

# Addressing the Rising Prices of Disease-Modifying Therapies for Multiple Sclerosis

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**In 1993**, the first disease modifying-therapy (DMT) for multiple sclerosis (MS), interferon beta-1b, was approved, and an untreatable disease that had disabled humans for hundreds of years became treatable. Since then, multiple drugs with varying mechanisms of action have been approved, and neurologists now have a palette of therapies that allows for individualizing therapy and effectively controlling relapsing MS in most patients. Regrettably, this achievement has come at a steep price. Interferon beta-1b entered the market with an annual price of approximately \$10 920 (\$19 313, inflation adjusted). While this price stunned many physicians at the time, the price for the first DMT for MS is now looked back at with nostalgia. The prices for DMTs for MS have risen dramatically over the last 15 years, far outpacing inflation, and now have a mean price of more than \$86 000 per year (Figure).

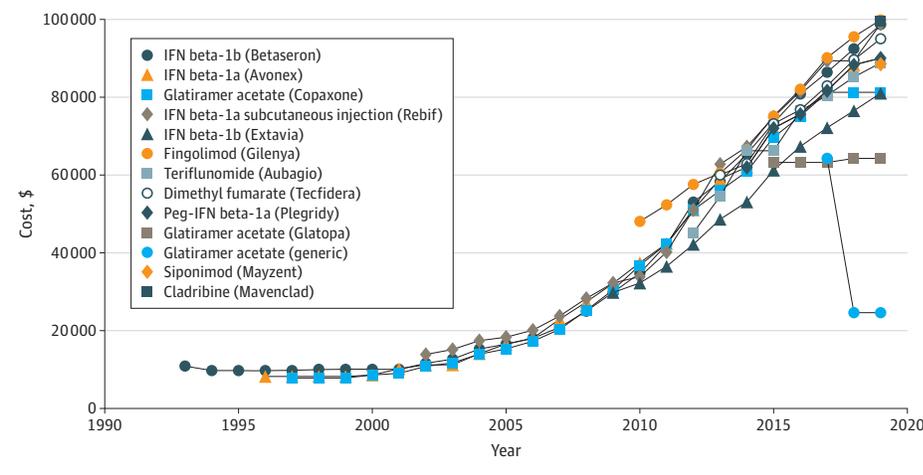
In this issue of *JAMA Neurology*, San-Juan-Rodriguez et al<sup>1</sup> provide a description of the effects of MS DMT price growth on the US Medicare Part D program. Using a 5% random sample of Medicare Part D claims data, they analyzed how the cost of self-administered DMTs for MS changed between 2006 and 2016. The authors estimate that over the 11-year period, the annual cost to the Medicare Part D program for DMTs rose from \$396.6 million to \$4.4 billion, which equates to a 10.2-fold increase per Medicare beneficiary. This increase was driven primarily by the annual cost of DMT treatment, which climbed more than 4-fold from \$18 660 to \$75 847, or nearly 13% an-

nually. The authors also note the disturbing trends that DMT costs increased in parallel and the entry of new products seems to only propel costs higher, phenomena previously noted<sup>2</sup> and also apparent in the Figure. As a consequence of escalating costs and Part D benefit design, the out-of-pocket expenses to patients during this same time rose 7-fold, from \$372 to \$2673 per 1000 beneficiaries.

This study by San-Juan-Rodriguez and colleagues<sup>1</sup> is an important addition to the literature on the rising cost of DMTs for MS. Their study documents the escalating costs that patients, Medicare Part D plans, and ultimately taxpayers are paying for these irrationally priced therapies. The US Medicare program is the single largest purchaser of DMTs for MS in the United States, and DMTs for MS are among the most expensive drugs purchased by the program.<sup>3,4</sup> In 2017, the Medicare Part D program spent more than \$5 billion on 11 self-administered DMTs. Medicare spent nearly \$1.5 billion on branded glatiramer acetate alone.<sup>5</sup> To put these numbers in perspective: in 2016, Medicare paid approximately \$1.4 billion to neurologists for all services and procedures through the Part B program. Medicare is thus spending more than 3 times as much for DMTs for this single illness as they pay to neurologists for all of the services that they provide.

