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# Prescription Trends in Branded Versus Generic Glatiramer Acetate Utilization Among Insurers for the Treatment of Multiple Sclerosis in the United States

Stephen G. Smith
*Medical University of South Carolina*

# PRESCRIPTION TRENDS IN BRANDED VERSUS GENERIC GLATIRAMER ACETATE UTILIZATION AMONG INSURERS FOR THE TREATMENT OF MULTIPLE SCLEROSIS IN THE UNITED STATES

BY

Stephen Gerald Smith, MBA

DHA Candidate, MUSC

A doctoral project submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree Doctor of Health Administration in the College of Health Professions

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Approved by:

| | | |
|---|---|---|
| Chair, Project Committee | Kit N. Simpson, DrPH | Date 4/19/19 |
| Member, Project Committee | Daniel Brinton, PhD | Date 4/15/2019 |
| Member, Project Committee | Erin R. Weeda, PharmD | Date 4.19.19 |

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TABLE OF CONTENTS


Acknowledgements ii

Table of Contents iii

List of Tables v

List of Figures vi

Abstract vii

I. INTRODUCTION 1
- a. Background of Glatiramer Acetate and Need for Analysis 1
- b. Problem Statement 4
- c. Research Question 6
- d. Population 6
- e. Assumptions 6

II. LITERATURE REVIEW 8
- a. Multiple Sclerosis & Disease Modifying Therapies 8
- b. Glatiramer Acetate 12
- c. Cost of Disease Modifying Therapies 17
- d. Healthcare Insurance Benefit Design 20
- e. Conclusion 26

III. METHODOLOGY 28
- a. Research Design 28
- b. Specification of Variables 28
- c. Data Source 28
- d. Data Set Construction 29
- e. Data Analysis 30
- f. Institutional Review Board 30
- f. Conceptual Model 31

IV. MANUSCRIPT
- a. Cover Letter 33
- b. Title Page 34
- c. Abstract 35
- d. Summary Bullets 36
- e. Introduction 38
- f. Methods 40
- g. Results 41
- h. Discussion 42
- i. Conclusion 48
- j. References 54

V. APPENDIX 58

VI. REFERENCES 61

LIST OF TABLES

Table 1: FDA Approved Multiple Sclerosis Disease Modifying Therapies 11

Table 2: FDA NDA vs ANDA Approval Requirements 16

Table 3: Symphony Health Integrated Dataverse® Data Set 58

LIST OF FIGURES

Figure 1: Axonal Damage Consequent to Demyelination 9

Figure 2: Glatiramer Acetate Mechanism in Immune Modulation 14

Figure 3: Commonly Prescribed MS DMT Annual Acquisition Cost 19

Figure 4: Insurer Benefit Design Coverage for Glatiramer Acetate Therapies 22

Figure 5: Project Conceptualization Chart. 31

# ABSTRACT

Abstract of Doctoral Project Presented to the
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By

Stephen Gerald Smith, MBA

Chairperson: Kit N. Simpson, DrPH
Professor, College of Health Professions
Department of Healthcare Leadership & Management
Medical University of South Carolina

Committee: Daniel Brinton, PhD
Assistant Professor, College of Health Professions
Department of Healthcare Leadership & Management
Medical University of South Carolina

Erin R. Weeda, PharmD
Assistant Professor, College of Pharmacy
Department of Clinical Pharmacy and Outcome Sciences
Medical University of South Carolina

**PURPOSE**: Multiple Sclerosis (MS) is a chronic condition managed by disease modifying pharmaceutical therapies (DMTs). Health care cost is increasing due to high prescription drug spending. The high cost of branded DMTs highlights the potential value of lower cost generic therapies. Using generic DMTs could reduce the spending in the prescription drug sector. Recently, generic glatiramer acetate (GA) that treats relapsing remitting multiple sclerosis has become available. Appropriate insurer policies and practices are imperative to promote the use and utilization of generics like GA. Notably, no study has specifically evaluated the differences in utilization uptake of branded vs generic GA among the major insurer categories. The purpose of this study is to establish whether i n s u r e r type affects the rate of utilization uptake of branded vs generic GA.

**METHODS**: Prescription claims data for branded or generic glatiramer acetate for Commercially insured patients, Medicare beneficiaries with supplemental insurance, and Medicaid patients were extracted from Symphony Health Integrated Dataverse® data set from Oct 2014 – Jan 2019. Patient claim cohorts were identified through branded Copaxone® 20 mg or 40 mg, generic Glatopa® 20 mg or 40 mg, and generic Mylan Glatiramer Acetate 20 mg or 40 mg national drug codes. Data was limited to 52 months of claims data inclusive of FDA post-approval of generic glatiramer acetate options. Projected glatiramer acetate utilization rates were estimated using exponential regression modeling. Patient out of pocket costs were captured as pharmacy transactional level insights from the patient's primary plan pay setting of the initial co-pay amount and additional plan pay from third-party utilization of copay cards subsidizing the prescription.

**RESULTS**: From October 2014 to January 2019, 111,906 patients with multiple sclerosis were prescribed glatiramer acetate by Neurologists (80%) and had 1,624,159 approved dispensed claims primarily through specialty mail (87%) and categorized by payment type as 63.2% Commercial, 25.4% Medicare, and 11.8% Medicaid. The market trend showed a consistent decline in branded glatiramer acetate claims offset by a rapid uptake in generic glatiramer acetate with its initial market entry but remained relatively flat until launch of an additional generic market entrant. Generic market share has continued to grow reaching an approximate 30% share of claims. Over the 52 months brand glatiramer acetate utilization has declined more than half at 56%, while generic claim volume has grown 155% over the past 16 months. Among the payer types, Medicare has observed the greatest brand decline at 70% and the second highest generic utilization uptake at a 28% share. Commercial insurers have the greatest category claim volume and greatest generic growth to a 26% share, while the brand has declined by 44%. Medicaid has had the lowest utilization volume and the greatest ratio of generic utilization among insurers at 45%. Patient out of pocket costs are highest with branded use across all insurer types, while Medicaid has the lowest patient out-of-pocket costs. Across all payment types, generics offer approximately a 20% discount to the brand in patient out of pocket costs.

**CONCLUSION**: The study revealed that generic glatiramer acetate adoption or utilization has been slow among insurers but increasing over the past sixteen months with additional generic GA entrants and increased price competition. The greatest trend in generic utilization is occurring within the Commercial channel followed by Medicare and Medicaid, which has had the lowest growth trend. The results indicate that barriers to generic glatiramer acetate may vary by insurer and influenced by prescriber or patient choice. Generic uptake is projected to increase across all insurer types reflective of trends during 2019 open enrollment and healthcare benefit design change associated with a new health insurance cycle. Lower patient out-of-pocket costs

and generic preferred formulary positioning will influence utilization rates, especially in beneficiaries or enrollees with the greatest financial cost shift risk.

**KEYWORDS**: Benefit Design, Copaxone®, Drug Utilization, Formulary Management, Generic, Glatiramer Acetate, Multiple Sclerosis, DHA, Doctor of Health Administration.

# CHAPTER 1

# INTRODUCTION

## Background of Glatiramer Acetate and Need for Analysis

Multiple sclerosis (MS) is a chronic, autoimmune, neurological disease affecting the central nervous system caused by the demyelinating of neurons, which results in an inability of nerve cells to transmit signals and producing a wide variety of symptoms (Freedman, Selchen, Prat, & Giacomini, 2018). MS affects approximately 1 million people in the US (Wallin, 2019). Multiple sclerosis is associated with progressive disability, reductions in quality of life, and is a tremendous economic burden for patients, families, and society (Naci, Fleurence, & Birt, 2010). It has been reported that total all-cause health care costs associated with MS including direct and indirect costs in the United States ranged from $8,528 to $52,244 per patient per year (Adelman, Rane, & Villa, 2013).

In the absence of a cure, MS therapy consists primarily of supportive care and symptomatic management, which may generate substantial direct costs. A mainstay for treatment is disease-modifying therapies (DMTs) or medications that alter immune response. With appropriate use of these DMTs, significant clinical benefit may be realized by slowing progression or altering the course of various forms of the disease. DMTs are considered specialty pharmaceuticals, a category associated with insurance restrictions like prior authorization, step therapy, formulary tiers and co-insurance due to their high cost, complexity of the disease they treat, and the need for enhanced clinical services to ensure safe use of the drug and to optimize therapeutic outcomes (Penington & Stubbings, 2016). Amongst these DMTs, Copaxone® or glatiramer acetate stands out due to its unique mechanism of action and demonstrated extensive

clinical experience supporting its efficacy, safety, and generally good patient tolerability (Caporro, Disanto, Gobbi, & Zecca).

Copaxone® has also been recognized as the DMT with the highest cost increases at greater than 1000%, which far exceeds standard prescription inflation rates. Branded Copaxone® initial cost when launched in 1996 was $9,000 a year and now has increased to over $85,000 a year contributing to higher cumulative direct healthcare costs (Hartung, Bourdette, Ahmed, & Whitham, 2015). In fact, recent research has found that most MS DMTs have increased in acquisitions cost to approximately $80,000 per patient per year (Hartung, Johnston, & Bourdette, 2018). The research confirms that the cost to treat MS with DMTs is extremely high. By itself, MS ranked eighth by drug invoice spending among the top therapeutic classes in the U.S. in 2016, representing nearly $19 billion in drug spending alone (IQVIA, 2017). The introduction of these expensive specialty DMTs for the treatment of MS has created the potential for patients with MS to become higher contributors to healthcare spending (Anderson & Philbrick, 2014). Specialty drugs have become a major driver of prescription drug costs for insurers as well as out-of-pocket expenses borne by the patient. Since about half of specialty drug spending is on self-administered agents covered under the pharmacy benefits, these have been the focus of payer efforts to control spending. Insurers and pharmacy benefit managers seeking to manage costs have largely been unable to use the traditional 3-tiered cost-sharing design to encourage utilization of lower-cost drugs since specialty drugs often have few close, less-expensive substitutes until recently.

The primary patent for Teva's brand Copaxone® (glatiramer acetate) 20 mg daily ended in May 2014. Its expiration or invalidation of remaining patents created the opportunity to develop generic alternatives, which could result in cost savings for patients and payers.

Following submission of an ANDA in December 2007, the first generic glatiramer acetate named GLATOPA® was approved by the FDA in April 2015, based on demonstration of equivalent physicochemical characteristics plus immunologic and clinical effects to Copaxone®. Subsequently, the Glatopa® 40 mg generic formulation was approved in February 2018. In parallel, Mylan Pharmaceuticals received approval of its 20 and 40 mg generic versions of glatiramer acetate in October 2017. Both generic versions were introduced at wholesale acquisition cost discounts of between 15 to 70% discount to branded Copaxone®. Generic drugs are one of the most effective checks on rising drug costs in the United States (Kohl & Shrank, 2007). Thus, the current MS treatment landscape may change with the approval of less expensive generic versions of DMTs for MS.

Reducing the cost of MS DMTs would have a significant impact on the cost-effectiveness of these drugs and patient costs (Owens, 2016). With increased availability and development of less expensive generic specialty pharmaceuticals, US insurers can implement appropriate prescription management strategies to control both overall utilization and costs within the MS category if they should choose. Key insurer management strategies for specialty pharmaceuticals could include the implementation of specialty tiers and complex formulary designs, drug restrictions through prior authorizations and quantity limits, co-payments and co-insurance rates that increase patient cost burden, and government regulation for pharmaceutical step-therapy interventions and drug price controls (Patel & Audet, 2014). Moreover, insurers may implement specialty pharmacy provider dispensing for drug distribution, medication therapy management programs to increase coordination of care, quality measures enforced through healthcare reform and accountable care organizations and increased use of evidence-based medicine.

Many insurers have already adopted incentive-based formularies to control prescription-

drug costs through generic utilization in other therapeutic categories. An incentive based, or tiered formulary provides financial incentives (i.e., lower copayments) for enrollees to choose drugs that are preferred by the payer. Different changes in formulary administration may have dramatically different effects on utilization and spending and may in some instances lead enrollees to discontinue therapy. The associated changes in copayments can substantially alter out-of-pocket spending by enrollees, the continuation of the use of medications, and possibly the quality of care (Happe, Clark, Holliday, & Young, 2014).

Differences in benefit design between insurer types (Commercial, Medicare, and Medicaid) and differences in patient out of pocket costs may lead to variations in the rate of utilization uptake of generic vs branded glatiramer acetate among patients depending on the type of insurance. Little is known regarding the impact or use of generic treatments in MS. Insight into MS market dynamics is important as it provides an opportunity to assess management and utilization of generic prescription medications in MS through insurance benefit design.

**Problem Statement**

This study investigates the utilization uptake of generic vs. branded glatiramer acetate in multiple sclerosis (MS) using prescription claims data to highlight any differences in uptake between the three primary insurance payer types through benefit coverage and design. The primary insurance types include Commercially insured, Medicare, and Medicaid payers. This is an important area of research because there are no studies examining current utilization incentives used by insurers to facilitate generic glatiramer acetate uptake as covered beneficiaries. Literature articles indicate that MS imposes a significant economic burden on patients and the US healthcare system utilization. MS prescription drug costs have risen in a

dramatic fashion. The cost of MS drugs in the United States is rising five to seven times faster than the normal rate of drug inflation (Hartung, Bourdette, Ahmed, & Whitham, 2015). Therefore, insurers have introduced multiple formulary reforms and initiatives to optimize the managed entry of new drugs, in addition, to help control expenditure of existing drugs through the encouraged use of prescription generics leveraging lower cost and increased competition. Increased utilization of generic MS drugs my increase treatment access and help in controlling costs.

## Research Question

Does generic glatiramer acetate availability lead to greater utilization among insurers in treatment of multiple sclerosis?

## Population

This is an archival data analysis of U.S. patients with multiple sclerosis that are Commercially insured, Medicare, and Medicaid beneficiary cohorts identified by branded or generic 20 mg or 40 mg glatiramer acetate utilization analyzed through de-identified claims data licensed from Symphony Health for a 52-month period from October 1, 2014 to January 31, 2019.

