

CADTH Reimbursement Review

Patient Input

GALCANEZUMAB (Emgality)
(Eli Lilly Canada Inc.)

Indication: Emgality is indicated for the prevention of migraine in adults who have at least four migraine days per month.

CADTH received patient input from:
Migraine Canada and Migraine Quebec (Joint Submission)

June 28, 2021

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CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	GALCANEZUMAB (EMGALITY)
Name of the Patient Group	Migraine Canada Migraine Quebec
Author of the Submission	[REDACTED]

1. About Your Patient Group

Migraine Canada is a national not for profit patient organization with a mission to provide support and education as well as raise awareness about the impact of migraines. We advocate for optimal care for those living with migraines and support research to find a cure. We educate patients, caregivers, and healthcare professionals by researching, developing, and sharing electronic and print materials containing the most current migraine information. We drive awareness and education through our website, social media, workshops, and forums. We provide patient support through participation in regional support groups, with more than 3,000 members on our Facebook page and by playing a role with various other online groups.

Migraine Quebec is a provincial non-profit patient organization whose mission is to provide support and information to people with the disease, as well as to educate the public about the repercussions of migraine. We advocate for optimal care for migraine sufferers and support research to find cures to improve the quality of life of patients with this chronic disease. We educate patients, caregivers and healthcare professionals by researching, developing and sharing electronic and print documents containing the most recent data on migraine. We promote awareness and education through our website, social media, workshops and forums. We help patients by playing a role with regional on-line support groups, with more than 5,000 members on our Facebook page) for the province of Quebec).

Both organizations have a broader reach by interacting with several other on-line associations and leverage traditional and social media channels to empower patients to share stories and experiences to advocate for the supports needed to live full and active lives while coping with migraines.

Website (English): www.migrainecanada.org

Facebook (English): <https://www.facebook.com/migrainecanada/>

Website(French): www.migrainequebec.com

Partage Migraine Quebec (French, private)

<https://www.facebook.com/groups/312758085805229/>

2. Information Gathering

In late 2018, an on-line survey that was promoted through the Migraine Canada Facebook community, twitter account and in migraine clinics across Canada. The survey was designed and

analyzed by Migraine Canada. A total of 597 patients participated in the survey. The majority of participants were between 26 and 54 years old, which reflect the migraine population. The group represented low frequency episodic (26%), high frequency episodic (32%) and chronic (42%) migraine. 22% of the group was on short- or long-term disability. 38% reported another health condition that could impact their function.

In May 2021, we circulated another survey very specific to CGRP's and Emgality to gain insights on these medications and the impact of migraine on Canadians. The survey was designed and analyzed by Migraine Canada. A total of 115 people participated in the survey (97% were female and 3% were male). Close to 90% of respondents were diagnosed with migraine and 73% experience 15 or more migraines each month.

The majority of patient quotes we have included in this submission are from the 2021 survey. A comprehensive report capturing all patient comments is also available for review from both surveys. The statistics referred to throughout the submission are from the 2018 survey unless otherwise noted.

Migraine Canada also received direct input from two Canadian patients that has been integrated into the submission and highlighted. The first patient will be referred to as Patient 1 patient is a 37 year old male and his spouse's perspective (35 year old female). The other patient is a 25 year old female who will be referred to as Patient 2.

3. Disease Experience

Migraines are not just headaches but are a neurological disease. Migraine's impact 1 billion people worldwide, or about 1 in 7 people. Migraine is most common between the ages of 25 and 55 but it can impact people of all ages including children. It affects three-times as many women as men.

Migraines are classified according to their monthly frequency. Episodic Migraine is defined as impacting less than 15 days per month and 12% of adults living with migraine fall into this group; Chronic Migraine impacts more than 15 days per month and 2% of the adult migraine populations. Migraines often present with severe, throbbing, recurring pain, usually on one side of the head (or both sides or no pain at all). Nausea, vomiting, dizziness, extreme sensitivity to sound, light, touch, and smell, and tingling or numbness in the extremities or face are also common symptoms. About 25% of migraine sufferers also have a visual disturbance called an aura, which usually lasts less than an hour. Attacks usually last between 4 and 72 hours and severe attack are recognized by the World Health Organization to be as disabling as advanced dementia and paralysis of four limbs.

Migraine is usually categorized according to accompanying symptoms (aura, vestibular, hemiplegic) but also according to monthly frequency of attacks. Episodic migraine refers to attacks occurring 14 days or less and is now further separated in low-frequency (1-6 days) and high frequency (7-14 days). Chronic migraine is diagnosed when patients have 15 or more headache days per month. Chronic migraine is associated with more disability and co-morbidities. It is also associated with medication overuse headache (MOH), a complication of frequent use of acute treatments that induce even more frequent and intractable headaches. The estimated prevalence of MOH varies according to countries but is usually between 0.5% and 2% of the global population (GBD 2015). Medication overuse feeds the headache cycle and patients are trapped in a vicious cycle, unable to get adequate pain relief.

