Medication Adherence in Myasthenia Gravis: Exploring Patient Characteristics and Treatment

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Background

- Myasthenia gravis (MG) is a rare, chronic neuromuscular disease characterized by weakness in the voluntary muscles. MG affects 37 out of every 100,000 people in the United States, with the most common age demographic affected being those 50 years and older.[1]
- Patients affected with MG have a normal life expectancy with potentially impaired quality of life due to symptoms affecting daily activities.[1] Symptoms include drooping eyelids or blurred vision, changes in walking, impaired speech and difficulty swallowing. Severe symptoms include myasthenic crisis, a medical emergency characterized by impaired respiratory muscles, causing respiratory failure.[2]
- Treatment options for MG include acetylcholinesterase inhibitors, immunosuppressants, intravenous immunoglobulin (IVIG), and a thymectomy. Treatment of refractory MG may require maintenance use of IVIG, cyclophosphamide, or a provider-administered biologic such as rituximab (Rituxan); eculizumab (Soliris); ravulizumab (Ultomiris); rozanolixizumab (Rystiggo); efgartigimod alfa (Vyvgart); and efgartigimod alfa + hyaluronidase (Vyvgart Hytrulo).[3]
- Since 2022, as biologics have been FDA approved for MG, per member per month spend has increased from being the 18[th] most expensive drug therapy category in 2023 to the 15[th] most expensive in 2024.[4] In addition, exacerbations in symptoms such as myasthenic crisis are associated with high patient burden.[5] While improved disease management such as medication adherence can prevent exacerbations, there is limited literature conducted on drug adherence to MG.
- This study assesses patient adherence to provider-administered medications for MG to identify patients likely to be non-adherent. Identification may allow for early intervention with targeted measures, decreasing risk of future exacerbations.

Objective

The objective is to identify patient characteristics associated with adherence to provider-administered medications in new-start MG patients.

Methods

- **Figure 1** displays the study methods as outlined.
- Sample:
  - The study consisted of a Medicare and commercially insured claims sample representing 14 million medical drug claims.
  - Patients had to be new-start patients to MG therapy as defined as those with one or more MG diagnosis codes and no targeted therapy in the 6 months prior to their first (index) claim.
  - Patients had to be over the age of 18 and continuously enrolled 6 months prior to and 12 months following their index claim.
  - Patients were included if they had at least 2 administrations on 2 different days if taking ravulizumab or eculizumab, and at least 3 administrations on 3 different days if taking efgartigimod alfa.
- Evaluation window:
  - Members were evaluated from index date – 12 months.
  - Index date could start any time in 2022.
- Outcomes:
  - Outcome of interest – adherence, as defined as no missed doses during the evaluation window.
  - Members were placed into the adherent group (ADH) if medical claims indicated that they were administered their drug of interest within the time frame as defined by the drug's package insert, or into the non-adherent group (NA) if they did not.
    - Defined time frames for medication administration[6–8]
      - Eculizumab – Within 2 days of the scheduled infusion day
      - Ravulizumab – Within 7 days of the scheduled infusion day
      - Efartigimod alfa – Within 3 days of the scheduled infusion day
- Analysis:
  - Age, site of care for index treatment, index drug, and Elixhauser Comorbidity Index (ELX)[9] were assessed and compared for each cohort.
  - Cohen's *h*, a standardized effect size,[10] was calculated between adherent (ADH) and non-adherent (NA) groups. Effect sizes ranging from 0.20–0.49 are considered small, values ranging from 0.50 to 0.79 are considered medium, and values of 0.80 or greater are considered large.