## Assumptions

Increasing healthcare expenditure has led healthcare authorities, providers, and patients to minimize costs and maximize savings relative to outcomes (Burke & Ryan, 2014). Brand medication cost is a key component from both an affordability and accessibility perspective (National Academies of Sciences, Engineering, and Medicine, 2017). Upon patent loss by the originator of a branded drug, generic drug entry is soon to follow pending FDA approval. The FDA has approved two generic forms of glatiramer acetate on the basis that they are bioequivalent to the brand. Generic drugs are usually priced at a discount to the originator and thus offer direct acquisition cost savings to the payer and patient savings in the form of lower copayments (Landon et al., 2007). Switching from branded to generic medication use is a common cost containment measure. Drug insurance plans typically encourage preferred vs non-preferred drug use through tiered pharmaceutical formularies to guide prescription-drug use, requiring relatively small patient copayments for inexpensive generic drugs and higher copayments for brand-name drugs (Kouvelis, Xiao, & Yang, 2015).

Pharmaceutical manufacturers, however, use coupons to reimburse patients for this

difference in copayments when they buy brand-name medications, so that, for people with commercial insurance coverage, the out of pocket costs are the same as those for generic drugs. Patients with commercial insurance like the coupons because they can help make expensive brand-name drugs more affordable. But the coupons may also discourage patients from considering appropriate lower-cost alternatives, including generics. It is however illegal under the federal anti-kickback law for drug manufacturers to offer any type of payment that might persuade a patient to purchase something that federal health care programs like Medicare and Medicaid might reimburse. Pharmaceutical manufacturers may sponsor patient assistance programs (PAPs) that provide financial assistance or drug free product (through in-kind product donations) to low income individuals to augment any existing prescription drug coverage. PAPs also can aid Part D enrollees and interface with Part D plans by operating "outside the Part D benefit" to ensure separateness of Part D benefits and PAP assistance. Theses Medicare Savings or Extra Help Programs can help pay for patient premiums and out-of-pocket costs, such as deductibles and coinsurance. Medicare currently identifies products costing over $670 per month as specialty tier products allowing to charge between 25 percent and 33 percent coinsurance for specialty tier drugs to enrollees. In addition, unlike commercial plans that cap members' out-of-pocket drug spending annually, Medicare has no limit for prescription medications in Part D, its prescription drug benefit.

As a result, Commercial patients may be shielded from cost-sharing initiatives, thus undermining Commercial insurers’ ability to influence generic drug utilization as may be found within Medicare and Medicaid beneficiaries. In addition, insurance providers with higher utilization uptake of generic glatiramer acetate occurs when initiatives to reduce prescribing costs drive use of MS generics by placing more restrictions on branded products compared to payers with less initiatives.

# CHAPTER 2

# LITERATURE

# REVIEW

## Overview

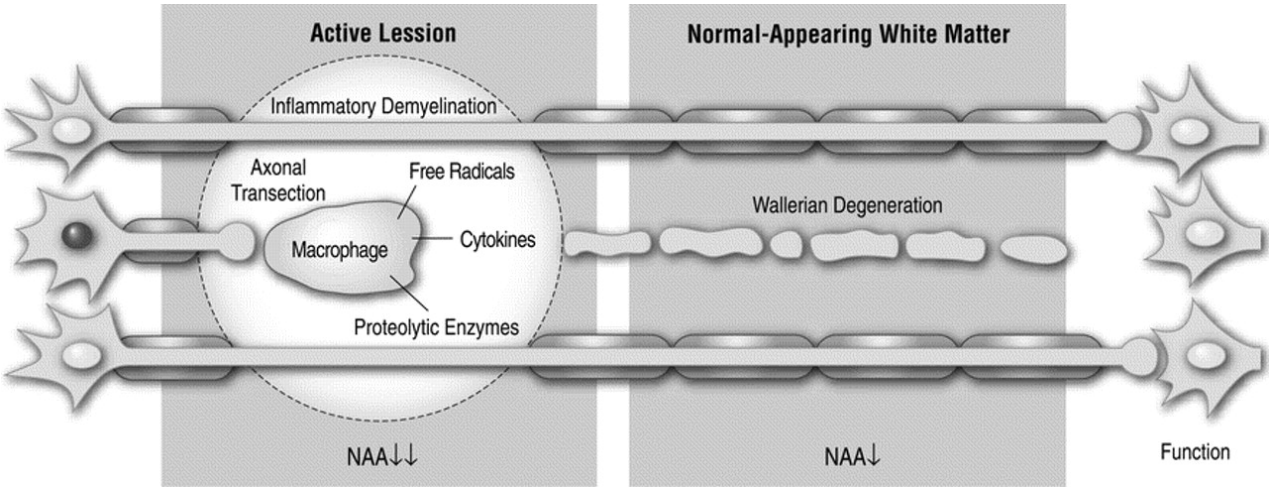
A literature review was conducted to expand on the background and unmet need for this study by analyzing previous research or available studies relating to my research question to assess any important findings to build on a theoretical foundation of knowledge and find applicable relevance in those insights. The primary objective of this literature review was to explore brand vs generic drug utilization trends in the treatment of multiple sclerosis and to gain an understanding on an optimal study design to approach research question.

## MS and Disease Modifying Therapies

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system (CNS) (Reich, Lucchinetti, & Calabresi, 2018). It is characterized by demyelination of axons (Figure 1) in the brain and spinal cord with axonal damage or destruction (English & Aloi, 2015). MS affects predominately patients aged 20-50 years with women affected twice as often as men (Gooch, Pracht, & Borenstein, 2017). The exact etiology is unknown and likely results from complex interactions of both environmental and genetic factors. The symptoms of MS vary depending in part on the location of lesions within the central nervous system. Common symptoms include sensory disturbances in the limbs, optic nerve dysfunction, pyramidal tract dysfunction, bladder or bowel dysfunction, sexual dysfunction, ataxia, and diplopia (Noyes & Weinstock-Guttman, 2013). Although there is large variability in symptom manifestation and disease progression, MS is still the most common cause of non- traumatic disability in young adults and is associated with an average reduction in life span of 5 to 10 years (English & Aloi, 2015). Current

MS classification is based upon different defined clinical courses and consensus on the nature of the disease. The first is relapsing-remitting MS (RRMS), which is characterized by interspersed self-limited clinical events known as “relapses” or “attacks” of neurologic dysfunction with periods of clinical remission without disease progression in approximately 85% of patients (Weinshenker, 1994). The second clinical course is secondary progressive MS (SPMS), which is comprised of about two-thirds of RRMS patients that progress in worsening neurological function due to accumulating axonal damage over years of active disease with or without attacks (Lublin, Reingold, & Cohen, et al).The third clinical type is primary progressive MS (PPMS), which is characterized by a continued steady decline in neurological function in about 10-15% patients from the first onset of a new attack or recurrent symptoms without any subsequent attacks (Koch, Kingwell, Rieckmann, & Tremlett). The fourth type is progressive–relapsing MS (PRMS), which also begins with a progressive course except patients do experience at least one occasional attack over a longer time period (Goodin, Frohman, & Garmany, et al, 2002).

**Figure 1: Axonal Damage Consequent to Demyelination.** One of the potential mechanisms accountable for axonal loss following demyelination is Wallerian degeneration, whereby axons degenerate distal to the site of damage resulting in function loss or downstream effect including decreased levels of the neuronal marker N-acetyl aspartate (Lisak, 2007).




There are no single clinical feature, laboratory test, or imaging findings that is enough to

diagnose that a person has MS. The diagnosis ultimately is a clinical decision based on weighing the factors that support the diagnosis against those that fail to support it or point to the possibility of an alternative diagnosis. The International Panel on MS Diagnosis criteria, also called the McDonald criteria, has set new diagnostic criteria for MS that incorporate the clinical characteristics and MRI features of CNS lesion "dissemination in space" (DIS – suggestions of damage in more than one place in the nervous system) and "dissemination in time" (DIT – suggestions that damage has occurred more than once) to speed the diagnostic process and reduce the chance of misdiagnosis thereby delaying treatment to limit permanent damage (Thompson, Banwell, & Barkhof, et al, 2018).

Even though MS is not a curable disease, drug treatment options are available to reduce frequency of attacks, manage symptoms, and slowing down disease progression by targeting the mechanisms that underlie inflammation. The selection of MS drug treatment(s) has become very challenging because of the number and availability of therapies including new agents with more complex mechanisms of action and greater risks of adverse effects that may influence initial and subsequent therapeutic choice. Patients with MS may benefit from treatment but individual response to a given therapy and adverse events occurrence are largely unpredictable and many cases need to change several drugs to stabilize their disease. Although much remains unknown about the long-term effects of using or switching between disease-modifying therapies (DMTs), factors such as presence of co-morbidities, desire for pregnancy, previous use of other immunosuppressant's, John Cunningham virus antibody seropositivity, geographical parameters, health insurance coverage, and patient/neurologist preferences can influence the treatment selection or sequence of treatment selection (Freedman, Selchen, Prat, & Giacomini, 2018). The choice of a specific agent should be individualized according to disease activity, patient values, and preferences. Currently, there are 17 DMTs approved by the U.S. Food and Drug Administration

(FDA) for the treatment of the various forms of MS as shown in Table 1.

**Table 1: FDA Approved Multiple Sclerosis Disease Modifying Therapies** (adapted from Freedman, Selchen, Prat, & Giacomini, 2018).

| Drug Chemical Name | Brand Name Manufacturer | Class | FDA Approved Dose | FDA Approved Indication |
|---|---|---|---|---|
| **Subcutaneous injection** | | | | |
| **Interferon β-1a** | Avonex® Biogen | Interferon | 30 mcg weekly | RRMS |
| | Rebif® EMD Serono | Interferon | 22 mcg or 44 mcg three times | RRMS |
| | Plegridy® Biogen | Peginterferon | 125 mcg every 14 days | RRMS |
| **Interferon β-1b** | Betaseron® Bayer | Interferon | 250 mcg every other day | RRMS |
| | Extavia® Novartis | Interferon | 250 mcg every other day | RRMS |
| **Glatiramer acetate (GA)** | Copaxone® Teva | Synthetic mixed polymers | 20 mg daily 40 mg three times | RRMS |
| | Glatopa® Sandoz/Novartis | Synthetic mixed polymers | 20 mg daily 40 mg three times | RRMS |
| | Generic GA Mylan | Synthetic mixed polymers | 20 mg daily 40 mg three times | RRMS |
| **Oral** | | | | |
| **Fingolimod** | Gilenya® Novartis | Sphingosine 1-phosphate receptor modulator | 0.5 mg once daily | RRMS |
| **Teriflunomide** | Aubagio® Sanofi Genzyme | Pyrimidine synthesis inhibitor | 7 mg or 14 mg daily | RRMS |
| **Dimethyl fumarate** | Tecfidera® Biogen) | Multifactorial | 240 mg twice daily | RRMS |
| **Siponimod** | Mayzent® Novartis | Sphingosine 1-phosphate receptor modulator | 0.25 mg once daily | RRMS SPMS |
| **Cladribine** | Mavenclad® EMD Serono | Purine antimetabolite | 10 mg tablet once daily for 4 or 5 days two times per year | RRMS SPMS |

| | | | | |
|---|---|---|---|---|
| **Intravenous Infusion** | | | | |
| **Mitoxantrone** | Novantrone® EMD Serono | Intercalates with DNA; inhibits topoisomerase II | 12 mg/$m^2$ every 3 months until a cumulative dose limit of approximately 140 mg/$m^2$ is reached | RRMS SPMS |
| **Natalizumab** | Tysabri® Biogen | Anti α4β1/ α4β7 integrin monoclonal antibody | 300 mg every 4 weeks | RRMS |
| **Alemtuzumab** | Lemtrada® Sanofi Genzyme | Anti-CD52 monoclonal antibody | 12 mg per day for 5 days in the first year, 3 days in second year | RRMS |
| **Ocrelizumab** | (Ocrevus®, Genentech) | Anti-CD20 monoclonal antibody | RRMS: 300 mg twice 14 days apart, then 600 mg once every 24 weeks<br>PPMS: 300 mg twice 14 days apart, cycle begins every 24 weeks | RRMS PPMS |

Recent studies have shown that early treatment with disease modifying therapies (DMTs) is associated with significant improvement in the patient's quality of life (Kobelt, Lindgren, & Parkin, et al, 2000). In addition, MS medications can help achieve treatment goals by treating acute relapses, improve health-related QOL, reduce the frequency and severity of relapses, delay disability accumulation, and postpone the onset of the progressive phase of the disease (Phillips, 2004; Philips, 2009). For example, when acute exacerbations occur (such as vision loss or loss of coordination), they are commonly treated with a short duration of high-dose oral or intravenous corticosteroid. If spasticity occurs, it can be addressed with muscle relaxants, however therapy with DMTs is designed to prevent relapses and progression of disability rather than treat specific

symptoms or exacerbations of the disease (Smith, Carson, & Fu, et al, 2010). These agents modify the immune response that occurs in MS through various anti-inflammatory, immunomodulatory or immunosuppressive effects. In 2018, the American Academy of Neurology (AAN) released new guidelines on the use of disease-modifying therapies (DMTs) in patients with MS to provide updated guidance on starting, switching, and stopping treatments including the recommendation for an earlier start to treatment rather than later in the disease course (Rae-Grant, Day, Marrie, et al, 2018).