There are two main states of life for a migraine patient: the active attack (ictal state) and in-between attacks (interictal state). During the attack itself, symptoms may prevent the person's ability to accomplish their tasks, work and interact with others. The pain is at least moderate and

often severe, throbbing, and diffuse. The nausea and vomiting are obviously disruptive and may prevent oral medications efficiency. The sensory hypersensitivity forces many patients to isolate themselves in a dark room and stop all activities. Auras are neurological deficits that can accompany migraines (including loss of vision, speech, and sensation, even muscle strength) which can last for hours. Some migraines are also accompanied with dizziness, vertigo, and loss of balance. People generally experience reduced cognition during a migraine, with slowed thinking, lack of focus, and difficulty reading and speaking. This typically disrupts most activities involving a computer or interacting with other people. A controlled migraine attack managed with effective treatment can be brief, but uncontrolled attacks may last multiple days in a row.

Migraine patients (15%) will visit an emergency department (ED) for an intractable attack every year. In our survey, 27% of respondents had been to the ED four times or more since the beginning of their disease. Most ED visits are difficult events, where migraine patients often feel stigmatized and blamed for wasting health care resources and the time of the health care providers.

Patients will often try to compensate for wasted time suffering from days of migraine and an ED visit, and will attempt to double efforts to catch up but often end up in a recurring loop of attached given that their brain is not allowed to rest and recover. ED visits are amongst other indirect harmful consequences of suffering from poorly controlled migraine attacks.

It is important to understand that, unlike other chronic pain conditions, migraine is not associated with permanent disability but with episodic disability during attacks.

In between headache attacks, patients can be otherwise completely healthy and contributing members of society's workforce. Our patient community members include accountants, engineers, physicians, nurses, lawyers, and other strong members of our society's workforce. These patients aim to be functional, thus making medication side effects unacceptable for the vast majority.

Migraine patient's quality of life is considerably (negatively) impacted during the interictal state. Survey respondents indicated in their comments that they live in fear of the next attack, and have difficulty planning ahead. Migraine sufferers end up dreading potential triggers and limit their activities, both personal and professional, to either avoid an attack or avoid blame by others for having to cancel an activity.

Migraine has a huge impact on the family unit.

Only 3% of respondents said that migraine had no impact on their family or intimate relationships. 48% said the impact was minor, 40% that the impact was major, and 9% said that migraine was the main reason why they had no family or intimate relationships.

We asked participants to describe the impact of migraine on their family and intimate life.

Comments, verbatim, are included in the full report. Common themes include the following:

1. Inability to care for children during a migraine attack, requiring the help from another person.
2. Financial repercussions of inability to work forcing the spouse to compensate and sacrifice career decisions
3. Inability to attend social and familial activities, forcing the family to stay at home and miss out on fun times.
4. Lack of understanding and support from the partner and children because migraines are invisible.
5. Difficulty with intimacy as migraine is exhausting.
6. Difficulty engaging in a relationship because of frequent migraine attacks.

Some key questions and responses from the survey are listed below in order to provide insights and feedback from people living with migraines.

Migraine is a negative impact on your family life / intimate relationship.

Migraines influence the family life for most patients as 49% of respondents indicate some level of negative impact. Survey respondents provided detailed comments on the impact migraines have in their relationships.

Some impactful comments include:

- “I deal daily with self-esteem, lack of energy and depression. I have been through cognitive behaviour therapy, which I still suffer with anxiety and stress. Guilt is a huge thing for me.”
- “It is very difficult being in chronic pain. It certainly impacts my mood and ability to function with common tasks such as driving, work and most activities of daily living. This in turn add more burden and often worry for my family.”
- “The impact is huge. My illness makes me very unreliable. I just went on medical leave from work and have difficulty taking care of my family.”
- “Physically and emotionally exhausting! The stress of going to work (nurse) and suddenly having to leave my patients and coworkers is upsetting. The unpredictability of migraine is stressful. The loss of freedom and independence is stressful. This mostly invisible chronic pain is stressful, almost overwhelmingly so.”
- “No quality of life right now. Can’t drive, can’t commit to plans, can’t work. Migraines every day.”
- “I’m just done. It is hard to be positive or see any end to the constant pain. I can’t plan my future or even my day to day and I hate asking for help all the time.”
- “My migraines are the main reason my husband and I do not have children. My husband currently has to work full time outside the house to support us since I am not working.”
- “Depression that accompanies migraine affects my personal relationships in that I avoid a lot of contact, I pretty much isolate myself.”
- “Migraines control every aspect of my life. Not an hour goes by where I don’t think about pain.
- Migraines have affected my family and friends and work as I am always in pain. It has caused serious depression including suicidal thoughts that have been treated with medication... not the root problem.”
- “Migraine is slowly destroying my life. I suffer from depression, an anxiety disorder and I often think of ending my life because I am so tired of being in pain, nauseated, vomiting, not sleeping, constantly tired.”

