

Calcitonin Gene-related Peptides (CGRPs) Uptake and Acute Migraine Medication Use among 15 Million Commercially Insured Members

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No external funding provided for this research

BACKGROUND

- Three self-injectable monoclonal antibody medications, working via antagonism of the calcitonin gene-related peptide (CGRP) receptor for intermittent migraine prophylaxis or chronic migraine prophylaxis treatment, were recently approved: erenumab-aooe (Aimovig®) in May 2018, and fremanezumab-vfrm (Ajovy™) and galcanezumab-gnlm (Emgality®) in September 2018.
- CGRP drugs represent the first biologic competition to Botox® (Onabotulinumtoxin A) for chronic migraine prevention.¹ In a real-world analysis of Botox® treatment persistency, less than half of individuals initiating therapy received the four annual recommended treatments during their first year of therapy, indicating there is a need for other treatments.²
- As all three CGRPs are priced at around \$600 monthly¹ before discounts, it is important to understand real-world CGRP uptake, adherence, switching and change in other acute medication use among those newly initiating a CGRP drug.
- Opioid use is a public health crisis³ and opioids are frequently prescribed to alleviate migraine pain. Therefore, understanding opioid real-world utilization before and after CGRP therapy initiation is important. Ideally, opioid use should decline after CGRP therapy initiation.
- Understanding CGRPs real-world utilization, costs, adherence, switching, and associated changes to concurrent acute migraine medication use will inform insurers' CGRP category management strategies.

OBJECTIVE

Using 15 million commercially insured members pharmacy claim data:

- Determine CGRP utilization uptake, cost, adherence, discontinuation rate, and switching among CGRP products.
- Assess acute migraine medication, opioid and triptan utilization change after CGRP therapy initiation.

METHODS

All analyses were conducted using pharmacy claims from 15 million commercially insured members.

CGRP Uptake, Utilization and Ingredient Costs

- Pharmacy claims data were queried from May 2018 through July 2019 (15 months) to identify all CGRP claims.
- Monthly count of members with at least one CGRP claim, CGRP claim count, and sum of all CGRP claims cost, defined as member and plan paid after pharmacy network discount, not including rebates or coupons.

CGRP Adherence, Switching and Acute Migraine Medication Utilization

- Because the first CGRP came to market in May 2018 and adherence, switching and acute migraine medication utilization required continuous enrollment six months after CGRP therapy initiation, members newly initiating a CGRP were identified from May 2018 through Jan 2019. The CGRP index date for members newly initiating CGRP was defined as the date of their first CGRP claim.
- Members were required to be continuously enrolled six months prior to (pre-index period) and six months after (post-index period) the CGRP index date.

Outcomes Measurements

- CGRP therapy discontinuation was defined as a gap of ≥ 45 days after the end of days-supply of a CGRP pharmacy claim, prior to the subsequent CGRP claim, during the 6-month post-index period.
- CGRP adherence was measured using the proportion of days covered (PDC) calculation. The CGRP PDC during the six months after therapy initiation is reported. When calculating the CGRP PDC, all CGRP claims with an overlap were adjusted to add the overlapping days to the end of the CGRP claim day supply. For a claim that straddles the end of the post-index period, only days in the post-index period were counted toward the PDC. The number of CGRP days covered were divided by the fixed interval of 182 days. Members were considered adherent if their PDC was $\geq 80\%$.

- Switching was defined as a pharmacy claim for a CGRP other than the index CGRP product in the 6-month post-index period.
- Opioid use in 6-month pre-index and 6-month post-index periods was defined in the following ways:
 - Separately calculating the proportion of members with at least one opioid claim in the pre-index period and post-index period with the change statistically compared using the McNemar's test.
 - Total morphine milligrams equivalent (MME) by month in each period where MME was calculated using the Centers for Medicare & Medicaid Services (CMS) overutilization monitoring system (OMS) method.^{4,5} The sum of the total MME for commercial members with six months of continuous enrollment in the pre-index and post-index periods initiating CGRPs was calculated for each month in the pre-index and post-index periods.