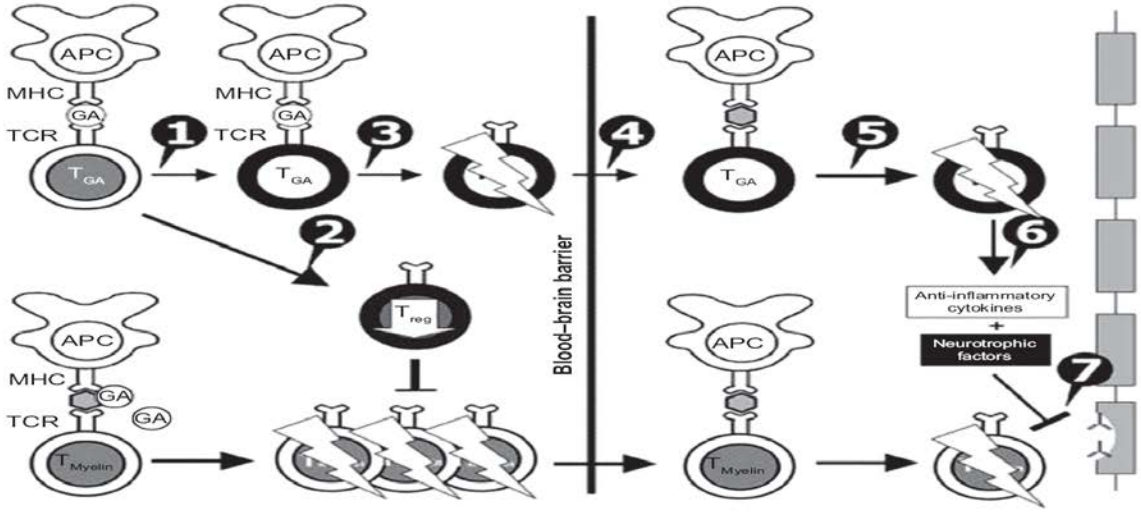
**Glatiramer Acetate**

Among the DMTs available, glatiramer acetate stands out due to its unique mechanism of action, and excellent long-term efficacy/safety data. Glatiramer acetate (GA) is the generic name of a multiple sclerosis drug produced by Teva Pharmaceuticals and sold under the commercial or brand name Copaxone®. Copaxone® (glaterimer acetate) was the first of the currently approved DMTs to be tested in human subjects and is considered a standard choice for first-line treatment of RRMS. Copaxone® (glatiramer acetae) was approved by the FDA in 1996 began development at the Weizmann Institute in the 1960's to study structural features of antigens involved in the induction of the animal model of MS (Varkony H, Weinstein V, Klinger E, et al., 2009). Glatiramer acetate is classified as a non-biological complex drug (NBCD) composed of a mixture of immunogenic polypeptides of varying amino acid sequences and sizes that are difficult to characterize even with state-of-the-art analytical methods (Weinstein, Schwartz, Grossman, 2015). Glatiramer acetate is best described as a heterogeneous mixture of amino acid copolymers. Thus, glatiramer acetate is not a single molecular entity, but a distinct synthetic polypeptide comprised of varying lengths of interconnected peptide chains, some containing up to 200 amino acids with structural complexity comparable to that of proteins, or even more complex than proteins (Varkony, et al., 2009). Glatiramer acetate is a manufactured amino acid

polymer of tyrosine, glutamate, alanine, and lysine analogous to biological products and thus is defined by its well-controlled manufacturing process. Glatiramer acetate resembles the myelin sheath components of myelin basic protein (MBP), which allows it to act as a decoy for immune targeting of myelin. Glatiramer acetate is administered by subcutaneous injection every day at the dose of 20 mg or alternatively three times a week at the 40 mg dose.

The exact mechanism of action (MOA) of glatiramer acetate is unknown, but it is believed to function via a multifaceted affect involving both immunomodulation and neuroprotection (Figure 2). Its MOA is hypothesized to involve competition with myelin autoantigens at the major histocompatibility complex class II binding site on antigen-presenting cells, induction of antigen-specific Th2 T cells leading to bystander suppression of inflammation, and stimulation of neurotrophic factor secretion by immune cells (Schrempf & Ziemssen, 2007).

**Figure 2: Glatiramer Acetate Mechanism in Immune Modulation.** The proposed mechanism of action relates to its immunologic effects such as the induction of antigen-specific suppressor T cells, inhibition of antigen presentation, displacing bound myelin basic protein (MBP), or causing an immune deviation in CD4_ T cells from a Th1 to a Th2 phenotype, which secrete anti-inflammatory cytokines in the CNS through cross-recognition with myelin autoantigens through a series of distinct steps (Schrempf & Ziemssen, 2007).




Across five randomized controlled clinical trials, glatiramer acetate 20 mg has consistently demonstrated efficacy in reducing relapse rate and MRI disease activity and slowing

of disability progression in patients with RRMS, while possessing a favorable and well-characterized safety record in both short and long-term studies (Boster, Ford, Neudorfer, & Gilgun-Sherki, 2015). Subsequently, the Glatiramer Acetate Low-Frequency Administration (GALA) study demonstrated the efficacy and safety of glatiramer acetate 40 mg 3 times a week in patients with RRMS (Khan, Rieckmann, Boyko, Selmaj, & Zivadonov, 2013).

Injectable DMTs such as glatiramer acetate have dominated the MS market for over two decades, but the situation has changed because of the recent patent expirations of Teva's Copaxone® (glatiramers acetate). This created an opportunity for approval of generics through the Abbreviated New Drug Application (ANDA) pathway established by the 1984 Hatch-Waxman Act (Mossinghoff, 1999), which permits FDA approval of applications to market generic versions of brand-name drugs without the need for costly and duplicative clinical trials. The FDA has made accelerated or expedited approval of less costly generic drugs a core objective in its mission designed to facilitate more generic competition, promote patient access, and improve the economics of developing generic medicines. Unlike the standard FDA drug-approval process that requires extensive preclinical (animal) and clinical (human) testing to establish safety and effectiveness (Van Norman, 2016), the approvals of generic drug products via the ANDA pathway do not generally require inclusion of preclinical and clinical data (Naziya, Sandeep, & Anoop, 2018). Instead, physicochemical equivalence and bioequivalence to the innovator drug must be demonstrated scientifically to establish therapeutic equivalence (Chow, 2014).

When an innovative (or brand-name) drug product is going off patent, pharmaceutical or generic companies may file an ANDA for generic approval, which in this scenario is for Copaxone®. Generic drug products are defined as drug products that are identical to an innovative (brand-name) drug which is based off an approved NDA with regards to active ingredient(s), route of administration, dosage form, strength, and conditions of use. Since ANDA submissions for

generic applications do not require lengthy clinical evaluation of the generic drugs under investigation (see Table 2), the price of a generic drugs is usually much lower than the cost of the originator brand. On average, generic entrants are about 30 - 60% of the price of the brand-name original (Zarowitz, 2008, Lewek & Kardas, 2010). As a result, increased use of less expensive generic drugs is encouraged as a means of healthcare savings and costs containment by policy makers, insurers, providers, and patients.

**Table 2: FDA NDA vs ANDA Approval Requirements** (Chow, 2014)

| NDA | ANDA |
|---|---|
| 1. Chemistry | 1. Chemistry |
| 2. Manufacturing | 2. Manufacturing |
| 3. Controls | 3. Controls |
| 4. Testing | 4. Testing |
| 5. Labeling | 5. Labeling |
| 6. PK/bioavailability | 6. PK/bioavailability |
| 7. Animal Studies | 7. ---- |
| 8. Clinical Safety & Efficacy Trials | 8. ---- |
| NDA = New Drug Application; ANDA = Abbreviated New Drug Application | |

In April 2015, the first generic version of the complex drug glatiramer acetate (Glatopa® 20 mg/mL) injection was approved in the United States as a fully substitutable AP-rated generic for all approved indications of the 20 mg branded glatiramer acetate (Copaxone®) dosage form. Despite glatiramer acetate's complex nature of being a chemically synthesized mixture of random peptide, the FDA approval occurred without conducting any clinical trials. Subsequently, the 40 mg Glatopa® formulation was approved in February 2018, while Mylan received FDA approval of both its generic formulations in October 2017. Teva contends that Copaxone® is too complex for another manufacturer to make an identical version of its drug, thus asserting that any new generic

version of Copaxone should be tested in clinical trials with MS patients to assure its safety and efficacy (FDA, 2015). Such a study has been conducted when the first phase III clinical trial to test a generic disease-modifying medication for multiple sclerosis treatment entitled the Glatiramer Acetate Clinical Trial to Assess Equivalence With Copaxone (GATE), demonstrated that glatiramer acetate, the generic drug, was equivalent to the trademark drug Copaxone® for the treatment of MS (Cohen, Belova,, Selmaj, et al., 2015). Despite this clinical validation of generic sameness to the originator or reference listed drug (RLD), lingering healthcare stakeholder perceptions of this sameness versus potential difference concerns may remain a key influencer in potential treatment utilization. As a result, some stakeholders may perceive that generics as less expensive versions of the RLD, while others may believe that they are never fully identical to the RLD.

**Cost of Disease Modifying Therapies**

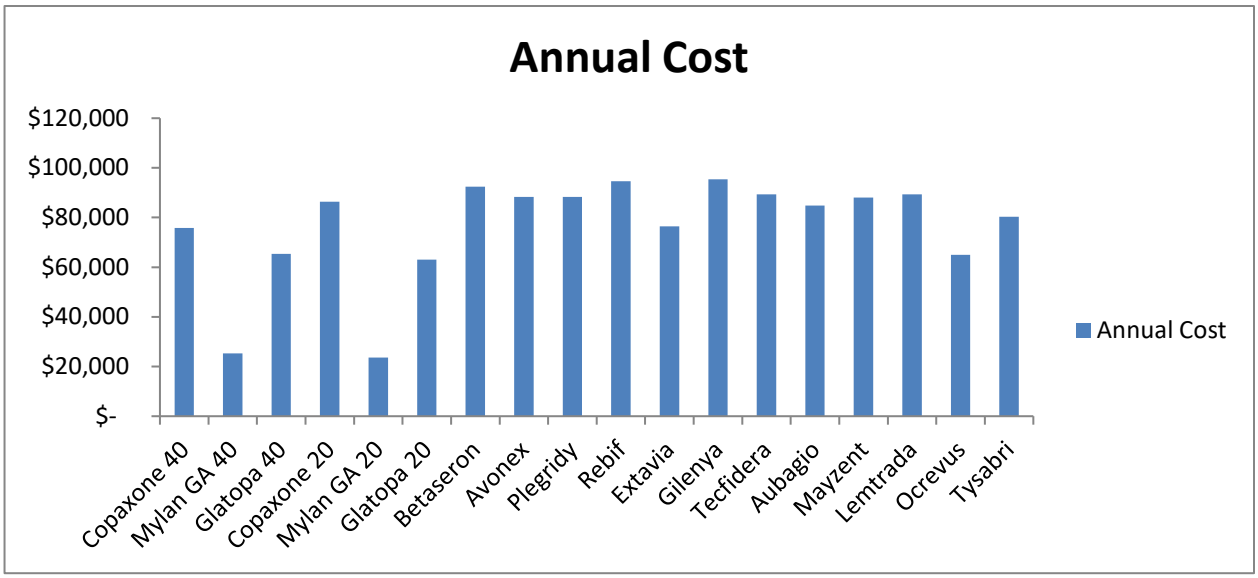
Spending on prescription drugs in the United States is on the rise and is projected to outpace growth in other parts of the healthcare sector in 2018 (Cuckler, 2017). In addition, in 2017 there was a 14.6% increase in per member specialty drug spending, up from 10.1% the prior year. Consequently, it is project that by 2022, specialty drugs will account for a projected 47% of the pharmacy industry's revenues. In 2017, four specialty classes accounted for over 75% of total expenditure for specialty drugs: (1) inflammatory conditions, (2) MS, (3) cancer, and (4) human immunodeficiency virus. Moreover, in recent years, the healthcare and managed care communities have witnessed a huge shift in expenditure from medical benefits towards pharmacy benefits, especially for newer oral agents that treat cancer or manage MS (Owens, 2013). Specialty drug spending now represents 46.5% of the net per-capital spending in the US. Of the $12 billion in net spending on new drugs, 75% was for specialty products exclusively (IQVIA, 2017). The IQVIA study also found that found the use of copay coupons in 42% of all specialty prescriptions compared

with 18% of all branded prescriptions filled through commercial plans. A contributing factor supporting high DMT costs and copay coupon use is the reality that most patients do not have to directly pay for their drugs. Copayments or out-of-pocket costs are meant to be paid by the patient, which should theoretically keep prices low. However, many pharmaceutical companies have counterattacked this by offering copayment coupons, which enable the company to pay some or all the patients' costs while raising drug prices (Dafny, Ody, & Schmitt, M.A, 2016). For specialty conditions in which the initial cost of drugs is extremely high such as autoimmune diseases, hepatitis C, and multiple sclerosis coupon usage rates are greater than 50% (IQVIA, 2017). This high utilization of copay coupons is consistent with a study looking at the impact of patient copays or co-insurance on the probability of receiving disease-modifying therapies and on being adherent with treatment in patients with multiple sclerosis. The study confirmed that MS patients are sensitive to cost sharing by having a lower probability of receiving DMTs, lower probability of treatment adherence, and higher risk of treatment discontinuation (Palmer, Abouzaid, Shi, Fowler, Lenhart, Dastani, & Kim, 2012). Patients who are not adherent to their DMTs have higher risk of relapse, more emergency department visits and hospitalizations, and higher medical costs, thus reducing cost barriers may improve initiation of DMTs and treatment adherence. Specialty copayments or coinsurance is variable depending on the insurer but can range from as low as 20 percent or as high as 50 percent of the cost of the medication. MS patients covered by Medicare Part D plans where drugs costing $670 or more per month are placed on a "specialty tier," may be subject to up to 33 percent coinsurance making it potentially difficult for Medicare patients to afford their medications (Doshi, Ladage, Pettit, & Taylor, 2016).

Despite the availability of more treatment options, costs for all MS DMTs have increased sharply in the United States (Sawad, Seoane-Vazquez, Rodriguez-Monguio, 2017). Between 2008 and 2012, U.S DMTs sales doubled from $4 billion to nearly $9 billion annually (Hartung,

Bourdette, Ahmed, & Whitham, 2015). By 2013, first generation DMTs like IFNß-1b (Betaseron®) and glatiramer acetate (Copaxone®) grew to an average annual cost of over $60,000. Second generation DMTs (Oral agents) cost have increased from 8 % to 17 % annually since their approval. For example: fingolimod cost $50,775 in 2010 but has increased in cost by 8% to $63,806 by 2013. Similarly, with teriflunomide and dimethyl fumerate cost $47,651 and $57,816 respectively at approval but increased in cost by 17% ($57,553) for teriflunomide and by 14% ($63,315) for dimethyl fumerate (Hartung, Bourdette, Ahmed, & Whitham, 2015). Current annual wholesale acquisition costs of commonly used DMTs are shown in below in Figure 3.