In both surveys, we asked the participants how their migraines impact their family members and loved ones. Full answers can be found in the detailed reports. Partners and children obviously find it difficult to see their mother/father/partner suffering. The fun aspects of family life are decreased because migraine sufferers must make up for lost time being in pain and catching up on work and chores. In more severe cases, survey responses indicated couples may decide not to have children because of migraine or be financially very restricted due to living on one salary. We have included a few comments participants shared about impact on family:

- “Financial. Husband bears brunt of all household and financial burden. Lost our home due to my inability to work.”
- “My family misses out on time with their mom, wife, daughter, sister.”
- “I literally cannot parent my child effectively. My husband and I are consistently facing troubles in our relations as we cannot connect because I am frequently ill. He doesn’t understand how to be a partner to someone who is well as there is little support out there for people in his position. I cannot build new relationships with friends, we cannot go out on

- “dates” as planning anything requires a babysitter, etc..and if I have a migraine all the money for nothing. This is huge.”
- “Lack of financial support from me as I’m off sick a lot and worried I may have to go on disability due to my migraines. Affecting relationships because I’m sick more times than not to the point of blindness (auras) being unstable on my fee, vomiting and diarrhea from the pain and meds.”
 - “Frustration and fatigue of hearing me complain. My husband does all the housework and cooking because I am often suffering. I cannot be the mother I want to be, and planning things is difficult as I never show if it is going to a bad migraine day that day.”

Migraine has a huge impact at work.

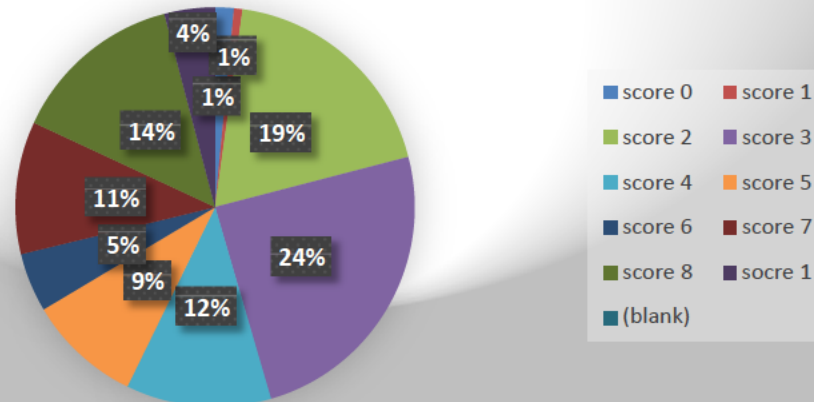
When patients miss work due to chronic pain, these missed workdays are labelled “absenteeism”; however, patients with migraine headaches often still show up to work, even though they are debilitated from the pain, a concept known as “presenteeism”. Migraine patients therefore suffer lost productivity when migraine frequency is poorly controlled, therefore “missed days at work” or “absenteeism” is not sufficient to measure the true financial burden of migraine sufferers. This crucial concept of “presenteeism” must be taken into consideration when assessing the cost-effectiveness of a migraine preventative pharmacological agent; it also helps us understand why for many migraine patients, it is unacceptable that, when they are migraine free, they continue to suffer from adverse medication side effects, such as cognitive impairment, drowsiness, and fatigue, as seen with topiramate, antidepressant tricyclics and betablockers.

Considering that the majority of migraine patients suffer from episodic and not chronic headaches, patients do not suffer a higher rate of comorbid disorders, such as depression, anxiety, bipolar disease, insomnia, epilepsy, hypertension, obesity, or angina in comparison to the general population. In fact, they are predominantly women under 50 years old, otherwise healthy and contributors of society’s workforce.

Survey results clearly demonstrate the impact of migraines on ability to work. On an 8-degree scale (see graph), 25% of participant were disabled and unable to work, 26% worked part-time or missed 3 or more days of work per month, 25% missed 1-2 days per month, and 25% did not miss work (but were still impacted in their personal life).

Only 1% chose the option <<I have no limitations>>.

Please rate the impact of migraine on your life during the last 3 months. If you are disabled by other health conditions than migraine, you may still choose the statement that reflects best your overall level of disability.



Legend

- score 0: I have no limitations
- score 1: I avoid triggers, but otherwise I function well
- score 2: I miss some personal activities, but I don't miss work
- score 3: I miss work (including childcare and home-making activities) on 1-2 days per month
- score 4: I miss work (including childcare and home-making activities) on 3-4 days per month
- score 5: I miss work (including childcare and home-making activities) on 5 or more days per month, but I am still working full time
- score 6: I work part-time
- score 7: I am disabled (not working), but can still do some desired activities
- score 8: I am disabled (not working) and dependent on others for many activities of daily living

Migraine can lead to anxiety and depression.