- Mean monthly MME in each period (i.e., pre-index and post-index) was defined as the sum of the total MME in the period divided by six.
- Mean daily MME by member in each period was calculated among members with an opioid claim for each month in the pre-index and post-index periods. The daily MME was defined as the total MME for all members in a specific month divided by the number of days on therapy for that month.

- Use of triptans with an FDA indication for acute migraine therapy in the pre-index and post-index periods was defined as:
 - Separately calculating the proportion of members with at least one triptan claim in the pre-index period and post-index period with the change statistically compared using the McNemar's test.
 - Triptan total monthly dosing units (number of tablets, nasal sprays, or injections) by month in each period was calculated using the units from the pharmacy claim.
 - Triptan mean monthly dosing unit in the pre-index and post-index period was defined as the sum of the total dosing units in the 6-month pre-index and post-index period divided by six.

RESULTS

CGRP Uptake and Economic Impact (Figure 1)

- The number of members new to CGRP therapy increased steadily from 6 members new to a CGRP in May 2018 to 1,809 in July 2019, a CGRP new start monthly accelerated growth rate of an additional 129 new members each month.
- CGRP utilizers by month grew slowly the first six months after the first CGRP launched May 2018 and has increased rapidly since January 2019, to 7,449 in July 2019.
- CGRPs monthly cost increase mirrors the utilizers over the 15-month period ending July 2019, with the CGRP cost of \$4,811,866 in July 2019.

CGRP Study Population Identification

- A total of 3,555 members initiated CGRP therapy during May 2018 through Jan 2019 (Table 1).
- 2,758 (77.6%) of 3,555 had six months of continuous enrollment in the pre-index and post-index period, for a total of 12 months total continuous enrollment.
- The mean age of members initiating a CGRP was 44.6 years and 86.0 percent were female.

Switching, Discontinuation and Adherence to CGRP Therapy

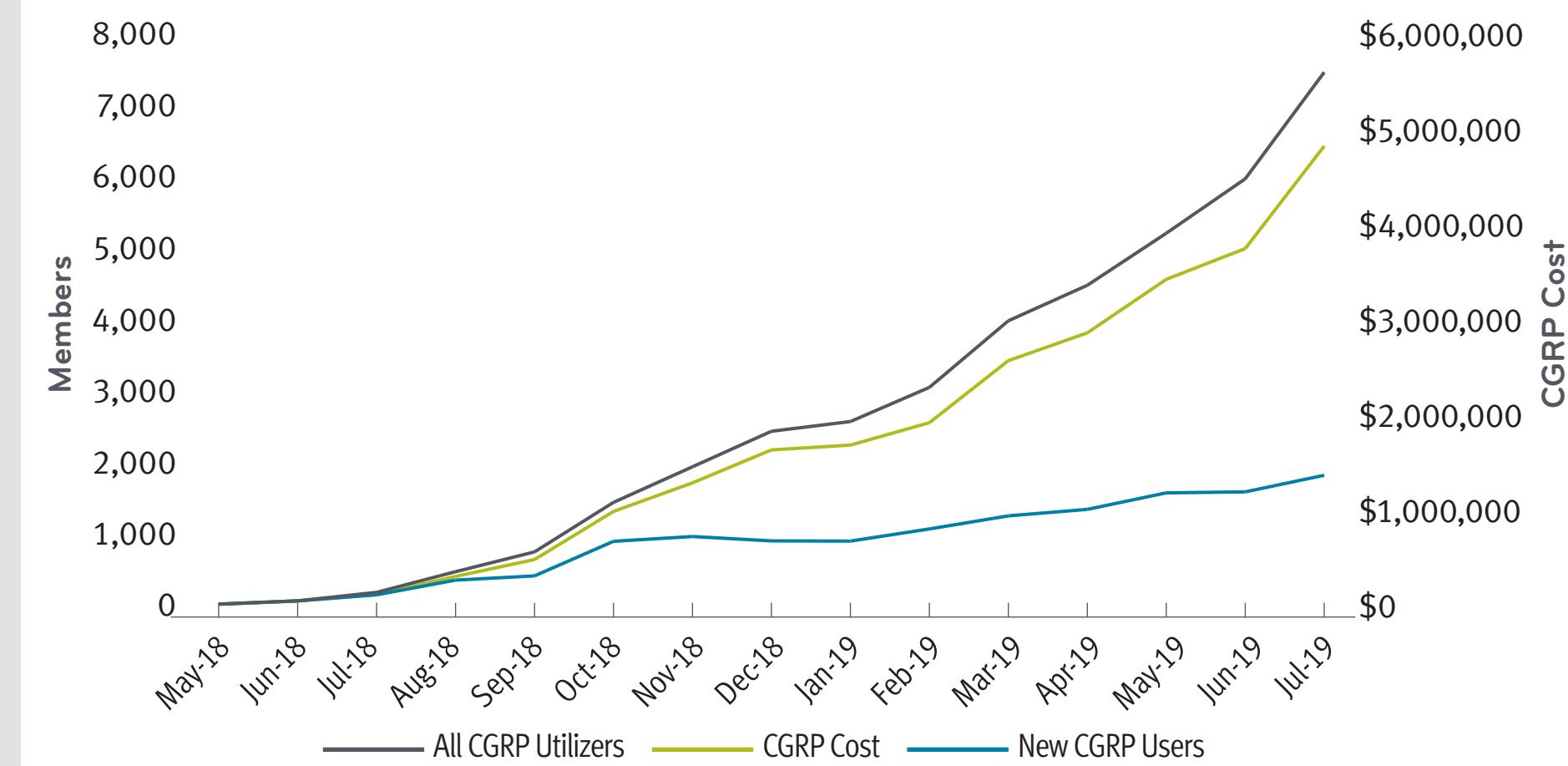
- 148 of 2,758 (5.4%) members switched to another CGRP therapy in the 6-month post-index period.
- 60.1% of members initiating CGRP therapy discontinued it; discontinuation was defined as a ≥ 45 -day gap in CGRP supply during the 6-month post-index period.
- The mean CGRP PDC in the post-index period was 70.6%. The proportion of members with a PDC $\geq 80\%$ was 50.5%.