**Figure 3: Commonly Prescribed MS DMT Annual Acquisition Cost** (AnalySource, 2019)




The high cost of MS DMTs in the United States is producing a cascade of negative effects upon patients with MS and their medical care. This can cause private insurers and public insurance regulatory bodies to require individuals with MS to meet specific criteria to obtain coverage for DMTs (Hohol, Orav, & Weiner, 1999) or require high copays (Minden, Frankel, Hadden, & Hoaglin, 2007). In what appears to be a direct response to the high cost of these drugs, insurance carriers have developed tiered formularies requiring step-wise DMT trials, with the tiers apparently determined by preferential pricing contracts rather than any objective analysis of risks and benefits

of the various therapies (Miller, Happe, Meyer, & Spear, 2012; Owens, 2013).

Overall, MS is a very costly chronic disease, with direct costs of prescription drugs and indirect costs being the most significant cost drivers, according to available data (Adelman, Rane, & Villa, 2013). The cost of providing health plan benefits and insurance coverage for MS therapy is one of the most rapidly growing segments of current healthcare expenditures. Evolving drug complexity portends increasing complexity for payers and health plans. Therefore, improved action plans must be developed that balance appropriate access to optimal therapies with the need to manage the high costs of DMTs and evolving treatments. Generic drugs are one of the most effective checks on rising drug costs in the United States (Kohl & Shrank, 2007). Today, about 9 out of 10 prescriptions filled with simple, small molecule generic drugs. However, most MS DMTs are complex agents and not exposed to price competition from generics, except for the recent availability within the glatiramer acetate category.

**Healthcare Insurance Benefit Design**

In the U.S., a health plan is an entity that provides or arranges for the insurance coverage of specific health services for an individual or group, either for a pre-determined price or by administering health benefits for entities like employers who opt to take on the financial risk themselves, often referred to as self-insuring (Morrisey, 2008). Today, health plans play a central role in the U.S. healthcare market by providing or administering health insurance as well as a range of services to its members on behalf of employers, individuals and government payers. As the country's largest healthcare payer, the U.S. government has always influenced the benefit design of Medicare, Medicaid, Veterans Affairs and the Department of Defense (Brown & American Enterprise Institute for Public Policy Research, 2010). The U.S. government has increased its influence by setting standards for more affordable and simplified benefit structures that are reshaping traditional commercial health plan products thru bundled and value-based

payment reimbursement.

In turn, private health plans must look for ways to control their expenses while maintaining enough quality to satisfy the needs of their clients and members. Pharmaceuticals, especially branded prescription drugs have been and will continue to be a top target for health plan cost control due to their high category growth and spend (Ballreich, Alexander, Socal, Karmarkar, & Anderson, 2017). However, health plans also know that pharmaceutical innovations create some of the greatest opportunities for better health and decreased overall costs. Government and private payers are trying to stabilize or reduce their healthcare spend by shifting more costs to consumers (Jencks, & Schieber, 1992). This is occurring across the market through higher deductibles, copays and premiums as well as greater use of coinsurance. It is most prominent in consumer-directed health plans (CDHPs) and the use of private exchanges, particularly for retirees. As consumers assume a higher share of healthcare costs, they face greater responsibility for healthcare choices and spending.

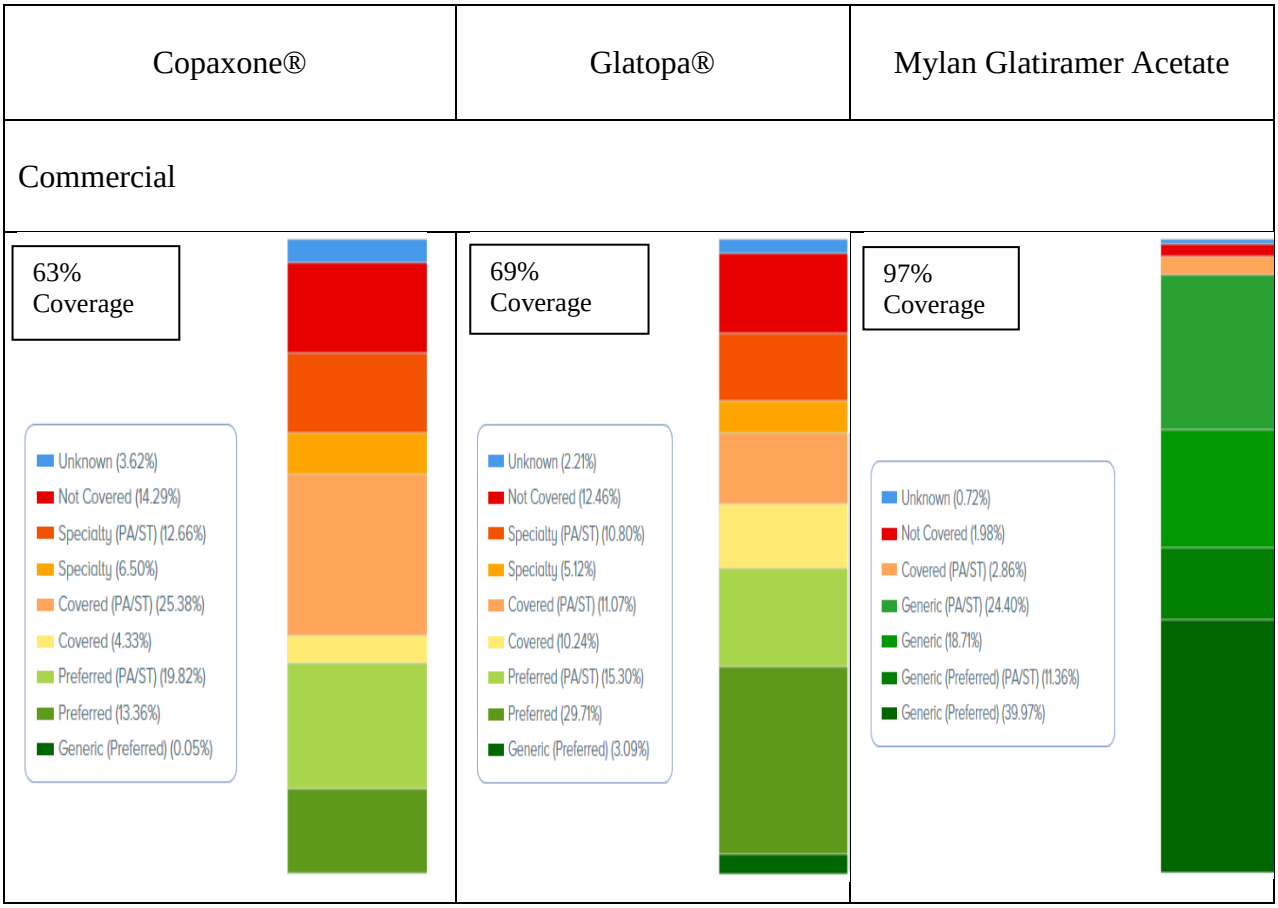
Health plans typically organize their insurance services into three distinct areas of coverage based on the patient lives that they cover (Hoffman, Klees, Curtis, 2000):

- **Commercial:** People under 65 may have access to what is often called group coverage as a benefit from their employer. If not covered under a group plan, the Affordable Care Act, (ACA) requires individuals to purchase coverage through a health plan exchange or face a penalty fee for remaining uninsured, but this is expected to end in 2019.
- **Medicare:** People 65 and older, as well as permanently disabled individuals of any age, have access to Medicare a federally-funded insurance program. Medicare beneficiaries can choose to enroll in “traditional Medicare,” which is administered directly by the federal government, or enroll in Medicare Advantage with a private plan that administers the benefit on the government’s behalf.

- **Medicaid:** People of all ages who meet a low income threshold may have access to Medicaid a federally and state-funded insurance program. State governments may choose to administer their Medicaid program themselves or outsource it to a private plan, often referred to as a Managed Medicaid plan.

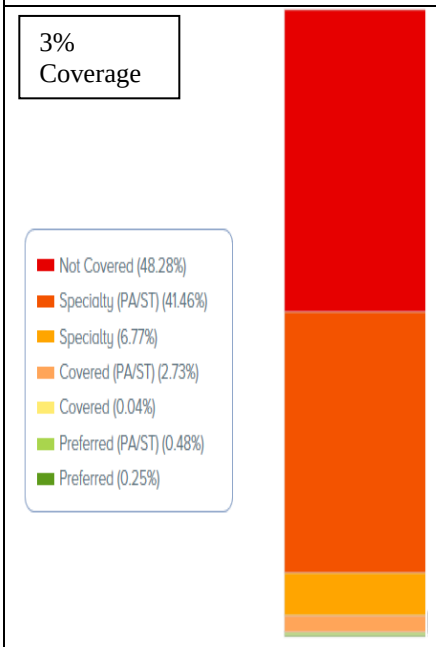
Over two-thirds of the U.S. population is enrolled in a commercial market plan (Barnett, & Berchick, 2017). In addition, the U.S. Census Bureau shows 60 percent of Americans are covered through an employer, 16.2 percent purchase health insurance directly, and the rest are covered by Medicare (16.7 percent) or Medicaid (19.4 percent) or remain uninsured. Within this payer mix, MS patients receiving glatiramer acetate treatment regiments will find varying degrees of formulary coverage and benefit design relative to their insurer as shown in Figure 4.

**Figure 4: Insurer Benefit Design Coverage for Glatiramer Acetate Therapies** (Managed Markets Insights & Technology, 2019)

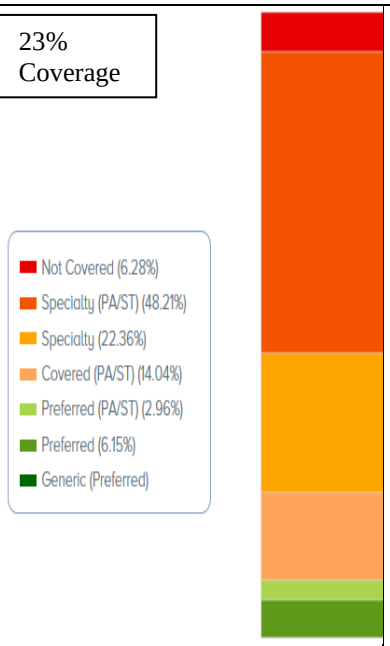


Medicare

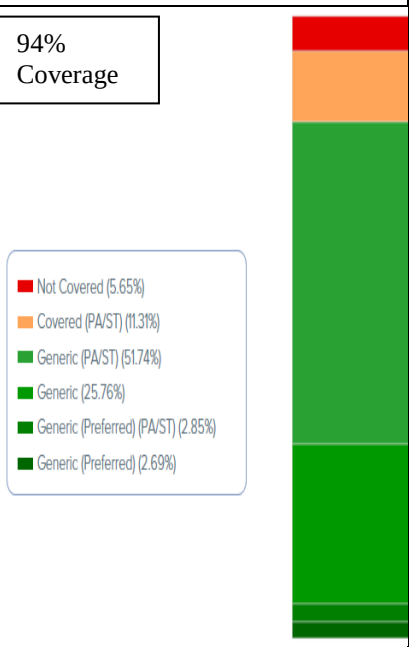
3% Coverage




23% Coverage

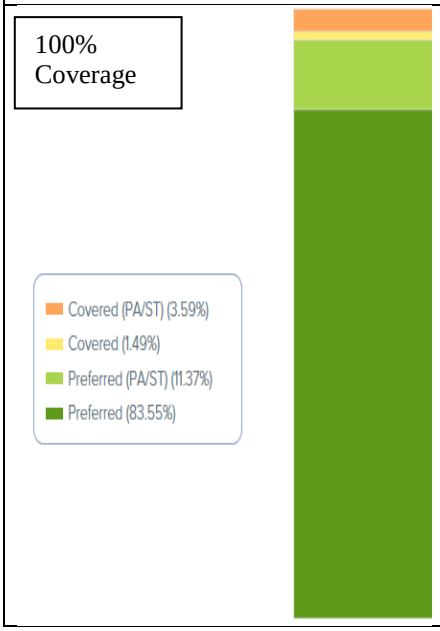



94% Coverage

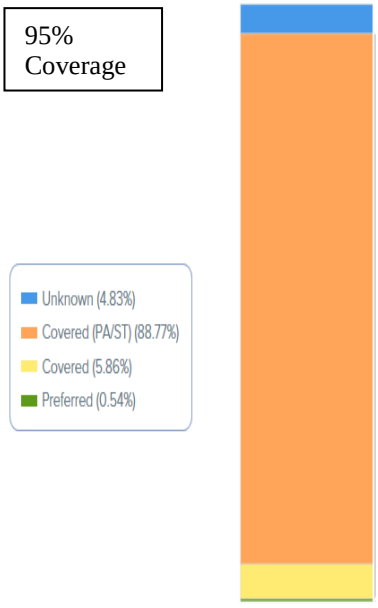



Medicaid

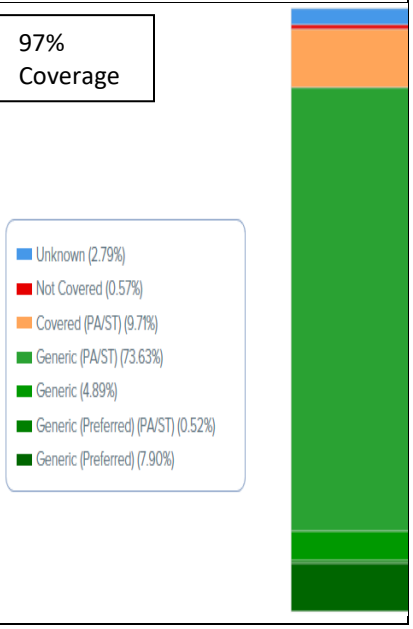
100% Coverage




95% Coverage




97% Coverage



Any private or public health plan that maintains a drug formulary irrespective of whether they contract or negotiate for product access will utilizes a Pharmacy and Therapeutics (P&T) Committee comprised of a medical director and/or prescribing physicians and the pharmacy director to assist in development and management of benefit design. P&T Committees may also include a nursing director or other allied care providers as well as a patient advocacy member representative of real-world clinical practice and community use. The committee is charged with developing and maintaining the drug formulary as well as analyzing new drug evaluations, new FDA approved indications for existing drugs, new clinical line extensions, and new published or clinical practice trends that may impact previous formulary placement decisions. Health plans increasingly include cost data as part of the P&T committee review process. In the absence of significant clinical differentiation, product formulary placement is likely to be financially oriented or incentive-based providing financial incentives (i.e., lower copayments) for enrollees to choose drugs that are preferred by the payer.