80% of participants stated that migraines led to anxiety or depression (mild for 46%, moderate or severe for 34%). This complicates life even further for those living with migraine as evidenced in patient feedback. Comments from survey respondents include:

- *"It limits our time together and our connection. It drastically limits the activities we can do together. It causes stress, anxiety, depression, guilt, anger and frustration."*
- *"I have missed out on several family functions in the past 15 years due to migraines. This has had a very negative impact on my life causing depression, and loneliness. It has negatively impacted my relationship with my spouse of 19 years as I never want to go anywhere because I always have a migraine."*
- *"I am too physically and emotionally exhausted from being "on" for others at the end of the day to even speak with my husband. I help with my 2-year-old daughter but even that's a struggle. My husband and I rarely see each other or have any time alone. We are rarely intimate. It is a struggle. We are seeing a psychologist to help with this."*

- *“Chronic migraine has turned my wife's life upside down. She suffers with bouts of depression, anxiety, and even suicidal thoughts. I can't even begin to be imagine the pain she suffers on an almost daily basis.”*

Migraine is stigmatized.

As an invisible disorder that affects women and is associated with psychological symptoms (that may be consequences of the chronic pain), migraine is stigmatized. Survey respondents shared the impact of stigmatization in all aspects of life. There is no objective diagnostic test for migraine, blood work or imaging, and that leads to a significant amount of skepticism from the social network, employers and even health care providers. Because migraine sufferers are often unable to perform activities without being able to show a proof of their condition, they end up being blamed and they develop significant guilt and even shame. Instead of getting the care and support they need, and that is provided for patients suffering from other conditions like cancer, diabetes, or epilepsy, they may be forced in social isolation.

Survey comments highlight the feeling of isolation and lack of understanding about life with migraines:

- *“It is invisible. It is stigmatised. It isolates and diminishes you. Constant pain symptoms from migraine wear on the body and soul. You are trapped unable to escape or explain. Unable to live your life or enjoy simple moments.”*
- *“He does not suffer from migraines or even get headache. He does not understand how debilitating they are.”*
- *“I am very alone. No one can even begin to understand how migraine feels unless they've experienced one. I live life with depression and extreme anxiety. This is no way to live. Any medication that can even improve people's lives a little bit should be accessible”.*

Patient 1: when the condition is uncontrolled, the result is daily migraines which require the patient to take multiple medications to make it through basic daily tasks including excessive amounts of triptan medications and opioids to combat/manage the pain. Sometimes even with the use of these medications, the patient finds himself unable to complete basic daily tasks – unable to work at times, very frequently unable to assist with childrearing due to exhaustion due to trying to make it through a work day, unable to participate in household chores/hobbies/social functions. Patient describes life as basically miserable and not worth living.

Most important aspects of the illness to control: frequency and severity of the migraines (and associated pain)

Patient 2:

Life before Emgality

My migraines started in year 2 of my university degree and gradually got worse, so much so, that I had to take a break from my studies to return living with my parents' to be cared for as I could no longer take care of my basic needs. I spend most days stuck in my dark, quite room bedridden in pain unable to do anything because of my sensitivity to light and sound. Due to the constant nausea from the migraines my relationship with food deteriorated. Finding food, I could stomach was a challenge, and I began to hate mealtimes. I hated eating and I struggled to maintain my weight. My mental health during this time was at an all time low. I did not see the point in living if I was not able to even have a life. I felt tormented and imprisoned in my own room by my own body with no hope for a life I felt had just started. A University degree had been my life dream and I had worked so hard to get there only to have migraines take it away from me. Everything good in my life migraines took away. There was no way I would ever be able to return to university, get a degree, get a job, travel, and see the world, meet people and maybe even get married if I could never leave my room. My anxiety over migraines got to the point where I was scared to leave the

house, as I had no way of knowing if while out, I would have a migraine attack and be unable to get myself home safely. I didn't attend any social events with friends as I either had a migraine, or was too scared I would get one while out and would become a burden to my friends and ruin the fun time. I lost friends due to my lack of ability to socialize and stay in touch. When I did leave the house, I preferred to go with someone who could drive me as I became scared that I would have an attack while driving and cause an accident. If I did leave myself, it was a short and quick trip. Migraines caused a lot of fatigue even on days when I did not have one. I remember that if that I got 3 pain free days in a row with no fatigue, I genuinely felt spoiled. A week of pain free days and it felt like I won the lottery. Then it would all be taken away by another migraine, causing me to not even want to hope for better days. It was easier to live in constant misery than to be given a glimmer of hope only to have it ripped away. During this time, I was trying all the standard prescribed migraine medications which were all ineffective and/or intolerable. I relied on strong painkillers to get me through the days which after years of chronic use caused other health complications.