Acute Migraine Medication Use Among 2,758 CGRP New Initiators

- 1,025 (37.2%) members had an opioid claim in the 6-month pre-index period compared to 976 (35.4%) in the 6-month post-index period, a 4.8% reduction ($p=0.041$).
- The monthly total MME was relatively steady in the 6-month pre-index period, decreasing in the two months after initiating CGRP therapy and then remaining stable (Figure 2).
- The mean monthly total MME in the pre-index period was 340,757 compared to 304,710 in the post-index period, a reduction of 10.6%.
- The mean daily MME was 47.9 in the pre-index period compared to 45.4 in the post-index period, a reduction of 5.2%.
- A total of 1,760 (63.8%) members had a pharmacy claim for a triptan in the pre-index period compared to 1,585 (57.5%) in the post-index period, a reduction of 9.9% ($p<0.001$).
- The mean monthly dosing unit of triptans in the pre-index period was 85.5 compared to 79.7 in the post-index period, a reduction of 6.8% (Figure 3).

FIGURE 1

Members Initiating CGRPs, Total CGRP Utilizers, and CGRP Month Cost from May 2018 through July 2019 Among 15 Million Commercially Insured Members



CGRP = Calcitonin Gene-related Peptides. The first CGRP came to market in May 2018.
New Users defined as the member count in the month with a CGRP claim who had no prior CGRP claim.
All utilizers defined as the member count with CGRP claim the month.
CGRP cost was defined as the sum of the CGRP claims member paid plus plan paid less pharmacy network discount, not including rebate or manufacturer coupons.