To slow and even reverse healthcare spend especially for specialty pharmaceuticals, health plans have focused on specific pharmacy cost controls, including (Pharmaceutical Care Management Association, 2016):

- **Changes to benefit design that shift costs to consumers**:
    - Increased premiums
    - Increased deductibles
    - Increasing co-pays, using co-insurance, including extending cost-sharing to drugs covered under the medical benefit, and increasing tier complexity.
    - Implementation of copay accumulator programs that enforces the patient's full payment of the deductible without subsidization from the manufacturer's copay program toward the cost of the drug.

- **Access and utilization management tactics**:
    - Employing approaches such as step therapy, prior authorization, the narrowing of formularies with limited brands to decrease use of high cost drugs, encourage use of lower cost options and generic utilization.
    - Implementing increasingly aggressive utilization management tools, including expanded use of formulary exclusions and introduction of new to market policies and NDC blocks.
    - Aggressively negotiating for price protection and rebates for preferred tier placement with drug manufacturers.

The need for pharmacy cost control and greater financial predictability is a key driving force behind pharmacy management tactics. Intense focus on specialty products have become a target. Plans have publicly stated their expectations on cost cutting by greater use of generics and biosimilars. Commercial, Medicare and Medicaid plans are increasingly challenged with controlling the costs associated with specialty medications. Active management of specialty drugs and the use of the best pharmacy go together in achieving great patient results with better savings.

Plans have always controlled pharmaceutical utilization through formulary management. However, the latest Utilization Management (UM) strategies particularly exclusion lists and New-to-Market Blocks are designed to address issues of higher product volume for non-preferred and/or high cost brands and pricing. These UM strategies continue to raise access hurdles and, in some cases, prohibit access. In a survey conducted by the National Disability Institute (NDI) and the Multiple Sclerosis Association of America (MSAA), results showed that access to health insurance is not a barrier for MS patients with only 7.7% uninsured and coverage consisting of

53.9% Commercial insurance and almost 39% received government funded healthcare, namely 32.5% Medicare and 6.0% Medicaid (National Disability Institute, 2012).

An additional system for driving generic drugs in the United States is one of "switching" from a brand product to a generic equivalent (usually an AP or AB-rated generic in the Orange Book). Depending upon individual State Law requirements and insurer, substitution may be performed by a pharmacist for a prescription most often written as a brand name product and without specified preference (i.e. dispense as written) to a less expensive generic option if available with appropriate consent. One consequence of this system of substitution is that patients may have their medication "switched" either from brand to generic or from one generic to another generic without input from or knowledge of the physician or the patient without appropriate notification (Shrank, et al, 2010).

**Conclusion**

MS is an inflammatory and degenerative disease of the CNS affecting young adults. The burden of the disease in the society is very high representing the second cause of disability in young patients. In addition, MS is a very costly disease with a significant economic burden to the healthcare system. Given the prevalence of MS and increasing DMT utilization and costs associated with management of the disease, economic evaluation is important in making informed decisions. In a cost-conscious healthcare environment with ever growing fiscal responsibility being placed upon healthcare delivery, cost effective therapies like generic DMTs in MS are likely to become an important part of the decision- making process to use resources efficiently in the face of rapidly escalating costs of MS.

This is an important area of research because of the very limited data analyzing the utilization uptake of generic glatiramer acetate post FDA approval using electronic prescription claims data. There currently are no large retrospective studies examining differences in generic

vs branded GA uptake in the MS prescription treatment category between payer types. Using prescription claims frequency or run rate trends, the investigators will create a linear regression to forecast future utilization of glatiramer acetate. Secondly, the investigators will compare patient out of pocket copayment costs between the three payer groups in addition to copayment card utilization within the Commercially insured group.

# CHAPTER 3

# METHODOLOGY

## Research Design

A retrospective, observational quantitative archival data analysis of Commercially insured, Medicare, and Medicaid prescription claims identified by 20 & 40 mg Copaxone®, Glatopa®, and Mylan glatiramer acetate national drug code utilization.

## Specification of Variables

Glatiramer acetate (GA) use was identified by approved and dispensed pharmacy prescription fills in Commercial, Medicare, and Medicaid claims using national drug codes to compare ratio of branded versus generic GA prescription claim volume to total GA DMT prescription utilization. Glatiramer acetate prescription claims consisted of Copaxone®, Glatopa®, and Mylan Glatiramer Acetate prescription utilization over 52-months inclusive of FDA approved generic glatiramer acetate entrant timing within each of the three key insurance channels. In addition, patients' out-of-pocket copayment amounts for specific drugs were compared between payer groups, as well as manufacturer prescription copayment coupon or foundational assistance utilization within the various payment channels.

## Data Sources

Symphony Health – Integrated Dataverse® data set from October 1, 2014 – January 31, 2019 licensed to Pfizer Inc. in connection to statement of work in de-identified format in compliance with the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations ("**HIPAA**"). Symphony Health – Integrated Dataverse® de-identified claims data set field**s** available for analysis are shown in Table 3 of the Appendix.

**Data Set Construction**

1. Monthly prescription claims for Copaxone®, Glatopa® and Mylan Glatiramer Acetate (numerators). Specific National Drug Code (NDC) numbers included in the data set:
    - **Copaxone®:** 06854631730 (20 mg 30 Pre-filled Glass Syringe Blister Pack in 1 Carton) and 06854632512 (40 mg 12 Pre-filled Glass Syringe Blister Pack in 1 Carton)
    - **Glatopa®:** 00781323434 (20 mg 30 Pre-filled Glass Syringe Blister Pack in 1 Carton) and 00781325089 (40 mg 12 Pre-filled Glass Syringe Blister Pack in 1 Carton)
    - **Mylan Glatiramer Acetate:** 00378696093 (20 mg 30 Pre-filled Glass Syringe Blister Pack in 1 Carton) and 00378696112 (40 mg 12 Pre-filled Glass Syringe Blister Pack in 1 Carton)
2. October 1, 2014 – January 31, 2019 total FDA approved glatiramer acetate DMT claims (denominator).

3. Prescription claim coverage and transactional specifics for Copaxone®, Glatopa® and Mylan Glatiramer Acetate including utilization of out-of-pocket support in the form of copay or secondary assistance from a prescription assistance program.

**Data Analysis**

1. Calculated monthly uptake of each glatiramer acetate (GA) by insurance payer (Commercial, Medicare, and Medicaid) by comparing prescription claim volume of utilization to total GA DMT utilization. The claims ratio is used to construct three different growth curves showing the uptake trends for each version of glatiramer acetate.
    - A future growth curve of branded and generic utilization was constructed based on percentage increases and compared to previous period to forecast projected utilization based upon regression analysis for the remainder of 2019 insurer benefit cycle.

2. Mean monthly dollar value of patient out-of-pocket costs compared between Commercial, Medicare and Medicaid insurance groups for each glatiramer acetate medication.
    - Percentage of claims with manufacturer or foundational copay assistance per insurer type.
        - Commercial insurance: Percent of claims that have utilized manufacturer copayment cards.
        - Medicare: Percent of claims with free or reduced cost prescription offers for those qualifying either for patient assistance programs or those eligible for Medicare "extra help" assistance.
        - Medicaid: Percent of claims with zero cost or prescription patient assistance as a low-income subsidy.

**Institutional Review Board**

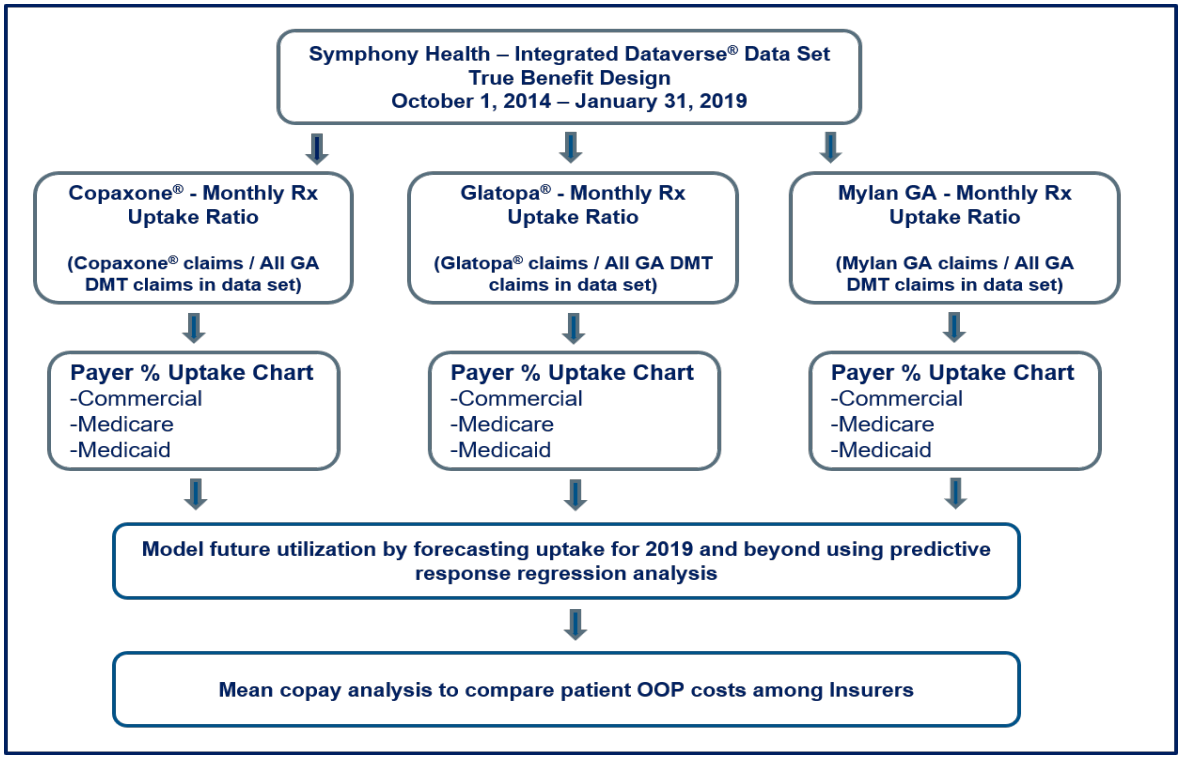
Symphony Health Integrated Dataverse® claims data set licensed by Pfizer Inc. is de-

identified and qualifies as non-human research as set forth by the guidelines of the MUSC Institutional Review Board.

## Conceptual Model

A review of the literature on brand vs generic glatiramer acetate utilization in the management of relapsing remitting multiple sclerosis reveals a lack of comprehensive theoretical framework for understanding these events and their complexities. Applying a process of conceptual framework analysis, as shown in Figure 5, will provide a theoretical framework to shed new light on the feasibility of implementing sustainable generic prescribing practices. This study will contribute important informational insights on MS brand vs generic utilization and help provide additional context to possible influences in generic drug prescribing or switching.

**Figure 5: Project Conceptualization Chart:** A conceptual diagram outlining the study methodology and data analysis.



# CHAPTER 4

## MANUSCRIPT FOR PUBLICATION

Target Journal: Journal of Managed Care and Specialty Pharmacy

Dear Editor,

Please find enclosed our manuscript submission entitled: “Prescription Trends in Branded Versus Generic Glatiramer Acetate Utilization Among Insurers for the Treatment of Multiple Sclerosis in the United States.” The study provides insight on current trends in generic glatiramer acetate (GA) utilization across various payment channels based upon recent availability. The utilization of lower cost generics over branded offering could result in healthcare savings.

Rising healthcare spend on multiple sclerosis (MS) drugs raises the question of what role does a generic glatiramer acetate have within MS treatment or acceptance by stakeholders. Notably, no study has specifically evaluated the differences in utilization uptake of branded vs generic GA among the major insurer categories. The purpose of this study is to establish whether insurer type affects the rate of utilization uptake of branded vs generic GA.

To address this research gap, we extracted glatiramer acetate prescription records from Symphony Health Integrated Dataverse® archival billing data for patients covered by Commercial, Medicare, and Medicaid for 52 months from Oct. 2014 – Jan. 2019. Our analysis of glatiramer acetate claim rates revealed a substantially lower utilization of generic glatiramer acetate across all payer types compared to the brand. The greatest increases in generic were observed in Commercial and Medicare patients. The results indicate a significant brand preference with low payer management directing glatiramer acetate prescriptions toward the generic options.

Thank you for considering our manuscript for publication. We appreciate your time and look forward to your response.

Respectfully,

Kit N. Simpson, DrPH
Professor

# PRESCRIPTION TRENDS IN BRANDED VERSUS GENERIC GLATIRAMER ACETATE UTILIZATION AMONG INSURERS FOR THE TREATMENT OF MULTIPLE SCLEROSIS IN THE UNITED STATES

Stephen G. Smith, MBA, DHA
Director, Specialty Marketing & Market Access
Pfizer Inc.
Biopharmaceutical Group
Phone: 908-901-1741
Stephen.g.smith@pfizer.com

**Corresponding Author:**
Kit N. Simpson, DrPH
Professor, Department of Healthcare Leadership & Management
Director, CEDAR Core (Comparative Effectiveness Data Analytics Resources)
Medical University of South Carolina
Phone: 843-792-0760
Simpsonk@musc.edu

Daniel Brinton, PhD
Assistant Professor, College of Health Professions
Department of Healthcare Leadership & Management
Medical University of South Carolina
Phone: 843-792-8383
Brintond@musc.edu

Erin R. Weeda, PharmD
Assistant Professor, College of Pharmacy
Department of Clinical Pharmacy and Outcome Sciences
Medical University of South Carolina
Phone: 843-792-1186
Weeda@musc.edu

**Disclosures:** Stephen Smith is employed by Pfizer and received funding sources for this research.

Word count: 3282; Abstract word count: 449; Number of tables and figures: 5

## ABSTRACT

**BACKGROUND:** Glatiramer acetate has been a core component of disease modifying therapy for multiple sclerosis since its introduction in 1996. However, branded glatiramer acetate has increased in acquisition cost by approximately 1000% to approximately $90,000 per year. Because of the drug's high cost and availability of alternative lower cost generic options, insurers may use various strategies to control branded utilization, while encouraging generic alternative use.