4. Experiences With Currently Available Treatments

The efficacy of currently available oral preventative treatments is completely insufficient. Furthermore, although when comparing monoclonal CGRP antibodies to placebo we only see approximately a two-day difference, which is similar to current conventional oral preventative drugs, we fail to recognize the spectrum of responders and we fail to acknowledge the 75-100% patient responders across the responders to CGRP monoclonal antibodies, including in long term studies up to 5 years, which is a striking benefit that has not been reported with any of the conventional oral preventatives.

Side effects are a major issue for patients and cause for discontinuation of preventive medications. Among participants who had tried oral preventives, 68% had experienced a side effect leading to the discontinuation of the drug.

In the 2018 cohort, 22% had tried 1-2 preventives, 22% had tried 3-4 preventives and 45% had tried 5 or more. Only 11% had never tried a preventive. It is important to note that this survey did have a high proportion of participants suffering from chronic migraine, who were referred to our survey via support groups and migraine clinics, and, therefore, who are diagnosed and being treated for migraines.

Moreover, other members of our online community having benefitted from the CGRP monoclonal antibodies are patients who were under patient support programs (Novartis and Eli Lilly); these were patients suffering from at least 8-month migraine days and having failed at least 2 conventional oral preventative medications. We cannot define responses from those patients who are living with migraines but not benefitting from appropriate diagnosis and treatment. However, the survey population is aligned with potential candidates for Emgality.

Patients are told that there is no cure for migraine, and that a 50% improvement in frequency and intensity should be acceptable. Even with such low expectations, it is disappointing to see that 74% of them did not find at least a >50% improvement, which is the usual outcome proposed by physicians for migraine prevention. Only 6% reported a 75% improvement with a preventive they tried.

Mentioned above, side effects are a major issue for patients and cause for discontinuation of preventive medications. Among participants who had tried preventives, 68% had experienced a side effect leading to the discontinuation of the drug. 25% reported side effects that were tolerable,

and only 7% said they did not have side effects. The most commonly reported side effects were somnolence (76%) and weight gain (54%), dizziness (58%), gastrointestinal upset (45%), mood difficulties (44%) and cognitive difficulties (53%). Quotes such as “do you prefer to be fat and drowsy or thin and stupid” are known in the migraine community when patients are faced with choosing amongst currently available migraine preventative medications. A better tolerability profile was evoked in many comments on what a good preventive should be (see next section).

Along with insufficient medication treatment options, patients also have limited access to care for migraine. Wait lists to see a neurologist or headache specialist are more than one year for 27% of patients. Satisfaction with care was surprisingly low. 54% of participants stated that they were very dissatisfied or dissatisfied with the care they received from their physicians (general practitioner or neurologist). They described no improvement (33%) or mild improvement (49%), only 14% were markedly improved.

In assessing cost-benefit ratio when comparing currently available oral preventative medications to new CGRP monoclonal antibodies, health authorities make two fundamentally wrong assumptions: patient comorbidities and a 100% adherence.

A key element that should be taken into consideration when comparing various prophylactic agents is the rate of adverse reactions, especially when these reactions are harmful to members society’s working class. A more just representation of these agents when comparing would have been to list potential adverse events and rate of occurrence. There is a stronger likelihood of these adverse events occurring than a migraine patient suffering from the comorbidities listed.

In that manner, we could imagine that it would cost society more to address a patient suffering lost work productivity from cognitive impairment caused by topiramate, depressive symptoms and fatigue by a betablocker or weight gain by an antidepressant, in an otherwise healthy migraine patient who did not suffer any of the comorbidities and who’s unique objective was headache reduction, in order to be more functional.

None of the currently available oral agents are better tolerated than this class of medication specifically designed for migraines. We believe that oral preventative drugs currently used for migraines benefit from an unjust comparison pedestal versus monoclonal antibodies, as they were approved by health authorities decades ago without undergoing rigorous criticism in regard to their poor effectiveness-tolerability ratio and, other than topiramate, their effectiveness in chronic migraine has not been proven but rather extrapolated from their benefit in episodic migraine.

Furthermore, the cost effectiveness table presented assumes a 100% adherence looking at a monoclonal antibody and conventional oral preventatives. This assumption is intrinsically false as the rate of dropout from studies of conventional oral preventatives far exceeds the less than 2% drop out rate of the CGRP monoclonal antibodies specifically designed for migraines, including in long term studies up to five years.