TABLE 1

Calcitonin Gene-related Peptides (CGRPs) Utilizing Members and Study Population Identification

Among 15 million Commercially Insured Members:	Members
Members newly initiating CGRP therapy from May 2018 through July 2019	10,234
Members newly initiating CGRP therapy from May 2018 through January 2019	3,555
Members with 6 months continuous enrollment prior to and after newly initiating CGRP therapy – study population for assessing adherence, CGRP product switching, and acute migraine drug utilization 6 months prior to CGRP therapy initiation compared to the 6 months post CGRP initiation	2,758 (77.6%) of 3,555

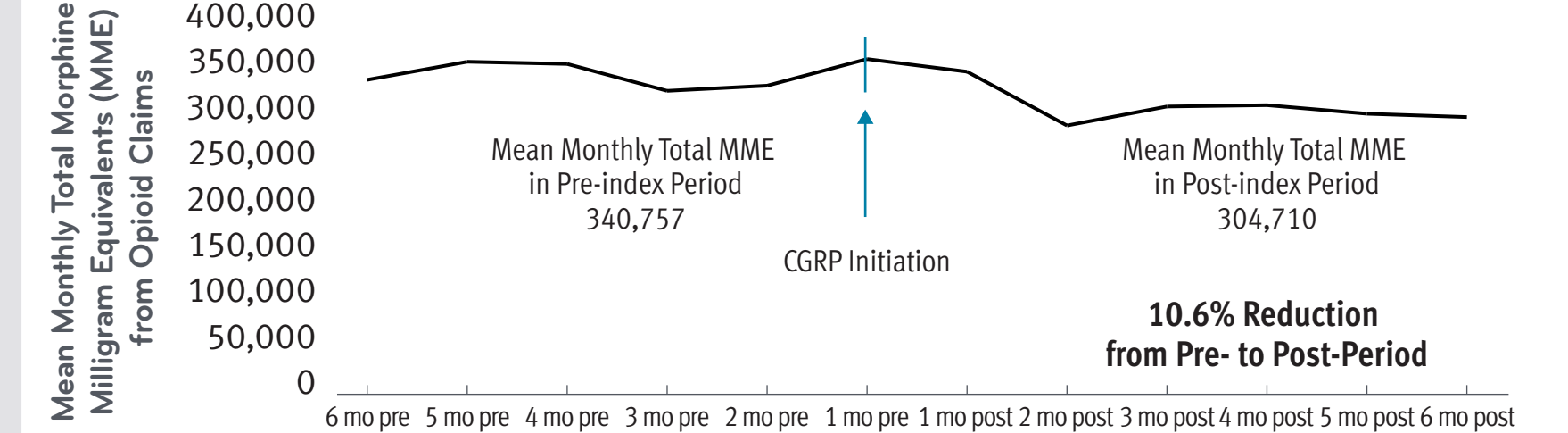
NOTE: The first CGRP came to the market May 2018.

CONCLUSIONS

- In this large commercially insured population, the real-world CGRP drug uptake was slow during the initial months after launch in May 2018 and has increased rapidly since January 2019, with a July 2019 utilization rate of 50 per 100,000 members.
- Prime Therapeutics is forecasting that in the month of December 2020, the CGRP expense will be \$15 million, a three-fold increase of the \$4.8 million in CGRP expense seen in July 2019.
- While few members were found to switch CGRP therapy, 60% of members newly initiating a CGRP discontinued their therapy in the first six months. It is important insurers have value-based contracts in place to recoup the costs for early CGRP discontinuation. The high discontinuation rate is not surprising for three reasons: first, the severe, difficult-to-treat migraine patients are most likely those initially receiving therapy; second, poor migraine prophylaxis drug adherence has been seen with other agents;⁶ and third, provider CGRP samples may have been used by members without insurers' knowledge.
- CGRP initiation was found to have a potentially positive impact on opioid and triptan acute migraine medication utilization. This real-world study resulted in a statistically significant 5% decrease in members with an opioid claim in the 6 months after starting CGRP therapy.
- Insurers will need to closely monitor CGRP utilization and costs as they are expected to triple in the coming year. The anticipated value in decreased opioid use and other acute migraine treatment medications needs further assessment.

