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CoLab Network

Summary Report

Calcitonin Gene–Related Peptide Inhibitors for Migraine Prophylaxis

Rapid Review Report Author

Michael Law

Drug Utilization Report Authors

Jason R. Randall, Huong Luu, Khanh Vu, Cristiano S. Moura, Houssem Missaoui, Karen Martins, Hassan Behlouli, Sarah Treit, Devin Manning, Zhaoyu Liu, Farnaz Amoozegar, Daniel Dutton, Jean-Luc Kaboré, Sasha Bernatsky, Scott Klarenbach

The rapid review was conducted independently by Michael Law, and the drug utilization study was conducted by the Alberta Drug and Technology Evaluation Consortium (ADTEC), the CAnadian Network for Advanced Interdisciplinary Methods (CAN-AIM), and the Institut national d'excellence en santé et en services sociaux (INESSS), both through the Post-Market Drug Evaluation CoLab Network.

Executive Summary

Recurrent migraine headaches can be debilitating. Calcitonin gene–related peptide (CGRP) inhibitors are prescribed for migraine prophylaxis (also known as migraine prevention) after standard therapies fail. There are several different formulations of CGRP inhibitors, and it is unclear whether switching from one CGRP inhibitor to another after treatment failure is a clinically or cost-effective treatment option.

A rapid review and drug utilization study aimed to examine the evidence on the effectiveness of switching to an alternate CGRP inhibitor after treatment failure and understand their trends in use and treatment patterns.

We found that, although some patients experience a reduction in monthly migraine days after switching, the evidence supporting this practice is very weak. The use of CGRP inhibitors is increasing, with a growing preference for newer medications. About 5.4% of new users switch to another CGRP inhibitor within the first year. Many also try other treatments or stop preventive treatment altogether. Some studies suggest that individuals who switch from one CGRP inhibitor to another tend to require moderately less rescue medication and fewer health care resources to manage migraines. Although the findings do not conclusively support the practice of switching from one CGRP inhibitor to another, there are indications that this practice may be beneficial to some. However, more evidence is required to confirm this finding.

Background

Migraines, which are a severe type of headache, are disabling for many people in Canada. Migraine prevention treatment strategies are typically recommended when individuals experience weekly migraines or have severe symptoms. CGRP inhibitors are a class of drugs used to prevent migraines. These drugs work by blocking CGRP, which helps reduce pain and inflammation. They are usually prescribed after an individual has tried and has not improved with 2 or more standard migraine therapies.

Policy Issue

While CGRP inhibitor medications have proven effective after failure on standard migraine therapies, it remains unclear whether switching from one CGRP inhibitor to another after failure is a clinically effective treatment option. When switching and trialling another drug is not beneficial, it can lead to unnecessary medication exposure, delays in effective treatment or care, and needless use of health care resources. More evidence is needed to inform policies guiding the use of CGRP inhibitors for migraine prevention in individuals who have previously tried a CGRP inhibitor.

Policy Question

1. Should CGRP inhibitors be reimbursed upon lack or loss of response to a previous CGRP inhibitor for migraine prevention?

Objectives

The rapid review aimed to examine the evidence on the effectiveness of using different CGRP inhibitors after a lack or loss of response to a first or second CGRP inhibitor.

The objective of the drug utilization study was to describe trends in the use of CGRP inhibitors, treatment patterns including switching from one CGRP inhibitor to another, and outcomes after switching. A secondary objective was to examine user characteristics, health care resource use, and indirect markers of effectiveness, such as the use of rescue medications that provide quick relief for active symptoms.

Findings

Effectiveness

We identified 1 systematic review of 7 nonrandomized observational studies, along with 3 additional nonrandomized observational studies and 2 clinical guidelines. However, we did not identify any randomized controlled trials or economic evaluations.

All included studies were published between 2022 and 2024 and focused on changes in the number of monthly migraine days after switching to a new CGRP inhibitor. The studies were generally small, conducted in various countries, and had significant issues with their methods. The 2 evidence-based guidelines were published in 2022 and designed for use in Germany and Europe. They were developed using a systematic process but did not undergo a formal bias assessment of the evidence.

The studies generally suggest that patients experience improvement with the second CGRP inhibitor, based on reported reductions in the number of monthly migraine days. There is some indication that this is particularly true when switching between medications with different mechanisms of action (e.g., CGRP inhibitor to CGRP receptor inhibitor) or after discontinuing a particular therapy due to medication-specific adverse events. Both guidelines conclude that there is not enough evidence to support switching after failure as evidence-based practice.