Figure 1

Study Design Diagram

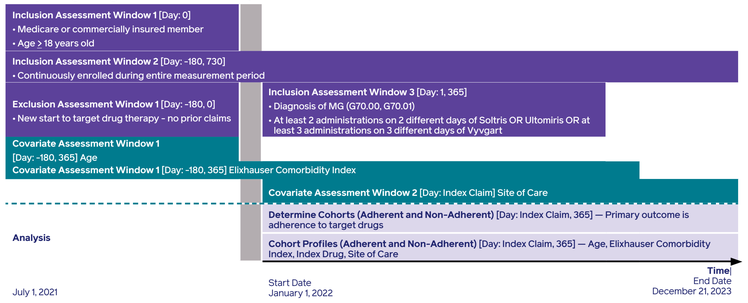


Table 1

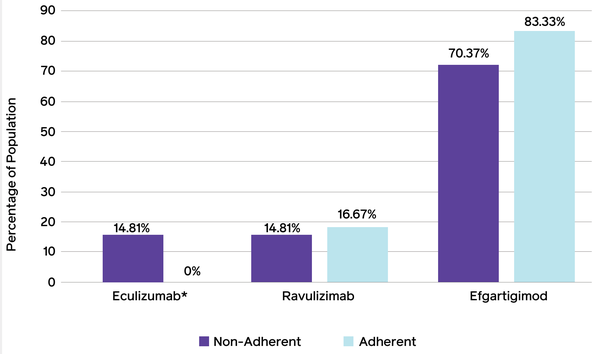
Comparison of Age, Elixhauser Comorbidity Index, Index Drug, and Site of Care Between the Non-Adherent and Adherent Groups

	Non-Adherent (n=27)		Adherent (n=18)			Overall	
	Mean/%	SD/ Count	Mean/%	SD/ Count	Cohen's *d*/*h**	Mean/%	SD/ Count
Age	49	14.74	58	14.44	0.62	52.60	15.13
Elixhauser Comorbidity Index	0.67	1.04	0.06	0.24	-0.74	0.42	0.87
Index Drug							
Eculizumab (Soliris)	14.81%	4	0%	0	0.79	8.89%	4
Ravulizimab (Ultomiris)	14.81%	4	16.7%	3	-0.05	15.56%	7
Efgartigimod alfa (Vyvgart)	70.37%	19	83.33%	15	-0.31	75.56%	34
Site of Care							
Hospital outpatient	11.11%	3	5.88%	1	0.19	9.09%	4
Physician's office	37.04%	10	47.06%	8	-0.20	40.91%	18
Home infusion	48.15%	13	47.06%	8	0.02	47.73%	21
Other	3.70%	1	0%	0	0.39	2.27%	1

*SD = standard deviation
*Age and Elixhauser Comorbidity Index: Reported as mean and SD and assessed with Cohen's *d*.
*Index drug and site of care: Reported as % and count and assessed with Cohen's *h*.

Figure 2

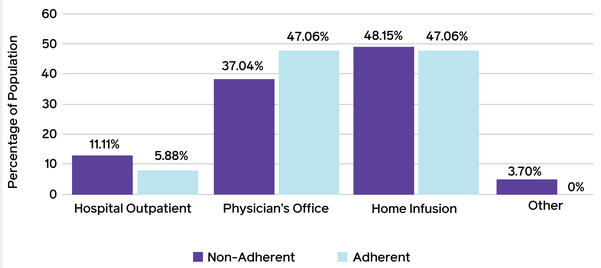
Comparison of Index Drug between the Non-Adherent and Adherent groups



* Medium effect size

Figure 3

Comparison of Site of Care between the Non-Adherent and Adherent groups



Results

- **Study Population**
  - After applying the inclusion and exclusion criteria, the study sample consisted of 45 members. A total of 27 members (60%) were in the NA cohort and 18 members (40%) were in the ADH cohort.
- **Age and ELX**
  - **Table 1** displays the mean values for age and ELX. The mean age was 52.60 (SD=15.13) and the mean ELX was 0.42 (SD=0.87). The mean age for the ADH group was 58.00 (SD=14.44) and mean ELX was 0.06 (SD=0.24). The NA group had a mean age of 49.00 (SD=14.74) and mean ELX of 0.67 (SD=1.04).
- **Index Drug**
  - **Table 1** displays the counts of index drug assessed. **Figure 2** compares the percentage of patients in the NA and ADH group receiving each index drug. None of the ADH group and 14.81% (n=4) of the NA group received eculizumab (Cohen's *h*=0.79). Efgartigimod alfa was received by 83.33% (n=15) of the ADH group and 70.37% (n=19) of the NA group (Cohen's *h*=0.31). Ravulizumab was received by 14.81% of the NA group and 16.67% of the ADH group (Cohen's *h*=0.05).
- **Site of Care**
  - **Table 1** displays the count of members administered their target drug for each site of care. **Figure 3** compares the percentage of patients in the NA and ADH group administered treatment at each site of care. The ADH cohort utilized a physician's office as site of care more than the NA cohort with 47.06% and 37.04% utilization, respectively (Cohen's *h*=0.20). The NA cohort utilized hospital outpatient as site of care more than the ADH cohort with 11.11% and 5.88% utilization, respectively (Cohen's *h*=0.19). Home infusion was utilized by 48.15% of the NA group and 47.06% of the ADH group with no difference between groups (Cohen's *h*=0.02).