FIGURE 2

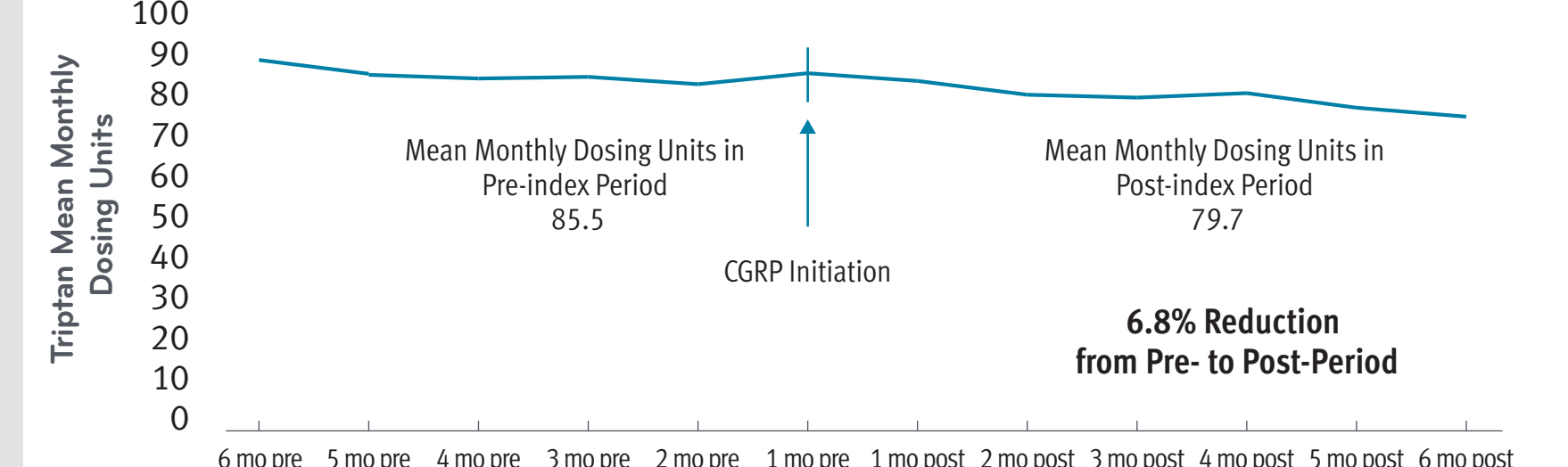
Monthly Mean Total Opioid MME for 2,758 Commercial Members* Initiating CGRP Therapy: Pre- to Post-CGRP Therapy Initiation Comparison



*6 months of continuous enrollment in the CGRP pre-index and post-index periods required. Each member's CGRP initiation was May 2018 through Jan 2019. NOTE: The first CGRP came to the market May 2018.
CGRP = Calcitonin Gene-related Peptides; CGRP initiation = date of first CGRP claim; mo = month.
1,025 (37.2%) of 2,758 members had an opioid claim in the pre-index period compared to 976 (35.4%) in the post-index period, $p=0.041$ using McNemar's test.
MME was calculated using the Centers for Medicare & Medicaid Services (CMS) overutilization monitoring system (OMS) method.^{4,5} The total MME sum was calculated each month. Mean monthly MME in each period was defined as the sum of the total MME in a period divided by 6.

FIGURE 3

Triptan Monthly Mean Dosing Units for 2,758 Commercial Members* Initiating CGRP Therapy: Pre- to Post-CGRP Therapy Initiation Comparison



*6 months of continuous enrollment in the CGRP pre-index and post-index periods required. Each member's CGRP initiation identification was May 2018 through Jan 2019. NOTE: The first CGRP came to the market May 2018.
CGRP = Calcitonin Gene-related Peptides; CGRP initiation = date of first CGRP claim; mo = month.
1,760 (63.8%) of 2,758 members initiating CGRP therapy had a triptan claim in the pre-index period compared to 1,585 (57.5%) in the post-index, $p<0.001$ using McNemar's test.
Triptan total monthly dosing units (number of tablets, nasal sprays, or injections) by month in each period was calculated using the units from the pharmacy claim. Mean monthly dosing unit in the pre-index and post-index period was defined as the sum of the total dosing units in the 6-month pre-index and post-index period divided by 6.

LIMITATIONS

- Provider CGRP sample dispensing may have artificially inflated the discontinuation rate.
- The study did not require a diagnosis of migraine and intermittent off-label use of CGRPs (e.g., cluster headaches) may have occurred.
- The data used in this study was limited to a commercial population and results are not generalizable to Medicare or Medicaid populations.

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