Drug Utilization

We identified 12,851 individuals taking CGRP inhibitors in Canada and 148,100 in the US. The data were gathered using health administrative and billing databases across 6 provinces in Canada (Alberta, British Columbia, Manitoba, Nova Scotia, Quebec, and Saskatchewan) and from the US.

We found that among both new and current users of CGRP inhibitors:

- The use of CGRP inhibitors is increasing over time in Canada and the US.
- In recent years, the newer CGRP inhibitors have become the most commonly used treatment.

The trends suggest CGRP inhibitor use may continue rising, with a growing preference for newer medications.

Approximately 5.4% of new users switch to an alternate CGRP inhibitor within the first year. Additionally, 9.3% switch to onabotulinumtoxinA, 12.0% switch to other preventive treatments, and 9.1% stop using preventive medication altogether within a year. Within 4 years of taking a CGRP inhibitor, 33% of users switch to another CGRP inhibitor.

For new CGRP inhibitor users, the need for rescue medication and health care resources for migraines was generally lower in the first year after starting treatment. For those who switched to another CGRP inhibitor, the use of rescue medications and health care resources for migraines was also generally lower in the year after switching.

Importantly, we did not find evidence to suggest that individuals who switched to an alternate CGRP inhibitor experienced lower effectiveness.

Limitations

Both the rapid review and drug utilization study had some key limitations.

All the studies in the rapid review, including the clinical guidelines, were conducted in other countries, so it is not clear how relevant their findings are to patients in Canada. All studies also had very significant methodological concerns, and their results should not be considered conclusive. In particular, all the primary studies were uncontrolled, meaning we cannot rule out the possibility of bias.

The drug utilization study could not analyze medication use in some provinces, like Ontario, because of missing data. Using administrative data instead of detailed medical records might lead to inaccuracies in the results. Changes in medication availability and reimbursement policies could influence treatment choices. While the study aimed to identify factors affecting the use of CGRP inhibitors, it did not assess their effectiveness or the reasons for stopping or switching treatments. Factors such as side effects and convenience may influence treatment choices.

Implications for Policy-Making

The studies included in the rapid review do not offer conclusive evidence in support of switching CGRP inhibitors after failure on a first CGRP inhibitor. However, existing studies do suggest some potential, particularly when switching between medications with different mechanisms of action (e.g., CGRP inhibitor to CGRP receptor inhibitor) or after discontinuing a particular therapy due to medication-specific adverse events. Clinical guidelines indicate that this might be a viable strategy for particular circumstances, but they acknowledge the lack of a solid evidence base to inform treatment recommendations.

The drug utilization study found that the rate of CGRP inhibitor use is increasing over time, with a trend indicating a preference for newer CGRP inhibitors. The reasons behind this trend are unclear and may involve various factors beyond clinical effectiveness. Individuals who begin using CGRP inhibitors tend to require moderately less rescue medication and fewer health care resources to manage migraines. This observation also holds true for those who switch from one CGRP inhibitor to another, relative to pre-switch treatment status.

Taken together, these studies suggest that, although there is not enough evidence to determine the effectiveness of switching CGRP inhibitors, patterns of lower rescue medication and migraine-associated health care resource use suggest that patients switching to a different CGRP inhibitor may experience some benefits.

Considerations

Post-Market Drug Evaluation (PMDE) projects aim to produce health policy issue evidence and are not linked to a recommendation.

This work was intended to inform health policy. Clinical questions regarding the use of CGRP inhibitors should be directed to a health care professional.

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For the full scientific reports, visit:

Switching Calcitonin Gene–Related Peptide Inhibitors for Migraine Prophylaxis

Calcitonin Gene–Related Peptide Inhibitors for Migraine Prophylaxis

This work was conducted by Michael Law, the Alberta Drug and Technology Evaluation Consortium (ADTEC), the CAnadian Network for Advanced Interdisciplinary Methods (CAN-AIM), and the Institut national d'excellence en santé et en services sociaux (INESSS) through the Post-Market Drug Evaluation CoLab Network. It was supported by Canada's Drug Agency (CDA-AMC) and its Post-Market Drug Evaluation Program through funding provided by Health Canada.

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CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with the Post-Market Drug Evaluation Program to produce credible and timely evidence on postmarket drug safety and effectiveness.

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