Taylor & Francis
Taylor & Francis Group

Current Medical Research and Opinion

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icmo20

Treatment patterns following initiation of generic glatiramer acetate among patients with multiple sclerosis from two large real-world databases in the United States

Jessica K. Alexander, Rinat Ariely, Ying Wu, Erin Hulbert, Allison Bryant, Zhaohui Su, Michaela Vardi & Jyotsna Kasturi

To cite this article: Jessica K. Alexander, Rinat Ariely, Ying Wu, Erin Hulbert, Allison Bryant, Zhaohui Su, Michaela Vardi & Jyotsna Kasturi (2021): Treatment patterns following initiation of generic glatiramer acetate among patients with multiple sclerosis from two large real-world databases in the United States, Current Medical Research and Opinion, DOI: 10.1080/03007995.2021.1929135

To link to this article: https://doi.org/10.1080/03007995.2021.1929135

CURRENT MEDICAL RESEARCH AND OPINION
https://doi.org/10.1080/03007995.2021.1929135
Article ST-0029.R1/1929135

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Treatment patterns following initiation of generic glatiramer acetate among patients with multiple sclerosis from two large real-world databases in the United States

Jessica K. Alexander[a], Rinat Ariely[a], Ying Wu[a], Erin Hulbert[b], Allison Bryant[c], Zhaohui Su[c], Michaela Vardi[a] and Jyotsna Kasturi[a]

[a]Teva Pharmaceuticals, Frazer, PA, USA; [b]OptumInsight Inc., Eden Prairie, MN, USA; [c]OM1 Inc., Boston, MA, USA

ABSTRACT

Introduction: To better understand treatment patterns in US patients with multiple sclerosis (MS) initiating generic glatiramer acetate (GA), this study examined adherence, discontinuation and switching patterns from generic follow-on glatiramer acetate (FOGA) therapy in real-world patient cohorts.

Methods: Retrospective analyses utilized data from two large US databases (administrative claims and linked electronic medical records). Eligible adult MS patients had ≥1 pharmacy claim for FOGA during the identification period; the first FOGA claim was the index date. All analyses were descriptive; proportion of days covered (PDC) was calculated as a measure of adherence to FOGA during the follow-up period.

Results: The first cohort consisted of 95 patients, with 93.6% having a branded GA claim for Copaxone during the baseline period. Half these patients (48.4%) had high adherence to FOGA therapy (PDC: 0.8–1.0). Fifty-five patients (57.9%) initially discontinued FOGA with a mean persistence of 112 days. Of those who discontinued, 7.3% had no subsequent disease-modifying therapy (DMT), 30.9% restarted FOGA and 61.8% did not restart FOGA. The second cohort consisted of 1957 patients, with 63.8% having a branded GA claim for Copaxone during the baseline period and 33.5% were treatment naïve. The majority of patients (61.9%) had high adherence to FOGA therapy. A total of 1597 patients (81.6%) initially discontinued FOGA with a mean persistence of 93 days. Of those who discontinued, 55.8% switched to another DMT, 16.7% restarted FOGA and 37.5% had no subsequent DMT.

Conclusion: Adherence to FOGA therapy was reasonably high across cohorts; however, most patients discontinued their initial FOGA within four months of the index date and most switches from FOGA were to branded GA products.

ARTICLE HISTORY
Received 13 January 2021
Revised 2 May 2021
Accepted 10 May 2021

KEYWORDS
Relapsing multiple sclerosis; disease-modifying therapies; treatment discontinuation; adherence; switching

Introduction

Relapsing multiple sclerosis (RMS) is a chronic inflammatory demyelinating disease that progresses over a long period of time, eventually leading to neurological disability[1]. The overall goal of disease-modifying therapies (DMTs) in RMS is to decrease the number of relapses, thus minimizing progression of disability over time. In the past 10–15 years, several new DMTs have entered the market in the US, significantly increasing the treatment options for patients[2]. These DMTs vary greatly in terms of tolerability, mode and frequency of administration. However, their effectiveness may be limited due to poor rates of adherence and persistence as well as treatment discontinuation, especially since DMTs for RMS are intended for long-term use[3,4]. Rates of RMS treatment discontinuation and persistence have been found to vary widely across studies and reasons for discontinuing DMTs are not always well documented[5–11]. An improved understanding of patterns of treatment discontinuation and switching among RMS patients receiving licensed doses of DMTs is critical given the potential impact of such factors on decision-making in clinical practice.