We’ve included some comments from patients about the current treatment they are on:

- *“I am not managing very well; my Chronic migraines are very debilitating. I use Zomig, Amitriptyline, Topamax, Emtec, some Advil and CBD oil”.*
- *“Nothing preventative has worked. Almotriptan and Toradol IM make the pain manageable but it’s still quite difficult to perform at work.”*
- *“Emgality has been my miracle drug after trialing every other treatment available. While I still have daily headaches, it has helped reduce the severity.”*
- *“Not very well. I’m on medical leave from work (1.5 years now). Still intractable (24/7) and abortive meds minimal work.”*

- *“Struggling! Now on CPP and LTD from work. I never have a migraine free day. My new neurologist is helping me to try different medications to see if we can something that will make them manageable.”*
- *“Not well at all. I have daily migraines and can barely work. Amitriptyline is not working anymore which is why I am currently looking into injection types of treatment recommended by my neurologist but a lot so them are not covered by my insurance or pharmacare.”*
- *“Not well. I’ve tried several preventatives and abortive medications as well as alternative therapies and still haven’t found a solution for my migraines.”*

Comments provided from people who are on a CGRP include:

- They are a godsend to those who have had migraine relief with them. The costs makes them unavailable to many unless they have a private insurance plan. Side effects for some migraineurs make it impossible to take them even if they provide relief
- Once a month injection is very convenient and its so wonderful not to be dulled by excessive pain meds all the time. Side effects for me are non-existent.
- Advantages are getting migraines under control with only one dose a month. Feel better in-between migraines. Only disadvantage is access to them and cost.
- Worked for me when nothing else worked. No side effects.
- Ease of use. Drastically reduced the number of severe migraines.
- Life changing. Gave me back my life.

Patient 1:

- Prior to being on Emgality, patient was very poorly managed with current treatments – control of pain at best and typically once pain controlled by triptans and/or opioids, the side effects of these options make it impossible to live a normal lifestyle (triptan side effects: burning/tingling in hands and feet, muscle weakness, overuse of the medication makes it less effective or can put you into a medication overuse headache, frequent urination and urine leakage, extreme irritability, not wanting to be around other people. Opioid side effects: drowsiness, unable to drive and unable to work or really do anything). No other available prophylactic options have worked to reduce the frequency and severity of migraines.

Patient 2:

- Tried all the normal prescribed medications that were ineffective and not well tolerated.

5. Improved Outcomes

We asked specifically what a meaningful, successful outcome for a preventive therapy would be. Unfortunately, survey participants do not have an expectation for a cure and seem ready to accept virtually any degree of relief. Many have mentioned that work is important to them, and a good preventive would help them to be more productive at work and with their family. Side effects are a significant concern. Affordability has been mentioned in many comments.

A small sample of patient feedback includes:

- *“If I had access to a preventive that I could take only once monthly, I would be thrilled.”*
- *“I would like something that has minimal mental side effects (I have reduced mental capacity and mental clarity on my preventative, and I really hate that I feel 'stupid' now when I know I'm capable of better/more). “*
- *“Anything that would help not have a chronic migraine would be amazing.”*
- *“I need something that will reduce frequency and intensity so that I can resume my professional activities. That's all.”*

- “Anything that would allow me to live a fruitful life — return to work, keep a relationship, allow me to see friends and family on a regular basis, allow me to go to events.”
- “Anything that would give me relief enough to have somewhat of a normal life. It would be nice to be able to spend time with friends and family, to be able to look after myself and my home, to be able to go for walks and be able to enjoy the outdoors and sunshine.”

Patient 1:

- New treatment: reduced frequency and severity of headache, reduction or elimination for need to use triptans/opioids, general improved quality of life with minimal side effects.
- Change to daily life: increased ability to participate fully in activities and daily life which includes participating in hobbies and extra-curricular activities, Improvement in relationships both inside and outside the family unit, ability to fully participate fully at work (reduction in use of sick days), reduced exhaustion due to just trying to muddle through life in pain or muddle through life battling the side effects of the medications that reduce the pain.
- Trade-offs: consider what are the side effects vs. benefits, what is the cost vs. benefit and can I afford it?

Patient 2:

- Improved outcomes would be any improvement in my quality of life pre Emgality.
- The ability to participate in activities and daily life would be amazing. Less fatigue from the migraines resulting in more energy on migraine free days to do things.
- Before Emgality, pretty severe nausea from the migraines and struggled to maintain a healthy weight. Less nausea, less side effects would be amazing.

6. Experience With Drug Under Review

Access to research protocols for migraine is limited in Canada. There are few headache specialists, many Neurology departments do not even have a dedicated Headache Clinic, and many headache specialists choose to practice in private outpatient clinics that allows them the flexibility needed for their practice. As a consequence, Canadian migraine sufferers cannot easily participate in clinical trials. Among people who were interested in participating to clinical research, 40% did mention it was impossible for them, and 22% said it was difficult. Only 17% said it was acceptable or easy to join a clinical trial.

We asked participants if an injectable form was acceptable, and 73% of them said they would prefer a monthly injection to a daily pill.