**OBJECTIVE:** To observe and report variances of generic vs branded glatiramer acetate utilization by insurance type.

**METHODS**: Final approved nationwide pharmacy transactional claims for Copaxone®, Glatopa®, and Mylan Glatiramer Acetate were extracted from Symphony Health Integrated Dataverse® data set from October 1, 2014 – January 31, 2019 for Commercially insured, Medicare beneficiaries with supplemental insurance, and Medicaid patients. Branded versus generic glatiramer utilization rates were calculated based upon volume and using simple percent change projection and regression modeling. Patient out-of-pocket costs and prescription assistance were categorized by insurance payment type.

**RESULTS:** Over the 52-month period, 111,906 patients with multiple sclerosis were prescribed glatiramer acetate by Neurologists (80%) and had 1,624,159 approved dispensed claims primarily through specialty mail (87%) and categorized by payment type as 63.2% Commercial, 25.4% Medicare, and 11.8% Medicaid. The market trend showed a consistent decline in branded glatiramer acetate claims offset by increasing uptake in generic glatiramer acetate with the launch of additional generic market entrants. Generic market share has continued to grow reaching an approximate 30% share of claims. Branded glatiramer acetate utilization has

declined by more than 56%, while generic claim volume has grown 155% over the past 16 months. Among the payer types, Medicare has observed the greatest brand decline at 70% and the second highest generic utilization. Commercial insurers have the greatest category claim volume and greatest generic growth to a 26% share, while the brand has declined by 44%. Medicaid has had the lowest utilization volume and the greatest ratio of generic utilization among insurers at 45%. Patient out of pocket costs are highest with branded use across all insurer types, while Medicaid has the lowest patient out-of-pocket costs.

**CONCLUSIONS:** The study revealed that generic glatiramer acetate adoption or utilization has been slow among insurers but increasing over the past sixteen months with additional generic glatiramer acetate entrants and increased price competition. The greatest trend in generic utilization is occurring within the Commercial channel followed by Medicare and then Medicaid, which has had the lowest growth trend. The results indicate that barriers to generic glatiramer acetate may vary by insurer and influenced by prescriber or patient choice. Generic uptake is projected to increase across all insurer types reflective of trends during 2019 open enrollment and healthcare benefit design change associated with a new health insurance cycle.

## SUMMARY BULLETS

**What is already known about this subject**

- Glatiramer acetate is a structurally complex, nonbiologic, established as an effective treatment for multiple sclerosis with a well-recognized safety and tolerable profile
- Branded multiple sclerosis drugs have high yearly costs adding to high long-term pharmacy costs.
- Strategies to decrease healthcare costs include increasing the use of generic drugs through brand-name drug utilization management.

**What this study adds**

- Examines differences in utilization rates by payer type for branded versus generic glatiramer acetate over the past 52 months.
- Forecasts future utilization of generic glatiramer acetate options relative to brand.
- Compares differences in the patient out-of-pocket costs between payment types.

## INTRODUCTION

Multiple sclerosis (MS) is a common neurologic disease affecting more than 1 million people in the United States.[1] The etiology is assumed to be an autoimmune process leading to an inflammatory condition that damages the myelin of the central nervous system and causes progressive neurologic impairment and frequently severe disability.[2]

In the absence of a cure, MS therapy consists primarily of supportive care and symptomatic management, which may generate substantial direct costs. Management of multiple sclerosis has evolved in recent years, due in part to the availability of first generation and newer disease modifying therapies (DMT) that are immunomodulating with improving efficacy, convenience, and higher associated cost.[3,4] However, these newer DMT's with improved clinical benefits are often associated with adverse events (AEs) that are uncommon, but significant, such as progressive multifocal leukoencephalopathy (PML) or cardiac arrhythmias.[5] Glatiramer acetate is the most frequently prescribed DMT for MS, with an efficacy, safety, and tolerability profile backed by over two decades of real-world and clinical data.[6]

Teva's glatiramer acetate (Copaxone®) is a first generation DMT approved in 1996 to treat multiple sclerosis. It has quickly proved effective, popular and a mainstay of first line treatment among healthcare professionals and patients, gaining a reputation for turning multiple sclerosis into a manageable chronic disease.[7,8] Glatiramer acetate is considered a high-cost specialty drug. Specialty drugs are typically high price products used to treat rare, complex conditions with characteristics that may impede generic substitution or interchangeability.[8] Branded glatiramer acetate (Copaxone®) has increased in price by 1000 percent and now costs approximately $7,000 per month/$88,000 per year.[10]

Payers encourage the use of generic drugs to lower total drug spending with generic drugs representing 89% of all prescriptions.[11] This can be achieved by increasing management utilization

of branded drugs such as prior authorization or step therapy, leveraging mandatory generic auto-substitution pharmacy switches or offering lower patient copayment on generic drugs.[12] Generic price competition has historically been a successful strategy for lowering prescription drug prices in the United States.[13] Specialty drugs, including injectables and generics may be an exception due their use in complex situations like critical care, cancer, and autoimmune disease due to higher escalating price increases that drive up cost.[14] In addition, pharmaceutical manufacturers differ in how they approach their pricing strategies, both for a new generic launch or for the defense of a brand name drug. As a result, the presence of pre-existing or re-negotiated contracts may create financial incentives (spread compensation) for a payer to stay with the branded drug for a longer time, rather than automatically switch to the new generic without the appropriate financial incentives[15].

In April of 2015, the FDA approved the first fully AP substitutable generic version of the glatiramer acetate called Glatopa in the United States.[16] As the first U.S. generic manufacturer of glatiramer acetate, Sandoz/Momenta launched the 20 mg generic formulation in June 2015 at a 15% discount to the wholesale acquisition (WAC) price of the brand-name Copaxone.[17] In October 2017, Mylan received Food and Drug Administration (FDA) approval of a second 20 mg generic version and the first 40 mg generic version of Teva's multiple sclerosis medicine Copaxone including pricing both at a 30% discount.[18] Subsequently, Sandoz/Momenta received approval on a 40 mg generic version of Teva's Copaxone in February 2018 matching the Mylan market pricing approach.[19] In June 2018, Mylan further reduced their WAC price discount compared to Teva's Copaxone by approximately 66% or a flat $1,950 per month acquisition cost.[20] As a result, Teva and Sandoz are likely to offer additional discounts or rebates to customers in an attempt match Mylan's pricing out of competitive pressure in order avoid losing formulary status or market share. Whether these negotiated discounts or rebates will be passed on to patients at pharmacy point of

sale points or withheld for insurer/pharmacy benefit manager profit remains to be determined.

Little is known about glatiramer acetate utilization in the treatment of patients with multiple sclerosis among insurers after expiration of market exclusivity for the brand-name medication (Copaxone®). In this study, we aim to examine trends in utilization and management among insurers associated with branded versus generic glatiramer acetate availability.

## METHODS

We conducted a retrospective analysis of de-identified prescription pharmacy claims and eligibility data extracted for the period October 1, 2014 – January 31, 2019 using Symphony Health Integrated Dataverse® claims data identifying Copaxone®, Glatopa®, and Mylan Glatiramer Acetate National Drug Code (NDC) numbers using final approved and dispensed prescription fills in patients with multiple sclerosis. To compare different formulation quantities of medication, fills were standardized to represent a single month's glatiramer acetate supply (30 day) for the recommended dose for relapsing remitting multiple sclerosis (20 mg/day and 40 mg three times a week) and aggregated.

Our primary aim was to understand shifts or trends in treatment usage from brand to generic glatiramer acetate agents over the study period. We calculated the market share of glatiramer acetate drugs over time among the generic option relative to brand for therapy. Uptake of generic glatiramer acetate was estimated as the percentage of all glatiramer acetate fills for which the generic product was dispensed relative to brand. Two forecasting growth charts were constructed to predict future uptake growth for glatiramer acetate within the Commercial, Medicare, and Medicaid insurance groups. Branded and generic growth is calculated using a fixed percentage change each month based on the observed rate each monthly period from October 2014 to January 2019, plus projected another 11 months for the brand.

Secondary analyses compared the mean monthly patient out of pocket costs across the three payment types. In addition, we examined the percentage of claims receiving prescription assistance either from a manufacturer copayment program or foundational assistance that effectively reduces or zero's patient out-of-pocket expense.

The study was exempt from institutional review board review, as only a limited dataset was accessed in full compliance with the Health Insurance Portability and Accountability Act of 1996.

## RESULTS

From October 2014 to January 2019, 111,906 patients with multiple sclerosis were prescribed glatiramer acetate. As shown in Table 1, patient demographics were consistent with disease epidemiology. Most patients were female (77%) between the age of 31 – 60 (67%) with a similar geographic distribution. Primary insurance coverage was 63.2% Commercial, 25.4% Medicare, and 11.8% Medicaid. The primary prescriber of glatiramer acetate is a Neurologists (80%) and the vast majority of the 1,624,159 approved claims dispensed were through a specialty mail order pharmacy (87%).

Figure 1 shows the market trend of a consistent branded glatiramer acetate claim decline offset by a rapid uptake in generic glatiramer acetate (Glatopa® 20 mg) with its initial market entry and then remaining flat until launch of next generic entrant (Mylan 20/40 mg GA). Generic market share has continued to grow reaching an approximate 30% share of claims as of January 2019. Over the 52 months brand glatiramer acetate utilization has declined more than half at 56%, while generic claim volume has grown 155% over the past 16 months.

Figure 2 shows the relative claim volume by payment type for comparison. Among the payer types, Medicare has observed the greatest brand decline at 70% and the second highest generic utilization uptake at a 28% share. Commercial insurers have the greatest category claim

volume and greatest generic growth to a 26% share, while the brand has declined by 44%. Medicaid has had the lowest utilization volume and the greatest ratio of generic utilization among insurers at 45%.

Figure 3 shows projected or forecast branded utilization decline is greatest within the public insurance channel (Medicaid & Medicare). Medicare has the greatest forecast decline in brand utilization. Figure 4 reflects the projected generic utilization rate being greatest within the Commercial channel, while lowest in Medicaid.

Table 2 compares mean monthly patient out-of-pocket (OOP) costs for glatiramer acetate versions between Commercial, Medicare, and Medicaid insurers. Medicare has the highest patient cost share among insurers with both branded and generic glatiramer acetate having the highest mean OOP cost ($403 vs $330). Lower mean patient out-of-pocket costs are generally observed with generic glatiramer acetate options based upon monthly medication fulfilment. Medicaid has the lowest cost share among the three insurer types. Across all payment types, generics offer approximately a 20% discount to the brand in patient out of pocket costs. Manufacturer copay coupon or foundational assistance is also provided for both brand and generic glatiramer acetate to assist with patient affordability. A greater degree or percent of assistance for $0 patient pay is observed within Medicaid, while Medicare patients also have benefited from foundational assistance and Commercial patients utilize manufacture copay coupons, which appears higher with generics than brand.

## DISCUSSION

Switching branded to generic medications has been a common cost containment measure among insurers.[21] Brand to generic switching is also common place across many therapeutic areas. In this retrospective, observational study of brand versus generic glatiramer acetate (GA) utilization among various insure types over 52 months, we found that generic utilization is occurring, but at a

much slower rate and still evolving among insurers. In our analysis there is still a disproportionally greater utilization of branded GA versus the generic glatiramer acetate across all insurer types, although it is declining over time. This preference for the brand may reflect historical brand loyalty or a lack of provider, patient, or insurer incentive to change to the generic unless by choice or select insurer mandate.[22] The decline in branded glatiramer acetate does not appear to be offset by the degree of increasing generic utilization, so it may be indicative that patients may be switching to other branded DMT therapies. In addition, standard generic switch models of brand conversion rely on mandatory generic auto-substitution by pharmacists, which does not appear to be occurring.[23] However, increasing generic utilization over the past 16 months has improved dramatically with the additional generic introduction of Mylan's glatiramer acetate at its significant discounted list price. The overall increased market utilization of generic glatiramer acetate appears to be consistent across insurers and the utilization trend appears to be continuing through at least the first month of the new 2019 benefit cycle. This may be indicative of changes in benefit design or formulary administration favoring greater preferred generics utilization that assists in controlling drug costs benefiting insurers, providers, and patients.

Healthcare benefit policies are continuously adjusted to improve value relative to quality healthcare delivery.[24] This can result in more costs being shifted to the beneficiaries, raising issues in affordability especially for the high cost specialty pharmacy category multiple sclerosis disease modifying therapies. These cost shifts can include higher yearly premium increases, rising deductible limits or implementation of copay accumulator programs, greater utilization of coinsurance requiring beneficiaries to pay a greater percentage of the full cost of a drug, and benefit design changes that may eliminate coverage of a drug or move a drug from a lower price tier to a higher one including generic drugs normally on the less expensive tier 1 or 2, to the much more expensive 4$^{th}$ or 5$^{th}$ specialty tiers.[25] This effectively eliminates any preferred drug advantage

between a generic vs brand option in a category like specialty multiple sclerosis drugs and requires patients to share a higher cost of these medications. It forces patients to pay increased out-of-pocket (OOP) costs for important specialty drugs that likely have no medically comparable alternatives for treating a serious condition cost effectively.[26] Patient OOP's are a key lever in product decision making and selection as many insurance beneficiaries are on fixed incomes such as retired or disabled Medicare patients, low income/uninsured Medicaid participants, or even middle class Commercial lives with low annual per capita incomes where high out-of-pocket health care costs can pose a challenge in those with significant medical needs that are having to pay more for healthcare delivery. Thus, the use of lower cost generic drugs would seem to make more sense from a patient affordability or economic perspective.