Glatiramer acetate (GA; Copaxone[i]) is indicated for the treatment of RMS, including clinically isolated syndrome, relapsing–remitting disease and active secondary progressive disease; it was initially approved by the Food and Drug Administration (FDA) in 1996[4]. Glatopa[ii] was the first FDA-approved generic follow-on glatiramer acetate (FOGA) product for MS patients, available in April 2015[5]. According to the FDA, generic drugs are the same as branded drugs in dosage, safety, strength, how the drug is taken, quality, performance and intended use[6]. Generic drugs may, however, differ in certain other characteristics, such as packaging, excipients and storage conditions, which can affect an individual patient's treatment experience[7]. In particular, there are compositional differences between branded GA and FOGA that may be associated with immunogenic and clinical outcomes[12].

CONTACT Jessica K. Alexander Jessica.Alexander@tevapharm.com Teva Pharmaceuticals – Medical Affairs, 111 Teva Way, Frazier, PA 881181, USA

Consequent to these differences, assessing adherence and persistence data in users of FOGA is timely and necessary to inform optimal clinical treatment decisions when different choices exist, including branded GA (daily 20 mg/mL or three times weekly 40 mg/mL) and other DMTs. To better understand treatment patterns in US patients initiating generic GA, we undertook descriptive analyses using data derived from two large real-world databases. The purpose of this study was to measure adherence and persistence to, discontinuation of and switching patterns from FOGA among patients who had previously been treated with a DMT or were treatment naïve.

Methods

This retrospective observational study utilized data from two different real-world databases representing patients with a wide age and geographic distribution in the US: administrative claims from the Optum Research Database (ORD; OptumInsight Inc., Eden Prairie, MN, USA) and linked administrative claims and electronic medical records (EMRs) from the OM1 Real-World Data Cloud (OM1 Inc., Boston, MA, USA). Both databases are fully de-identified and compliant with the Health Insurance Portability and Accountability Act (HIPAA) and this research was exempt from institutional review board (IRB) review.

Group 1 (ORD) study design

Group 1 utilized administrative claims data for Medicare Advantage enrollees with Part D (MAPD) coverage from the ORD. The ORD is a research database that contains eligibility-controlled paid medical and pharmacy claims. MS patients on disability are automatically enrolled in Medicare after about a year and the ORD includes MS patients under 65 years of age with MAPD[13]. MAPD members in the ORD are geographically diverse with age and gender distributions that are similar to the overall US Medicare Part D patient population.

The ORD analysis consisted of MS patients with $\geq$1 pharmacy claim for FOGA (i.e. Glatopa 20 mg/mL) during the identification period between 1 June 2015 and 30 June 2016; the date of the first FOGA claim was denoted as the index date. In order to be included in the study, patients must have been at least 18 years old at the index date and had continuous enrollment in the health plan 6 months before (baseline period) and $\geq$3 months after (follow-up period) the index date. For purposes of inclusion, patients were not required to have one or more diagnosis codes for MS; it was presumed based on exposure to FOGA (which is only indicated for the treatment of RMS). Exposure to branded GA during the pre-index/baseline period was also not required. Observation extended through the earlier of a patient's disenrollment from the health plan or 31 December 2016, whichever came sooner. Patients with missing or unknown age, gender, insurance type or geographic region were excluded from the study sample.

Group 2 (OM1) study design

The second data source was the OM1 Real-World Data Cloud, a large, geographically representative US healthcare claims and EMR database, including medical and pharmacy claims with billing and coding history on inpatient and outpatient encounters from acute care facilities, ambulatory surgery centers and clinics.

Group 2 consisted of patients with $\geq$1 pharmacy claim or written prescription for FOGA during the identification period between 1 June 2015 and 30 September 2017 (the date of the first FOGA claim was also denoted as the index date). In order to be eligible for the study, patients must have been at least 18 years old at the index date. As with Group 1, patients were not required to have a diagnosis code for MS nor exposure to branded GA during the pre-index period. The pre-index (baseline) and post-index (follow-up) periods were of variable length and included all available patient data starting 1 January 2013 through the last encounter date (follow-up data available through 6 February 2018).