From the survey circulated in May 2021, 40% (36 respondents) have experience with Emgality

- “I am on Emgality and since I started this medication, I am 99.5% migraine free monthly injection.”
- This past year on Emgality has been life changing. I am functioning well at work, my sick time has drastically improved. My mood is upbeat, I look forward to life so much more without constantly feeling like I can't do the things I enjoy. I feel more reliable and pleasant to be around
- Benefits were awesome, my migraines severity went down. I went from daily migraine/headache to 9-10 Free Days!! Severity I rank from 0-5 I went from average of 3-5s to 1-3 with only a few 4 or 5. The BIG disadvantage was vertigo. The last month I took Emgality I lost 15 pounds due to vertigo...vomiting and unable to eat. It was a 17 day straight, some days needing my husband's help me walk just to use the washroom.
- Convenient, effective, once monthly verses daily
- Over 60% reduction in chronic migraine, no side effects. Has given me my life back.
- I am almost migraine free. Only one shot a month instead of daily pills
- Big reduction in migraine days and better response from acute meds when needed

When asked how did the benefits or disadvantages of Emgality impact your life or your caregiver/families lives we've included some examples of themes:

- “Less time in bed in the dark, less emerg visits, less medication.”
- “Greatly improved by quality of life which in turn has made my families lives happier”.
- “Was able to start having day swihtout migraine and symptoms. However, the possibility of having to stop treatment due to cost is very stressful”
- “They are so happy I finally found something that worked, and I can actually be a mom, daughter, wife that I've always wanted to be.”
- “My husband and my son are elated at the difference because I am able to be more present in our family and participate in activities that were impossible before my first Emgality shot. The symptoms get better with each subsequent injection as well.”

The majority of people who have experience on Emgality seemed to have few or no side effective and were tolerated.

- “Not really, nothing too noticeable.”
- “Some increased dizziness in the first week and a lit bit of constipation but very well tolerated.”
- “Constipation and managed pain/tenderness at site of injection but goes away after a few minutes.”
- “Side effects were minor and tolerated.”

Compared to other therapies, comments about Emgality were fairly similar:

- “The monthly injections were easy to administer myself.”
- “More convenient.”
- “About the same.”

- “Yes, because it’s just once a month and don’t have to do something every day. Also, I think it absorbs better especially since a lot of people with migraine have GI issues and the meds might not be absorbing.”
- “Once month shots are convenient.”

Patient 1:

- Access to drug under review: via prescription from neurologist and with help from the Eli Lilly patient support coverage
- Benefits: It actually works. It’s the only prophylactic medication that has had sustained and consistent benefit for reducing this patient’s migraines. It has dramatically reduced the frequency and severity of migraines from daily to occasional (once or twice per month, and at worst it is 2 – 3 times per week during a bad allergy season (an unavoidable trigger for this patient). The migraines are less severe and have enabled him to reduce his effective dose of triptan to one half or one quarter of his previous dose to get rid of the migraine which has resulted in less side effects from the triptan as well (such as reduced irritability, improved concentration and stamina, less nerve pain, still able to exercise and do other activities when needing to use a lower dose of the triptan).
- Disadvantages: no disadvantages, no negative side effects – perhaps only disadvantage is worrying about how patient will be able to afford the Emgality if it is not added to the provincial formulary
- Only side effect experienced from Emgality is very minor injection site pain for about 20 seconds after a dose. The patient states that it is significantly easier to use than other medications he has been prescribed in the past as he can easily administer to himself at home and doesn’t have to go to his neurologist’s clinic for it to be given.
- This drug is most likely particularly helpful for those who have a significant amount of migraine headaches where you are in a significant amount of pain who have failed on other prophylactic medications.
- The thought of losing access to this medication has caused the patient severe anxiety due to the cost of the medication because he considers it to have literally “brought him back from the dead.”
- Sequence of Treatments: the patient has tried many prophylactic medications over many years including but not limited to:
 - Tricyclic antidepressants: amitriptyline, nortriptyline, doxepin
 - Beta-blockers: propranolol
 - Calcium channel blockers: flunarizine, verapamil
 - Anti-Epileptics: topiramate
 - Botox administered by neurologist – stopped working after about one year with suspicion that patient developed antibodies to the botox
 - Lidocaine nerve block administered by neurologist – had twice and did not work
 - Aimovig – stopped working after about 6 – 8 months with suspicion that patient developed antibodies
 - Other: venlafaxine, magnesium, riboflavin
 - Used Cephaly device along with abortive meds (triptans)
 - Emgality has been working so far for about one year with no reduction in effectiveness and is the only prophylactic medication that is making a difference for reducing frequency and severity of migraine attacks
- The last option that the patient hasn’t tried yet is a more invasive nerve stimulator implant

Summary statement: sustained reduction in frequency and severity of migraine attacks while allowing patient to live a relatively normal life.

Patient 2:

- Accessing Emgality through the patient support program.