Economics or financial incentives may also be a key influencer in insurer decision regarding preferred brand or generic utilization.[27] Insurers may be motivated to shift financial risk exposure to the patient or improve internal operating margins. This influence can create misaligned incentives whereby insurers or their pharmacy benefit managers (PBM) structure benefit design based on self-benefiting financial profit motives relative to manufacturer negotiated preferred product formulary tier positions that lead to greater retained rebates and discounts paid for insurers. In theory, these discounts or formulary structures should benefit patient product access or affordability directly at a pharmacy point of sale where a prescription is dispensed leading to both lower patient OOP's and pharmacy drug costs. Unfortunately, most patients pay their out-of-pocket costs based on the list price of the drug, not on the discounted price given by the drug company. As a result, insurers may have incentives to continue using an expensive specialty branded drug like Copaxone® instead of a generic simply based upon the economics. To address both high costs and access restrictions to all available multiple sclerosis treatments, greater transparency and financial disclosures between policy makers, insures, and pharmaceutical companies are required. However,

for commercial patients, high out-of-pocket cost shifts can also be addressed by drug manufactures in the form of copay assistance cards that manufacturers provide to patients in order increase the utilization of branded drugs despite the cost. These copay coupons or vouchers work by paying the patient's required portion of payment and could also explain why branded glatiramer acetate is used disproportionately to the generic.

Public insurers like Medicare, created to increase access to prescription drug treatment among beneficiaries, may also shift costs of specialty drugs to beneficiaries. Medicare plans, which are administered by the same Commercial insurers and PBMs can charge between 25% and 33% coinsurance for specialty tier drugs before enrollees reach the coverage gap or "doughnut hole" where they have paid anywhere for 25-45% of the cost of their drugs. Once their total out-of-pocket spending exceeds an annual threshold of $5,100 in 2019, enrollees pay 5% of the total drug costs above the catastrophic coverage threshold.[28] As a result, Medicare beneficiaries may pay more for the brand in theory, but secondary insurance obtained as part of a retirement benefit or prescription assistance programs from foundations can cover or offset the higher monthly cost of using a brand. This would explain why brand utilization is still dominate in our study. The importance of secondary assistance is captured in our data analysis by the observation of a significant drop in brand utilization in second quarter 2016, when the Department of Health and Human Services Office of Inspector General (OIG) issued an OIG Advisory opinion stating that charity prescription assistance programs (PAP) cannot be supported through drug manufacturer donor (or its affiliate) contributions that exerts any direct or indirect influence or control over the PAP due to perceived violation of Anti-Kickback Statutes. The elimination of donations by manufacturers and the closure of PAP charities resulted in a decrease in secondary assistance available to help pay for the higher costing brand. As a result, the beneficiary cost shift not only helps explain the dramatic drop in brand utilization but also may explain the more recent increase

in generic utilization simply based upon affordability for some patients. Medicare patient out-of-pocket costs in general for specialty products are higher for the brand compared to a less expensive generic alternative.

In our analysis, Medicaid had the lowest utilization of either brand or generic GA compared to either Commercial or Medicare payment types. As stated previously, Medicaid provides health coverage for some low-income and uninsured individuals or nonelderly adults that are the least likely to be able to afford expensive specialty drugs. Oversight by the Department of Health and Human Services requires states to provide drugs to Medicaid beneficiaries without excluding even these high cost specialty therapies. However, Medicaid pays some of the lowest costs for pharmaceuticals as Medicaid plans receive supplemental rebates from manufacturers to lower government spending on prescription drugs. This allows states to create a preferred drug list encouraging physician to only prescribe therapies on that list, which are often more affordable and have the greatest negotiated supplemental rebates provided by manufacturers. Although prior authorization normally is utilized to manage high cost drugs by encouraging generics or excluding non-preferred tier drugs, states are almost always required to provide access to drugs from manufacturers that have signed a rebate agreement with the state. This allows brand manufacturers to not only compete on price with generics, but also gain preferred coverage status and higher potential utilization as seen in our analysis. Even with healthcare reform expanding Medicaid eligibility in many states thereby improving access to MS treatments, the high cost of MS DMTs can still be prohibitive even if supported by prescription assistance programs that may even assist in covering costs of high risk insurance plans or even elderly patients Medicare premiums if eligible.

Considering generic glatiramer has been availability since 2015, decreased usage may reflect delayed formulary inclusion because of benefit design negotiations cycles or insufficient

stakeholder motivation for action either from an economic, clinical, or behavioral perspective. Despite obvious lower list prices with generics and the potential impact of direct multiple sclerosis pharmacy cost reductions and patient OOPs, some stakeholders may harbor clinical reservations or concerns about using these newer generic options in an immune mediated condition without more patient exposure experience or until insurer incentives are employed that mandate generic first use or incentivize pharmacy mediated auto-substitution. Either should be achieved through an aligned process of strong insurer incentives to drive generic utilization via standard benefit design and formulary management, improved communication between payers, physicians, pharmacists, and patients on generic advantage to decrease healthcare costs, and educational initiatives to improve confidence and trust in generic use in multiple sclerosis as a safe and effective alternative to the brand. It is critical to effectively manage patient outcomes and associated costs by selecting and using the most cost-effective drugs for formulary inclusion with the appropriate utilization management incentives to drive usage.

The strength of this study is our ability to report changes in utilization patterns of brand versus generic glatiramer acetate over 52 months inclusive of two generic entrants. However, several limitations are warranted for consideration. First, this claims data set does not identify intent of medication prescribing or usage by either physician or patient. Improved data reporting and analysis could be improved by factoring prescriber/patient longitudinal information to more accurately show insights on claim trends and volume. Second, the Symphony Health Integrated Dataverse® claims data set is a blend of captured adjudicated pharmacy life cycle claims (43%), final pharmacy non-life cycle claims that are only report final transactional status (51%), and a small proportion of medical benefit claims (6%). As a result, not all data sets or fields are available thus limiting depth of analysis and basis for categorization as an un-projected data set.

# CONCLUSION

The purpose of this study was to examine whether insurance type affected the rate of utilization uptake of generic glatiramer acetate over 52 months inclusive of FDA approval of these new low-cost options for multiple sclerosis treatment. The study revealed that utilization of generic glatiramer acetate has been limited among insurers but has been increasing over the past sixteen months as more generic GA options are available and price competition increases. Generic uptake is projected to increase across all insurer types. A recent increase in generic utilization over the past five months is indicative of a changing benefit design and reflective of 2019 open enrollment and in anticipation/execution of a new health insurance coverage cycle. Lower patient out-of-pocket costs and generic preferred formulary positioning will drive uptake rates for those with the greatest cost shift risk. Patients in our analysis had higher out-of-pocket costs when using the brand versus the generic option.

**Table 1: Baseline descriptors of pharmacy claims data set for glatiramer acetate from October 2014 through January 2019**

| ***Patient Characteristics*** *(n=111,906)* | ***n*** | ***%*** |
|---|---|---|
| **Sex** | | |
| **Female** | **86,283** | **77.10** |
| **Male** | **25,500** | **22.79** |
| **Other** | **123** | **0.11** |
| **Age Distribution** | | |
| **0 - 10** | **18** | **0.02** |
| **11 - 20** | **627** | **0.56** |
| **21 - 30** | **6,085** | **5.44** |
| **31 - 40** | **18,128** | **16.20** |
| **41 - 50** | **25,981** | **23.22** |
| **51 - 60** | **31,099** | **27.79** |
| **61 - 70** | **22,998** | **20.55** |
| **71 - 80** | **6,968** | **6.23** |
| **Unknown** | **2** | **0.00** |
| **Payer Type** | | |
| **Commercial/other** | **70,725** | **63.20** |
| **Medicare** | **28,442** | **25.42** |
| **Medicaid** | **12,739** | **11.38** |
| **Geographic Region** | | |
| **Northeast** | **26,237** | **23.45** |
| **Midwest** | **27,010** | **24.14** |
| **South** | **36,124** | **32.28** |
| **West** | **21,494** | **19.21** |
| **Other** | **1041** | **0.93** |

| ***Claim Characteristic*** *(n=1,624,159)* | ***n*** | ***%*** |
|---|---|---|
| **Pharmacy Type** | | |
| **Mail Order** | **1,408,597** | **86.73** |
| **Retail** | **140,636** | **8.66** |
| **Non-retail** | **65,434** | **4.03** |
| **Specialty** | **9,492** | **0.58** |
| **Physician Specialty** | | |
| **Neurology** | **1,290,990** | **79.49** |
| **Neurophysiology, Clinical** | **73,198** | **4.51** |
| **Family Practice** | **63,385** | **3.90** |
| **Family Medicine** | **55,459** | **3.41** |
| **Internal Medicine** | **34,263** | **2.11** |
| **Other** | **106,864** | **6.57** |

**Figure 1:** Over the course of 52 months branded glatiramer acetate has been declining, while generic utilization has increase based upon new market entrant launches and market price adjustments. Branded glatiramer acetate utilization has declined 56%, while generic claim volume has grown 155% over the past 16 months. The decline in branded utilization may be contributed to generic utilization, switches to other MS DMT products, or treatment termination.

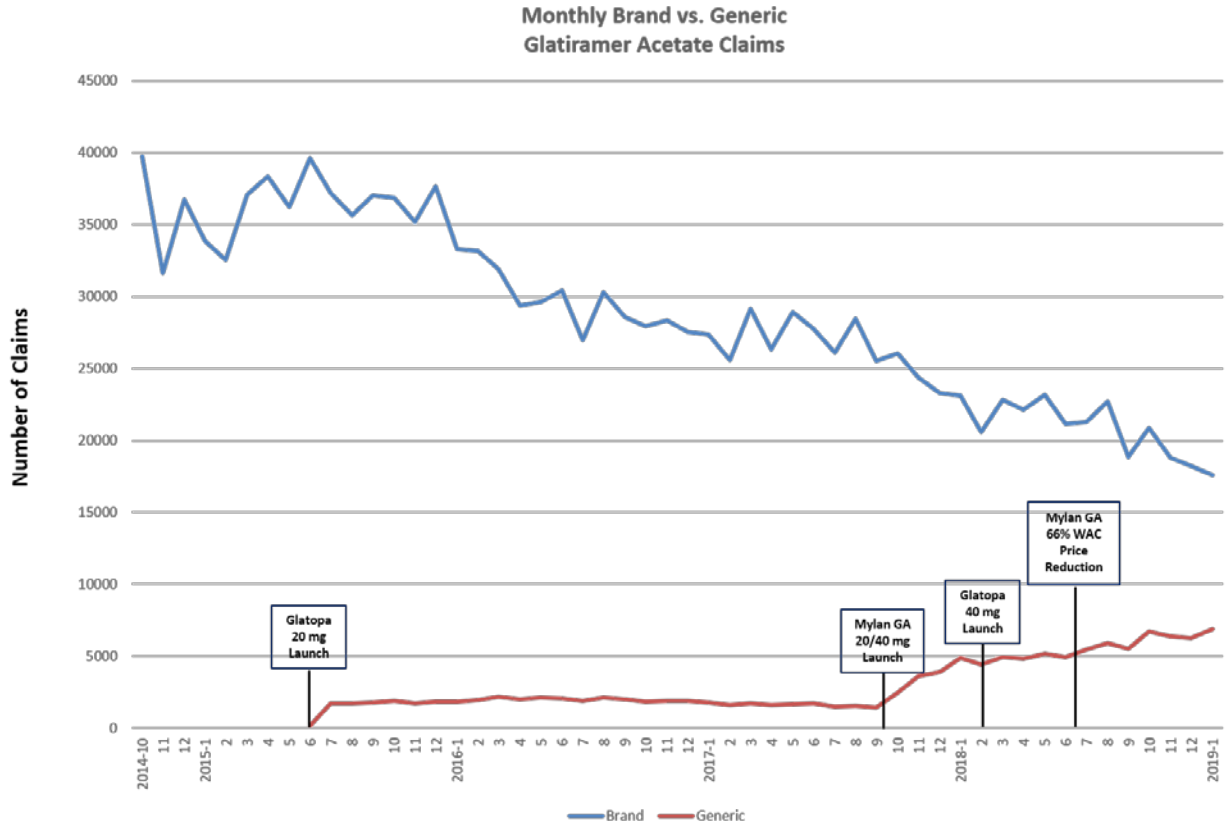


**Figure 2:** Bar chart depiction of monthly brand versus generic glatiramer acetate claim volume by primary insurer type. Commercially insured accounts for the greatest volume of both brand and generic utilization followed by Medicare, while Medicaid has the lowest utilization volume.

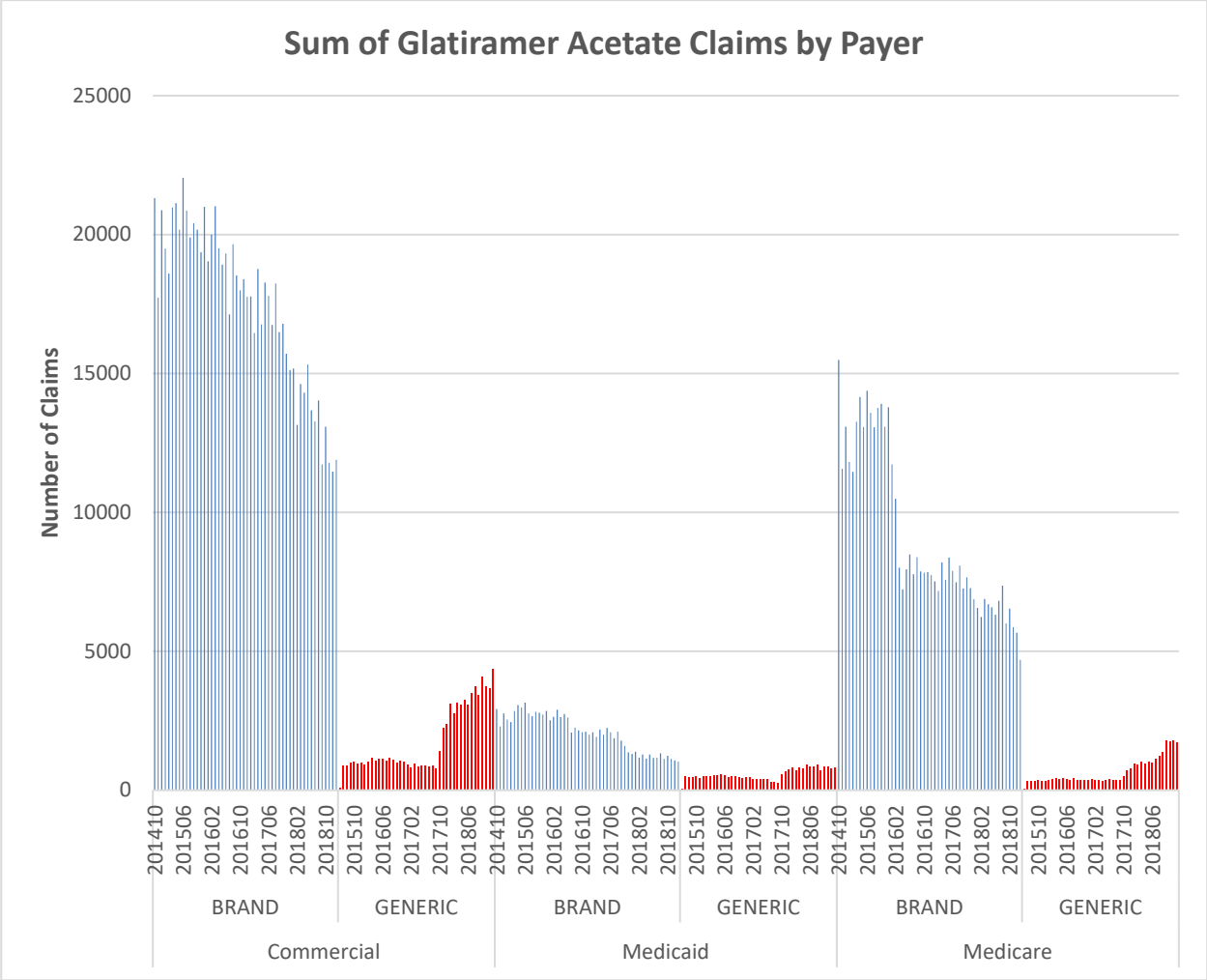


**Figure 3:** Trends in brand and generic glatiramer acetate utilization from October 2014 – January 2019 including projection through the next eleven months to December 2019. The projected percent change decline in brand use is lowest within the Medicare channel, while greatest in Medicaid. Generic utilization rate is greatest within the Medicare channel, while lowest in Medicaid.