Study outcomes

As the objective of this study was to describe treatment patterns following initiation of FOGA among MS patients (not to compare the cohorts derived from different data sources), all analyses were descriptive in nature and no statistical tests were performed. These analyses were conducted separately for each cohort, with similar but not identical methodology.

The proportion of days covered (PDC), as a measure of adherence to FOGA therapy, was calculated by dividing the number of days on which medication was available (based on filled prescriptions) by the number of days between the index date and the end of the follow-up period (censored at the initial switch to another DMT)[14]. PDC was reported as a categorical measure stratified into five equal categories from 0.0 to 1.0. A PDC of 1.0 means 100% adherence, indicating the patient had claims at the appropriate times. Persistence with FOGA therapy was based on number of days from the index date to the earlier date of either therapy switch or discontinuation. Patients were considered persistent with FOGA if they remained on therapy in the follow-up period without a fill for another DMT and without a gap exceeding 60 days after the run-out date of the last observed claim for the FOGA therapy.

Discontinuation of FOGA was defined as a gap in therapy of at least 30 days (Group 1), 60 days (Group 2) or switch to another DMT. If patients did not experience discontinuation before the end of their follow-up period, they were considered ongoing. Restart was defined as an additional fill of FOGA after the discontinuation date. The first switch from FOGA to another DMT was evaluated post-index; switches to a second DMT were also evaluated if available.

Results

Group 1 (ORD)

A total of 95 MS patients were identified and included in the analysis. The mean age of the cohort was 60.7 years,

Table 1. Patient demographics for Group 1 (ORD).

Demographic	Group 1 (ORD) $N = 95$	
	N	%
Gender		
Female	72	75.8
Male	23	24.2
Age group		
18–34 years	0	0.0
35–44 years	8	8.4
45–54 years	19	20.0
55–64 years	30	31.6
65+ years	38	40.0
Geographic region		
Northeast	36	37.9
Midwest	16	16.8
South	28	29.5
West	15	15.8
Other	0	0.0
Charlson comorbidity score categories		
0	55	57.9
1–2	25	26.3
3–4	11	11.6
5+	4	4.2
Multiple sclerosis diagnosis	89	93.7
Duration of follow-up		
90–180 days	4	4.2
181–270 days	7	7.4
271–365 days	13	13.7
366+ days	71	74.7
	Mean	**SD**
Age (years)	60.7	10.6
Charlson comorbidity score	1.1	1.6
Duration of follow-up (days)	428.2	115.6

Abbreviation. SD, Standard deviation.

Table 2. FOGA adherence during the follow-up period.

PDC* category	Group 1 (ORD) $N = 95$	Group 2 (OM1) $N = 1137$
0.0 to <0.2	21 (22.1%)	76 (6.7%)
0.2 to <0.4	14 (14.7%)	124 (10.9%)
0.4 to <0.6	7 (7.4%)	116 (10.2%)
0.6 to <0.8	7 (7.4%)	117 (10.3%)
0.8 to ≤1.0	46 (48.4%)	704 (61.9%)

*Calculated by dividing the number of days on which medication was available (based on filled prescriptions) by the total number of days. A PDC of 1.0 indicates full adherence.

three-quarters were female (75.8%), the majority lived in either the Northeast (37.9%) or the South (29.5%) and had a Charlson comorbidity score of 0 (57.9%) (see Table 1). The mean duration of the follow-up period was 1.17 years. A total of 84 patients (88.4%) had a claim for branded GA 20 mg/mL (COP20) and five patients (5.3%) had a claim for branded GA 40 mg/mL (COP40) during the 6 month baseline period.

Approximately half of the patients (48.4%) had adherence to FOGA therapy (as measured by PDC) between 0.8 and 1.0 during the follow-up period (Table 2). Fifty-five patients (57.9%) were non-persistent with FOGA, either due to discontinuation without evidence of another therapy or due to switching to another therapy. The mean FOGA persistence of the total cohort was 241 (standard deviation [SD] = 184) days. Among the 40 patients remaining on FOGA, mean persistence was 412 (SD = 122) days, whereas among the 55 non-persistent patients, mean persistence was 112 (SD = 101) days.