Limitations

- Analysis is based on real-world claims data. Services performed but not billed are not captured in the data. Claims data analyzed represents data submitted by the provider and validated within tolerance limits. Undetectable data quality issues may exist that are common to all claims data sources such as submitting a valid code but not the code that was intended.
- Claims data is limited to member enrollment. Patients identified as new start may have received the target drugs with a different coverage.
- The patient population used consisted of those enrolled in commercial or Medicare. Results may not be applicable to other groups (e.g., Medicaid).
- The scheduled infusion day for each patient was estimated using the established dosing regimen for each target drug and may not represent the patient's actual infusion day.
- Agents FDA approved in 2023, efgartigimod alfa + hyaluronidase and rozanolixizumab, have increased in utilization since approval, but could not be included due to limitations in the evaluation window.
- As MG is a rare disease, a small sample size was identified, and descriptive statistics were utilized as inferential statistics could not be calculated. Results may not be generalizable to a larger sample and additional research should be conducted.

Discussion

- As more provider-administered medications have been FDA approved for myasthenia gravis (MG), spend for this disease state has continued to increase.[4] Adherence is essential for patients to achieve the best outcomes from these high-cost medications.
- Age and Elixhauser Comorbidity Index were characteristics that affected adherence. On average, the adherent group was older with less comorbidities than the non-adherent group, both with a large effect size. However, the average age of the non-adherent and adherent groups are within the same age range of middle age and may not be clinically significant.
- For index drug, patients on eculizumab were more likely to be non-adherent, with a medium effect size. Potential factors of influence include its frequent (biweekly) and indefinite dosing schedule and the intravenous route of administration. Patients taking efgartigimod alfa were more likely to be in the adherent group than the non-adherent group, although effect size was small, suggesting marginal clinical significance. This could be due to the drug holiday associated with efgartigimod alfa, which may allow for more convenient administration scheduling and less opportunity for poor adherence compared to a drug administered indefinitely.
- Although effect size was small, the non-adherent group utilized hospital outpatient as site of care more often, while the adherent group utilized a physician's office as site of care more often. This suggests potential for adherence benefits in utilizing an alternative site of care to the hospital outpatient setting.
- Results suggest that there could be benefit to the utilization of efgartigimod alfa + hyaluronidase and rozanolixizumab given their subcutaneous administration, potential for administration outside of a hospital outpatient setting, and the drug holiday between administrations, which lead patients away from common drivers of poor adherence.
- Currently, limited program offerings exist to assess and enhance a patient's adherence to intravenous, medical benefit drugs. The findings of this study may support the development of such a program. The patient characteristics evaluated in this study could be used to identify those likely to be non-adherent for intervention.

Conclusions

- Overall, adherence to provider-administered treatments for MG was impacted by age, comorbidities, treatment, and site of care.
- Results show that patients receiving eculizumab, an intravenous and indefinitely dosed drug, were more likely to be non-adherent. This suggests there could be an adherence benefit to utilizing subcutaneous agents like efgartigimod alfa + hyaluronidase and rozanolixizumab.
- While effect size is small, results illustrate that the non-adherent group was more likely to utilize hospital outpatient as site of care, suggesting there may be an adherence benefit to using a site of service program to drive patients to non-hospital outpatient settings.
- Currently, limited programs exist to assess and enhance a patient's adherence to medical benefit drugs. The results of this study may indicate a potential advantage to the development of such a program. The patient characteristics evaluated in this study could be used to identify patients for intervention that are likely to be non-adherent.

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