**Table 2:** Table comparing mean monthly patient out-of-pocket (OOP) costs between Commercial, Medicare, and Medicaid insurers. Greatest patient cost share is associated with branded glatiramer acetate use and highest within the Medicare channel where higher coinsurance is predominant. Lower patient out-of-pocket costs are observed with generic glatiramer acetate options based upon monthly medication fulfilment. Medicaid has the lowest cost share among the three insurer types, but also has the largest proportions of patients receiving prescription assistance. All insurer types have a proportion of patients receiving prescription assistance.

| | Share of $0 Patient Pay | Mean Monthly OOP | Minimum OOP | Maximum OOP |
|---|---|---|---|---|
| **Commercial** | | | | |
| **Copaxone** | 13% | $300 | $0 | $9,279 |
| **Glatopa** | 43% | $201 | $0 | $6,988 |
| **Mylan GA** | 23% | $224 | $0 | $6,988 |
| **Medicare** | | | | |
| **Copaxone** | 21% | $403 | $0 | $9,273 |
| **Glatopa** | 38% | $339 | $0 | $3,900 |
| **Mylan GA** | 32% | $317 | $0 | $3,986 |
| **Medicaid** | | | | |
| **Copaxone** | 34% | $80 | $0 | $7,003 |
| **Glatopa** | 45% | $3 | $0 | $1845 |
| **Mylan GA** | 47% | $16 | $0 | $4,499 |

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# APPENDIX

**Table 3: Symphony Health -Integrated Dataverse® True Benefit Design de-identified claims data set fields licensed by Pfizer Inc.**

| ColumnName | ColID | DataType |
|---|---|---|
| PATIENT_ID | 1 | VARCHAR2 (20 Byte) |
| CLUSTER_ID | 2 | VARCHAR2 (61 Byte) |
| RX_ORDER | 3 | NUMBER |
| YEAR_MONTH | 4 | VARCHAR2 (6 Byte) 'YYYYMM' |
| FLAG_LIFE | 5 | VARCHAR2 (14 Byte) |
| PHARMACY_TYPE | 6 | VARCHAR2 (30 Byte) |
| PATIENT_AGE_GRP | 7 | VARCHAR2 (7 Byte) |
| PATIENT_GENDER | 8 | VARCHAR2 (6 Byte) |
| INITIAL_PRODUCT | 9 | VARCHAR2 (60 Byte) |
| INITIAL_DRUG | 10 | VARCHAR2 (60 Byte) |
| INITIAL_GENERIC | 11 | VARCHAR2 (60 Byte) |
| INITIAL_BRAND_GENERIC_IND | 12 | CHAR (1 Byte) |
| INITIAL_PRODUCT_STRENGTH | 13 | VARCHAR2 (10 Byte) |
| INITIAL_DRUG_QTY | 14 | NUMBER |
| INITIAL_PRODUCT_FORM | 15 | VARCHAR2 (40 Byte) |
| INITIAL_NDC | 16 | CHAR (11 Byte) |
| INITIAL_DAYS_SUPPLY_GROUP | 17 | VARCHAR2 (7 Byte) |
| INTERIM_PRODUCT | 18 | VARCHAR2 (60 Byte) |
| INTERIM_DRUG | 19 | VARCHAR2 (60 Byte) |
| INTERIM_GENERIC | 20 | VARCHAR2 (60 Byte) |
| INTERIM_BRAND_GENERIC_IND | 21 | CHAR (1 Byte) |
| INTERIM_PRODUCT_STRENGTH | 22 | VARCHAR2 (10 Byte) |
| INTERIM_DRUG_QTY | 23 | NUMBER |
| INTERIM_PRODUCT_FORM | 24 | VARCHAR2 (40 Byte) |
| INTERIM_NDC | 25 | CHAR (11 Byte) |
| INTERIM_DAYS_SUPPLY_GROUP | 26 | VARCHAR2 (7 Byte) |
| FINAL_PRODUCT | 27 | VARCHAR2 (60 Byte) |
| FINAL_DRUG | 28 | VARCHAR2 (60 Byte) |
| FINAL_GENERIC | 29 | VARCHAR2 (60 Byte) |
| FINAL_BRAND_GENERIC_IND | 30 | CHAR (1 Byte) |
| FINAL_PRODUCT_STRENGTH | 31 | VARCHAR2 (10 Byte) |
| FINAL_DRUG_QTY | 32 | NUMBER |
| FINAL_PRODUCT_FORM | 33 | VARCHAR2 (40 Byte) |
| FINAL_NDC | 34 | CHAR (11 Byte) |
| FINAL_DAYS_SUPPLY_GROUP | 35 | VARCHAR2 (7 Byte) |
| SUBSTITUTION_FLAG | 36 | CHAR (1 Byte) |
| MULTI_PAYER_FLAG | 37 | CHAR (1 Byte) |

| | | |
|---|---|---|
| COPAY_CARD_FLAG | 38 | CHAR (1 Byte) |
| INITIAL_PAYMENT_TYPE | 39 | VARCHAR2 (10 Byte) |
| INITIAL_BADMIN_NAME | 40 | VARCHAR2 (250 Byte) |
| INITIAL_MCO_NAME | 41 | VARCHAR2 (250 Byte) |
| INITIAL_PLAN_NAME | 42 | VARCHAR2 (250 Byte) |
| INITIAL_PLAN_TYPE | 43 | VARCHAR2 (10 Byte) |
| INITIAL_PLAN_SUB_TYPE | 44 | VARCHAR2 (10 Byte) |
| INTERIM_PAYMENT_TYPE | 45 | VARCHAR2 (10 Byte) |
| INTERIM_BADMIN_NAME | 46 | VARCHAR2 (250 Byte) |
| INTERIM_MCO_NAME | 47 | VARCHAR2 (250 Byte) |
| INTERIM_PLAN_NAME | 48 | VARCHAR2 (250 Byte) |
| INTERIM_PLAN_TYPE | 49 | VARCHAR2 (10 Byte) |
| INTERIM_PLAN_SUB_TYPE | 50 | VARCHAR2 (10 Byte) |
| FINAL_PAYMENT_TYPE | 51 | VARCHAR2 (10 Byte) |
| FINAL_BADMIN_NAME | 52 | VARCHAR2 (250 Byte) |
| FINAL_MCO_NAME | 53 | VARCHAR2 (250 Byte) |
| FINAL_PLAN_NAME | 54 | VARCHAR2 (250 Byte) |
| FINAL_PLAN_TYPE | 55 | VARCHAR2 (10 Byte) |
| FINAL_PLAN_SUB_TYPE | 56 | VARCHAR2 (10 Byte) |
| INITIAL_CLAIM_STATUS | 57 | CHAR (8 Byte) |
| INITIAL_REJECT_CDE | 58 | VARCHAR2 (10 Byte) |
| INITIAL_REJECT_REASON | 59 | VARCHAR2 (100 Byte) |
| INITIAL_REJECT_GROUP | 60 | VARCHAR2 (60 Byte) |
| INITIAL_MACRO_REJ_GROUP | 61 | VARCHAR2 (13 Byte) |
| INITIAL_SOB | 62 | VARCHAR2 (13 Byte) |
| INTERIM_CLAIM_STATUS | 63 | CHAR (8 Byte) |
| INTERIM_REJECT_CDE | 64 | VARCHAR2 (10 Byte) |
| INTERIM_REJECT_REASON | 65 | VARCHAR2 (100 Byte) |
| INTERIM_REJECT_GROUP | 66 | VARCHAR2 (60 Byte) |
| INTERIM_MACRO_REJ_GROUP | 67 | VARCHAR2 (13 Byte) |
| INTERIM_SOB | 68 | VARCHAR2 (13 Byte) |
| FINAL_CLAIM_STATUS | 69 | CHAR (8 Byte) |
| FINAL_REJECT_CDE | 70 | VARCHAR2 (10 Byte) |
| FINAL_REJECT_REASON | 71 | VARCHAR2 (100 Byte) |
| FINAL_REJECT_GROUP | 72 | VARCHAR2 (60 Byte) |
| FINAL_MACRO_REJ_GROUP | 73 | VARCHAR2 (13 Byte) |
| FINAL_SOB | 74 | VARCHAR2 (13 Byte) |
| INTERIM_TIME_TO_FILL | 75 | NUMBER |
| FINAL_TIME_TO_FILL | 76 | NUMBER |
| MEDICARE_ELIGIBILITY | 77 | VARCHAR2 (11 Byte) |
| INITIAL_APP_CLAIM_CNT | 78 | NUMBER |
| INITIAL_REJ_CLAIM_CNT | 79 | NUMBER |
| NN_INITIAL_APP_CLAIM_CNT | 80 | NUMBER |

| | | |
|---|---|---|
| NNZ_INITIAL_APP_CLAIM_CNT | 81 | NUMBER |
| INITIAL_APP_PAT_PAY | 82 | NUMBER |
| INITIAL_PLAN_APP_PLAN_PAY | 83 | NUMBER |
| INTERIM_APP_CLAIM_CNT | 84 | NUMBER |
| INTERIM_REJ_CLAIM_CNT | 85 | NUMBER |
| INTERIM_REV_CLAIM_CNT | 86 | NUMBER |
| INTERIM_PLAN_APP_CLAIM_CNT | 87 | NUMBER |
| NN_INTERIM_APP_CLAIM_CNT | 88 | NUMBER |
| NNZ_INTERIM_APP_CLAIM_CNT | 89 | NUMBER |
| NN_INTERIM_REV_CLAIM_CNT | 90 | NUMBER |
| NNZ_INTERIM_REV_CLAIM_CNT | 91 | NUMBER |
| NN_INTRM_PLN_APP_CLM_CNT | 92 | NUMBER |
| NNZ_INTRM_PLN_APP_CLM_CNT | 93 | NUMBER |
| INTERIM_APP_PAT_PAY | 94 | NUMBER |
| INTERIM_REV_PAT_PAY | 95 | NUMBER |
| INTERIM_PLAN_APP_PAT_PAY | 96 | NUMBER |
| INTERIM_PLAN_APP_PLAN_PAY | 97 | NUMBER |
| FINAL_APP_CLAIM_CNT | 98 | NUMBER |
| FINAL_REJ_CLAIM_CNT | 99 | NUMBER |
| FINAL_REV_CLAIM_CNT | 100 | NUMBER |
| FINAL_PLAN_APP_CLAIM_CNT | 101 | NUMBER |
| NN_FINAL_APP_CLAIM_CNT | 102 | NUMBER |
| NNZ_FINAL_APP_CLAIM_CNT | 103 | NUMBER |
| NN_FINAL_REV_CLAIM_CNT | 104 | NUMBER |
| NNZ_FINAL_REV_CLAIM_CNT | 105 | NUMBER |
| NN_FINAL_PLN_APP_CLM_CNT | 106 | NUMBER |
| NNZ_FINAL_PLN_APP_CLM_CNT | 107 | NUMBER |
| FINAL_APP_PAT_PAY | 108 | NUMBER |
| FINAL_REV_PAT_PAY | 109 | NUMBER |
| FINAL_PLAN_APP_PAT_PAY | 110 | NUMBER |
| FINAL_PLAN_APP_PLAN_PAY | 111 | NUMBER |
| PRACTITIONER_ID | 112 | NUMBER (18) |
| PHYSICIAN_LAST_NAME | 113 | VARCHAR2 (60 Byte) |
| PHYSICIAN_FIRST_NAME | 114 | VARCHAR2 (25 Byte) |
| PHYSICIAN_ADDRESS | 115 | VARCHAR2 (100 Byte) |
| PHYSICIAN_CITY | 116 | VARCHAR2 (28 Byte) |
| PHYSICIAN_STATE_CODE | 117 | CHAR (2 Byte) |
| PHYSICIAN_ZIP_CODE | 118 | CHAR (5 Byte) |
| PHYSICIAN_SPECIALTY | 119 | VARCHAR2 (75 Byte) |
| AMA_NO_CONTACT | 120 | CHAR (1 Byte) |
| AMA_PDRP_FLAG | 121 | CHAR (1 Byte) |
| AMA_PDRP_DATE | 122 | DATE ('DD-MON-YY') |
| NPI | 123 | VARCHAR2 (10 Byte) |

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