Of the 55 patients who discontinued FOGA, 4 (7.3%) had no record of any subsequent DMT during follow-up, 17 (30.9%) restarted FOGA and 34 (61.8%) did not restart FOGA (Figure 1(A)). Forty-one patients (43.2%) initially switched to another DMT from FOGA; of these, 31 (75.6%) and 9 (22.0%) switched to COP20 and COP40, respectively, and 1 patient switched to teriflunomide (Figure 1(B)). Seven of these 41 patients then restarted FOGA.

Group 2 (OM1)

A total of 1957 MS patients who had a FOGA index date during the identification period were identified from the OM1 dataset. The average age of the cohort was 51.0 years, 74.8% were female and 76.0% had a Charlson comorbidity score of 0. The majority of the patients (55.1%) had commercial insurance and 24.3% were covered by Medicare (see Table 3). The median duration of the follow-up period was 1.36 years. A total of 655 patients (33.5%) had no record of another DMT (i.e. were treatment naïve) prior to their FOGA index date. Of the 1302 patients who had a DMT record prior to the index date, the most common prior DMTs were COP20 ($n = 1116$;

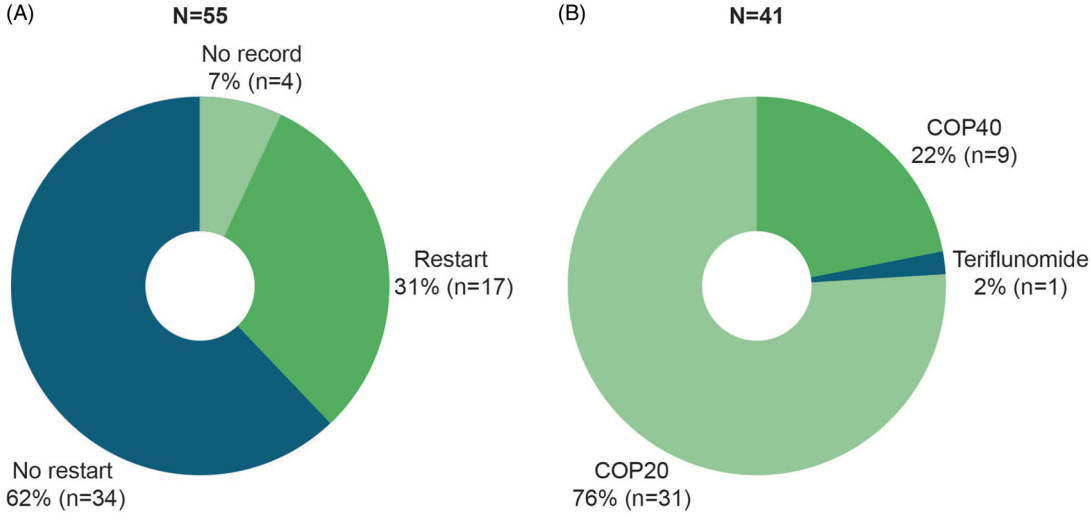


Figure 1. FOGA restarts (A) and initial switch medications (B) in Group 1 (ORD).
COP20: branded glatiramer acetate 20 mg/mL once daily; COP40: branded glatiramer acetate 40 mg/mL three times weekly; FOGA: follow-on glatiramer acetate.

Table 3. Patient demographics for Group 2 (OM1).

Demographic	Group 2 (OM1) $N = 1957$	
	N	%
Gender		
Female	1464	74.8
Male	493	25.2
Age group		
18–34 years	217	11.1
35–44 years	375	19.2
45–54 years	551	28.2
55–64 years	527	26.9
65+ years	287	14.7
Race		
Black	56	9.8
White	500	87.9
Other	13	2.3
Unknown	1388	70.9
Geographic region		
East North Central	309	16.1
East South Central	68	3.5
Middle Atlantic	342	17.8
Mountain	191	10.0
New England	125	6.5
Pacific	382	19.9
South Atlantic	230	12.0
West North Central	134	7.0
West South Central	137	7.1
Unknown	39	2.0
Charlson comorbidity score categories		
0	1488	76.0
1–2	350	17.9
3–4	82	4.2
5+	37	1.9
Multiple sclerosis diagnosis	1743	89.1
Insurance coverage		
Commercial	1079	55.1
Medicaid	146	7.5
Medicare	475	24.3
More than one insurance	102	5.2
Other/unknown	155	7.9
	Mean	**SD**
Age (years)	51.0	12.6
Charlson comorbidity score	0.5	1.1

Abbreviations. SD, Standard deviation; FOGA, Follow-on glatiramer acetate; PDC, Proportion of days covered.

