a Medicaid Population

By James T. Kenney, RPh, MBA
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DRUG MAKERS: Multiple sclerosis (MS) has been a challenging disease state for commercial and public (Medicare and Medicaid) plans for many years. According to the study by Elsisi and colleagues in this issue of the journal, the number of therapeutic options for MS expanded significantly over the 10-year study period from 2008 to 2018, with an increase in the number of US Food and Drug Administration–approved drugs from 6 to 16. Glatiramer acetate is the only generic drug that is currently available for the treatment of MS, offering some cost relief to health plans and patients.

PATIENTS: All brand-name drugs for MS have a very high per-patient per-year cost. Despite the availability of some rebate contracts to offset the cost, the net costs remain very high. Manufacturers of MS drugs understand the difficulty of driving patients to the use of preferred agents or of activating a therapeutic intervention or a drug-switching program.

MS is a chronic and debilitating disease that often progresses without patients’ awareness, unless they undergo noticeable physical or mental health changes or have an acute disease flare or relapse. The primary goals of disease-modifying therapies are to reduce or eliminate disease relapses and to achieve disease remission.

PAYERS: A patient’s disease can relapse at any time, regardless of whether the patient is receiving a disease-modifying drug. This can be challenging for formulary managers, who may want to apply utilization management to this drug category, select preferred agents, or potentially drive the market to these agents. This activity poses a high degree of risk, because any disease relapse that occurs after the patient is switching from the current drug to another drug may be blamed on that drug switch, and indirectly on the formulary. This may lead formulary managers to identify treatment-naïve patients and apply a step-edit process through 1 or 2 preferred agents before moving to a less-preferred treatment option. Given the size of the patient population with MS, and the variability of the available treatments used, the pool of treatment-naïve patients is relatively small and does not offer a large enough group to achieve significant cost-savings.

Historically, the costs for MS as a class have been high, with the annual price increases contributing to a significant budget impact over a 10-year period. The patient population with MS has increased as a result of the expansion of the Medicaid program under the Affordable Care Act (ACA), which drove the utilization of MS disease-modifying therapy to increase by 128.7%. The newly approved drugs have launched at premium prices versus existing therapies, which has fueled price increases from the older agents to essentially shadow the prices of the new innovator drugs. All these factors placed the category of MS drugs in the top 5 categories of specialty drugs during the current study’s time period, according to Express Scripts’ 2018 Annual Drug Trend Report.

Therapies for MS include several agents that are used off-patent; however, for biologics, the biosimilar pathway must be followed to launch direct competitors to the innovator brands. This process has been very slow, and the older agents in the class have efficacy profiles that are not as compelling as some of the newer oral drugs and provider-administered injectables. Ocrelizumab launched at a significant discount versus other drugs for the treatment of MS and has offered a compelling clinical, safety, and cost profile to health plans. Ocrelizumab is typically managed under the medical benefit and would require coordination across the medical and pharmacy benefits to target this as a preferred agent for cost-savings by Medicaid plans.

MEDICAID PLANS: One advantage that state Medicaid plans have is mandatory best price–driven rebates on covered drugs. For many of the older MS agents, the actual cost to the state may be nearly eliminated as a result of the inflation penalties added to Medicaid best price calculations for these agents over the drug’s lifetime. Any price increases in excess of the Consumer Price Index for pharmaceuticals in a given year are added to the guaranteed Medicaid best-price calculation baseline of 23.1% on a quarterly basis and are carried forward to a maximum rebate of 100%, which was capped under the ACA. The
newer agents with fewer price increases will drive costs to the Medicaid plans and could also be targets for potential value-based agreements in the healthcare market.

Several Medicaid plans—including in Oklahoma, Louisiana, California, Colorado, Kansas, and Wisconsin—are now entering into value-based agreements with pharmaceutical companies as a method to bend the cost curve and reduce expenses in this costly MS category. This methodology requires drug manufacturers to stand behind their drugs and guarantee a certain level of outcomes or provide price relief to the payer. These contracts could be used as a backdrop for driving patients to some of the newer agents that have reduced relapse rates compared with some of the traditional agents for MS.

Medicaid plans have a real challenge to manage patients with MS with significant drug variability by dosing option, mechanism of action, safety profile, as well as disease variability in each unique patient. There will likely be additional generic drug launches in the near future, including oral agents, toward which it may be easier to steer patients, thanks to their convenience of administration, lack of an injectable requirement, and their potential offer of budgetary relief.

In addition, MS agents such as cladribine and alemtuzumab have the potential to be given over a 2-year period, without the need for additional doses in years 3, 4, and beyond. The future collection of real-world evidence regarding patients' response to drug treatments and actual rates of reduction in disease relapse and improved remission may drive formulary managers to shift their focus to agents that offer a true benefit over the long-term.