As has been pointed out elsewhere and documented in the current study, nearly all DMTs for MS increased in price in parallel, and the introduction of new therapies seems to only propel prices higher.<sup>2,6-8</sup> We now have 19 US Food and Drug Ad-

Figure. Annual Prices of Disease-Modifying Therapies for Multiple Sclerosis



Each observation is based on 12-month supply using the wholesale acquisition cost in December of each year. The data for 2019 are based on the wholesale acquisition cost in June 2019. The wholesale acquisition cost is from the First DataBank Drug Database. For each glatiramer acetate product, we report the median price of the 20-mg and 40-mg formulations. IFN indicates interferon.

ministration-approved DMTs for MS in 10 different mechanistic classes. So despite the existence of multiple treatment options, the price of most DMTs for MS continues to rise. The pharmaceutical and biotechnology industries claim that the high prices reflect the expense of research and development and need to incentivize continued innovation. These claims are never backed up with transparent data. In addition, they do not explain the continuous rise in the 3 drugs originally approved for MS, interferon beta-1b (Betaseron), interferon beta-1a (Avonex), and glatiramer acetate (Copaxone). These drugs have long since recouped any cost of drug development, yet their prices have continued to rise. As can be seen from the Figure, these platform therapies had only modest increases in price until 2002 when another interferon beta-1a (Rebif) was introduced at a price approximately 30% higher than the existing approved therapies. This initiated the ever-increasing prices of DMTs for MS. What is driving this increase is uncertain. However, the simplest explanation is that pharmaceutical and biotechnology companies increase prices because they can, they do it to increase their profit margins, and there are few limits on what they can charge.

Should neurologists care about the rising cost of MS DMTs? After all, clinicians are helping patients by using these drugs to control their MS. Between private and public health insurance and programs provided by the manufacturers of MS therapies, most can receive treatment.<sup>9</sup> While not denying the benefit of MS DMTs, we believe that neurologists should be concerned about these rising prices. Neurologists should feel a responsibility to the health care system that is bearing the burden of the cost of these medications. They also should be concerned about rising out-of-pocket expenses to patients. Neurologists are cognizant of the toxicity and tolerability of these medications and often tailor therapy based on patient preferences for adverse effect profiles. Yet they rarely think of the financial toxicity these therapies impart. Recent analyses suggest out-of-pocket costs for 1 DMT for MS for a patient receiving Medicare can exceed \$6000 per year.<sup>6</sup> Surveys of patients with MS reveal that out-of-pocket costs are the most important attribute that affects DMT treatment decisions, outranking efficacy, safety, and route of administration.<sup>10</sup> Neurologists should be seeking to minimize the financial adverse effects of these therapies as much as they try to minimize physical adverse effects.

What can neurologists and others do about the rising prices? At the patient level, it is important to note that the price for the Mylan generic formulation of glatiramer acetate (20 mg and 40 mg) dropped by 60% (to about \$2000 a month, vs approximately \$6000 for branded glatiramer acetate) in June 2018 and is now the lowest-cost DMT on the market. For individuals with Medicare, this translates into dramatically lower out-of-pocket costs. As individuals and members of national organizations, such as the American Academy of Neurology, neurologists can urge state and federal lawmakers to pass legislation addressing runaway drug prices for MS therapies and other drugs. Many states have enacted or are considering bills seeking to provide financial relief for patients through enhanced pricing transparency, bulk purchasing, cost-sharing maximums, importation from other countries, and other initiatives. At the federal level, Medicare is statutorily prohibited from negotiating price directly with drug makers. However, many argue that allowing direct negotiation could dramatically bring down prices, similar to what is done in the Department of Veterans Affairs.<sup>11</sup> The Trump administration has recently proposed radical regulatory changes that reshape reimbursement of pharmaceuticals for Part D. One proposal essentially prohibits rebates unless they are directly shared with patients at the point of sale. While these initiatives may benefit individuals with high out-of-pocket expenses, its effect on total pharmaceutical expenditures is unclear.<sup>12</sup> Another proposed initiative is the development of a pricing structure for Part B drugs (physician-administered infusions) that ties reimbursement to an international pricing index based on prices paid in comparable foreign countries.<sup>13</sup> The ultimate effects of these proposals on the unending rise in prescription drug prices are uncertain, because they are based on a number of assumptions about how the pharmaceutical industry will respond; however, it is known that prices will continue to rise if no efforts are made.

Finally, neurologists should look carefully at their relationships with pharmaceutical and biotechnology companies and call them to task for unreasonable increases in prices. Remaining silent should not be an option. The development of DMT for MS has been one of the great achievements of neurology in the past 25 years. Neurologists should not allow the unfettered increases in price for these drugs hurt the health care system or patients.

#### ARTICLE INFORMATION

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