85.7%) and COP40 ($n = 357$; 27.4%) during the 6 month baseline period (see Figure 2).

The majority of patients (61.9%) had adherence to FOGA therapy (as measured by PDC) between 0.8 and 1.0 during the follow-up period (see Table 2). Three hundred and sixty patients (18.4%) were persistent with FOGA (i.e. remained on treatment) compared to 1597 patients (81.6%) who discontinued. The mean FOGA persistence among the 1597 patients who discontinued was 93 (SD = 137) days.

Of the 1597 patients who initially discontinued FOGA, 267 (16.7%) restarted FOGA during the follow-up period and 599 (37.5%) had no record of any subsequent DMT; 891 patients (55.8%) switched to another DMT from FOGA (Figure 3). Of the patients who switched, 748 (84.0%) switched to either COP20 or COP40. Among the 267 patients who restarted FOGA during the follow-up period, 107 (40.0%) restarted after a gap in therapy of at least 60 days (no other DMT), 18 (6.7%) restarted after a gap and prior to another DMT switch, and 142 (53.2%) restarted after another DMT. Two hundred and eighty patients (31.4% of the 891 switchers) switched more than once (see Figure 3).

To understand the duration of FOGA treatment before switch, initial DMT switches from FOGA were calculated over 6 months, cumulatively, starting from switches that occurred within the first month. By 6 months, 77.7% ($n = 692$) of all initial switches had occurred, with 89.7% ($n = 621$) switching to either COP20 or COP40 (Figure 4(A)). Stratification by prior branded GA treatment during the baseline period (Figure 4(B)) demonstrated that initial FOGA discontinuation was higher for patients who had prior branded GA use (COP20: 83.7%; COP40: 88.7%; both COP20 and COP40: 89.3%) when compared to patients with no prior branded GA use (75.1%). Switches away from FOGA to any DMT occurred more frequently in patients with prior branded GA use compared to those with no prior use (53.2% versus

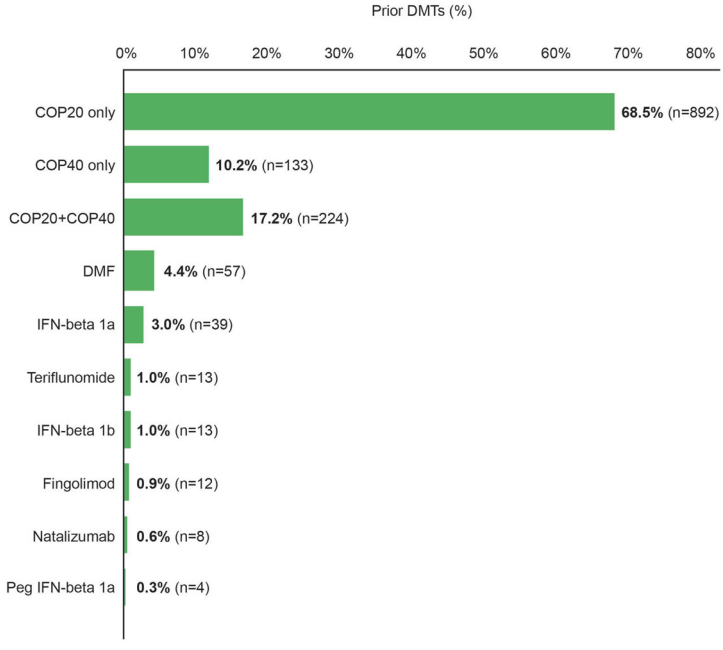


Figure 2. Pre-index date DMT use in Group 2 (OM1).
COP20: branded glatiramer acetate 20 mg/mL once daily; COP40: branded glatiramer acetate 40 mg/mL three times weekly; DMF: dimethyl fumarate; DMT: disease-modifying therapy; IFN: interferon.

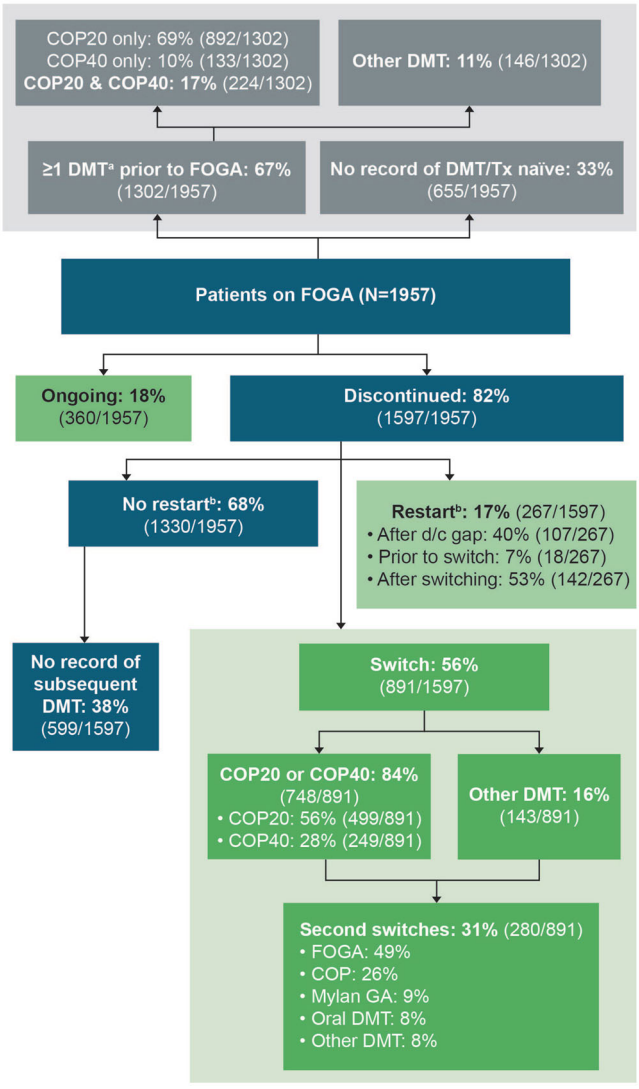


Figure 3. FOGA discontinuation, restarts and medication switching in Group 2 (OM1).
[a]Patient can be counted in multiple DMTs.
[b]Not mutually exclusive from the switch group.
COP20: branded glatiramer acetate 20 mg/mL once daily; COP40: branded glatiramer acetate 40 mg/mL three times weekly; d/c: discontinuation; DMT: disease-modifying therapy; FOGA: follow-on glatiramer acetate; Tx: treatment.

31.9%). Patients with prior branded GA experience showed reduced time to initial switch from FOGA (Figure 4(C)).

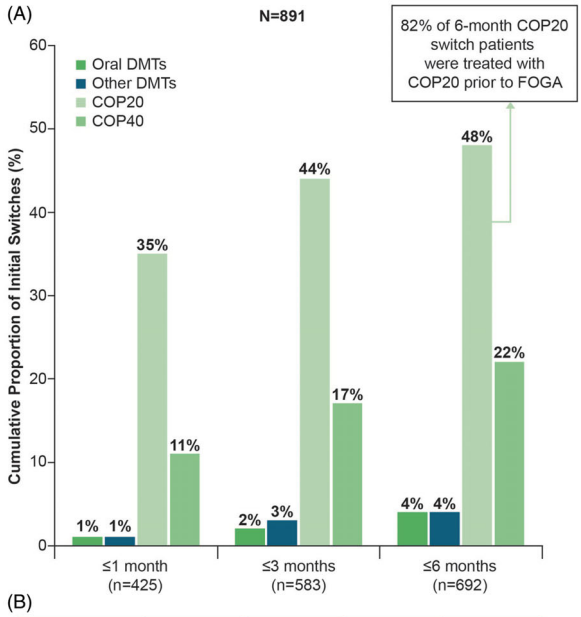
Discussion

With a focus on real-world data, the ORD (Group 1) and OM1 (Group 2) databases were utilized to describe treatment patterns and patient characteristics associated with the first FDA-approved generic DMT for RMS. Among patients who initiated FOGA, the majority were previously treated with branded COP20. Initial post-index adherence to FOGA was reasonably high for both cohorts, with a PDC of greater than or equal to 0.8 reported in 48% of Group 1 and 62% of Group 2 patients. Differences in the observation periods could account for the differences in PDC among the groups. Additionally, Group 1 was composed exclusively of MAPD patients; the lower adherence rate for this patient population may be worth further examination.

Poor persistence with initial FOGA therapy was apparent across both data sources, including Medicare and commercial patient populations. In Group 1, 58% of patients were non-persistent/discontinued FOGA, with a mean persistence of 112 days. Furthermore, three-quarters of the 41 patients who initially switched to another DMT switched to branded GA, primarily COP20. As only 22% of patients (9 of 41) initially switched to COP40, it appears unlikely that this switching behavior was driven by the ease of administration associated with the three times weekly 40 mg/mL formulation. In Group 2, 82% of all patients were non-persistent/discontinued FOGA therapy with a mean persistence of 93 days. In the discontinuation cohort, 56% switched to another DMT, 17% restarted FOGA and 38% discontinued with no record of any DMT in the follow-up period. At the initial switch, 84% switched to COP20 or COP40, whereas at the second (or subsequent) switch, 49% of switches were to FOGA. Although relatively few of these patients switched more than once, multiple switches between GA products (both branded and generic) warrants further research into the reasons for multiple switches and any associated clinical impact across DMTs. Additional research is also needed to understand the outcomes of patients who discontinued FOGA and had no record of subsequent DMTs, as these patients may be at risk for increased likelihood of relapse and disability progression.

Challenges in interpretation of these real-world data include the use of a retrospective study design and secondary use of data, which do not provide reasons for discontinuation or switching. Each database was sourced from different data (administrative claims and/or EMR) and there were some differences in methodology which could contribute to the minor differences seen in the results among cohorts. It is also the case that adherence and persistence were measured using available clinical and claims data, rather than from verifiable assessment of each patient's behavior. During the study period, the study medications were not included in the formularies[15], which may have had an effect on whether patients filled prescriptions or continued to use them. In addition, there was incomplete information on pharmacy claim reversals (transactions used by a pharmacy to reverse claims that were previously processed, including prescription abandonment, price checking, or substitution driven by physician/patient preference or co-pay amount) in the Group 2 analysis (Group 1 analysis only included paid claims). Although all known reversed FOGA index claim records and any subsequent reversed records were excluded from the analysis, some reversals may not have appeared in the data and thus may have affected measures of discontinuations and switches.

The strengths of this study include the use of two large-scale real-world databases with strong representation of the US population and similar, but not identical, methodologies. Importantly, results from these independent databases show a proportion of FOGA users with low adherence and persistence. Future research should assess the impact of the multiple FOGA therapies and dose strengths now available on



(B)

Rates (%)	Prior COP20	Prior COP40	Prior Both COP	No Prior COP
FOGA d/c	83.7	88.7	89.3	75.1
Switch	50.6	49.6	66.1	31.9

(C)

Median Days (range)	Prior COP20	Prior COP40	Prior Both COP	No Prior COP	Total
To FOGA d/c	30 (11-131)	30 (5-55)	30 (5-98)	30 (30.0-107.5)	30 (13-113)
To restart	109 (41-213)	67 (23.5-114.5)	79 (42-144)	94 (37-187)	96 (39-196)
To initial switch	28 (6-152)	28 (6-132)	22 (5-117)	79 (14-220)	35 (7-157)

Figure 4. DMT switches within 6 months of FOGA index date (A), discontinuation and switch rates (B), and median time to discontinuation and restart of initial switch in Group 2 (OM1).
COP20: branded glatiramer acetate 20 mg/mL once daily; COP40: branded glatiramer acetate 40 mg/mL three times weekly; d/c: discontinuation; DMT: disease-modifying therapy; FOGA: follow-on glatiramer acetate.

the US market. The reasons for initial and subsequent switches are not available from these insurance claims analyses, and ideally would be further investigated through surveys or chart review to inform clinical decisions (including changes in patient out-of-pocket costs). In general, these real-world data demonstrate a high and early discontinuation rate from FOGA treatment and subsequent switch to branded GA, for which future research into the reasons for switching is warranted.

Conclusion

This study attempts to describe the treatment patterns of MS patients initiating FOGA therapy in the US. Initial adherence to FOGA was reasonably high for both cohorts; however, the majority of patients overall discontinued their initial FOGA, and more than two-thirds of these patients did not restart FOGA at any time during the follow-up period. Initial discontinuation typically occurred within four months and most switches from FOGA were to branded GA (either daily 20 mg/mL or three times weekly 40 mg/mL). Future research on reasons for discontinuation and switching could help inform treatment decisions and thus potentially contribute to maintaining or enhancing patient care.

Notes

i. Copaxone is a registered trade name of Teva Pharmaceuticals USA Inc., Parsippany, NJ, USA.
ii. Glatopa is a registered trade name of Sandoz Inc., Princeton, NJ, USA.

Transparency

Declaration of funding

This study was funded by Teva Pharmaceuticals.

Declaration of financial/other relationships

J.K.A., R.A., M.V. and J.K. have disclosed that they are employees of and own stock in Teva Pharmaceuticals. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. *CMRO* peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgements

The authors wish to thank Jason Allaire PhD of Generativity Health Economics and Outcomes Research for help with editing this paper.

References

[1] Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014; 83(3):278–286.

[2] Jongen PJ. Health-related quality of life in patients with multiple sclerosis: impact of disease-modifying drugs. CNS Drugs. 2017; 31(7):585–602.

[3] Saiz A, Mora S, Blanco J. Therapeutic compliance of first line disease-modifying therapies in patients with multiple sclerosis. Compliance study. Neurologia. 2015;30(4):214–222.

[4] Tan H, Cai Q, Agarwal S, et al. Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis. Adv Ther. 2011;28(1):51–61.

[5] Johnson KM, Zhou H, Lin F, et al. Real-world adherence and persistence to oral disease-modifying therapies in multiple sclerosis patients over 1 year. J Manag Care Spec Pharm. 2017;23(8): 844–852.

[6] Menzin J, Caon C, Nichols C, et al. Narrative review of the literature on adherence to disease-modifying therapies among patients with multiple sclerosis. J Manag Care Spec Pharm. 2013; 19(1 Supp A):S24–S40.

[7] Burks J, Marshall TS, Ye X. Adherence to disease-modifying therapies and its impact on relapse, health resource utilization, and costs among patients with multiple sclerosis. CEOR. 2017;9: 251–260.

[8] Haddad P, Duquette P, Yeung M, et al. Comparison of compliance and discontinuation rates among MS patients treated with fingolimod and other disease-modifying therapies: a Canadian retrospective claims analysis. Value Health. 2015;18(7):A760.

[9] Vermersch P, Suchet L, Colamarino R, et al. An analysis of first-line disease-modifying therapies in patients with relapsing-remitting multiple sclerosis using the French nationwide health claims database from 2014 to 2017. Mult Scler Relat Disord. 2020;46: 102521.

[10] Moccia M, Lanzillo R, Brescia Morra V, et al. Assessing disability and relapses in multiple sclerosis on tele-neurology. Neurol Sci. 2020;41(6):1369–1371. Jun

[11] Lanzillo R, Prosperini L, Gasperini C, et al. A multicentRE observational analysis of persistence to treatment in the new multiple sclerosis era: the RESPECT study. J Neurol. 2018;265(5):1174–1183.

[12] Melamed-Gal S, Loupe P, Timan B, et al. Physicochemical, biological, functional and toxicological characterization of the European follow-on glatiramer acetate product as compared with Copaxone. eNeurologicalSci. 2018;12:19–30.

[13] Nicholas J, Halpern R, Ziehn M, et al. Real-world cost of treatment for multiple sclerosis patients initiating and receiving infused disease-modifying therapies per recommended label in the United States. J Med Econ. 2020;23(8):885–893.

[14] Raebel MA, Schmittdiel J, Karter AJ, et al. Standardizing terminology and definitions of medication adherence and persistence in research employing electronic databases. Med Care. 2013;51(8 Suppl 3):S11–S21.

[15] United Healthcare Pharmacy Clinical Pharmacy Programs [cited 2020 Oct 15]. Available from: https://www.uhc.com/member-resources/pharmacy-benefits/pharmacy-support-programs