- Emgality, even though I don't like needles, is able to easily self-administer at home which is convenient.
- Minor irritation at site of injection for the first 6 or 7 months but doesn't experience it any longer.
- Noticed an improvement within a couple days of the first injection. Pain began to dwindle and then eventually went away and didn't experience anything for 3 weeks vs 20-25 days of migraine prior to Emgality.
- Since the first month, after injection I would be have 3 weeks with only a couple migraines and by 4th week I'd start to experience an increase in migraine frequency and a few days after injection, migraine's free up and don't see same frequency. This pattern has held for 8 months. Being able to increase dosage would maybe be helpful in reducing frequency.
- Emgality has given me back my life. I can take care of myself. I can cook. I can go out and socialize with friends. I feel like I actually have a life versus being bedridden and stuck at home.
- My mental health was not in a good state because I was stuck in my room in pain and not able to do anything. Forced to leave school and move back with parents. My mental health is better now because she is not in pain all the time, I have more energy, less fatigue. I have a better perspective on life, and am more hopeful about the future.

7. Companion Diagnostic Test

There is no companion test for migraine diagnosis for Emgality prescription.

8. Anything Else?

Migraine Canada and Migraine Quebec represent and speak on behalf of patient across Canada. We hear from patients on a daily basis how hopeful they are to know there are new effective medications now available in Canada that may help them.

We are concerned that the new biologic treatments for migraine will not be reimbursed in part because migraine is stigmatized, unrecognized and not understood. As stated in the World Health Organization's Atlas of Headache Disorders and Resources, migraine patients are underdiagnosed and undertreated. Migraine is a severely neglected chronic illness in comparison to other diseases, such as diabetes, epilepsy, or multiple sclerosis, and is associated to significant years lost to disability.

Canadians living with migraine are desperate to find a treatment that may improve their quality of life. Until a cure is found, patients are looking for improved outcomes. Many are desperate to have any degree of normalcy returned to their lives. New treatment options may allow patients the ability to return to work, interact with their family and friends and feel like they are contributing to society.

We strongly believe a positive recommendation for Emgality will lead to reimbursement of novel CGRP monoclonal antibodies. Favourable societal cost-effectiveness outcomes will be realized, especially when considering that the migraine population is a younger pain population and a strong contributor to the workforce.

Moreover, considering that 80% of migraine sufferers are low frequency episodic sufferers, coverage for Emgality would only be applicable for the 20% minority of migraine sufferers, 15% are high frequency episodic (8-14 monthly migraine days) & 5% are chronic (≥ 15 monthly migraine days).

Canadians are hopeful to access new treatment options approved by Health Canada. When asked how might daily life and quality of life be different if the new treatment provides you with desired improvements, some comments included:

- “If a new treatment worked for my chronic migraines in either less attacks per month or less severity, it would change my life for the better in every way in positive changes for a change to live rather than trying to survive life with chronic migraine.”
- I can’t even imagine how much better my life would be if a preventative migraine treatment worked for me. I would have more money. I’d have a better outlook on life. I’d be less because because I’d actually be able to be contributing member of society. People wouldn’t call me useless or a faker anymore. My family would be better able to identify with me. My fiancé would be able to rely on me. My stepdaughter wouldn’t think I’m dying all the time.”
- “I can be in school full time and obtain my university degree. I can hang out with friends and have less anxiety and overall stress about being in pain.”
- I was considering medically assisted euthanasia before Emgality. Quality of life has improved dramatically since Emgality, has made life possible again.”
- My life has completely changed since starting a CGRP. I haven't missed any work, I haven't had to work while dealing with a screaming migraine and nausea, I have started making social plans because I am not afraid, I will have to cancel.
- I might be able to actually live - go back to work and school. I could get off disability. I could visit with friends and not worry about “overdoing it”. Go to church, volunteer again doing things I love.
- CGRP’s have the potential to be lifesaving. I have no other treatment options available except brain surgery. Without effective treatment I rapidly become suicidal, and it is highly likely I would take my own life. CGRP’s have the potential to enable me to live my life to the full, continue with my career and enjoy my time with my family and friends. It has also enabled me to start exercising again. It would increase my happiness level so much. I could plan activities with abandon and not be afraid. I could wake up each morning without the dread of wondering if this is going to be a migraine day. I could get together with friends and socialize to my heart's content without getting a migraine. I could exercise as hard or as much as I wanted without getting a migraine. I could go out to eat with ending up with a migraine. Lots more, but that's enough.”

Patient 1:

- This drug has changed the patient’s life – going from literally contemplating suicide at times to actually living life again. It is a ‘miracle drug’ as the patient is actually able to participate in relationships, child rearing, daily activities, hobbies, etc and is not continuously fighting a battle between continuous pain or terrible medication side effects.

Patient 2:

Life After Emgality

- It didn’t take long after starting Emgality that I noticed a drastic change in my migraines. For the first time in years, I felt like there was hope for a future. I got a part of my life back. I could start doing all the little things that most people probably take for granted. I could cook a meal and eat it, do my own laundry, and leave the house without all the fear and anxiety of having a migraine attack. While that is still a possibility it no longer scares me as it did before. Migraines robbed me of all of life’s little joys but Emgality has given some of those back to me. I can engage in hobbies like music, something I loved before migraines but could not do because of my sound sensitivities. I was able to start an aquarium, get house plants and keep up with the maintenance. Little things that migraines and the fatigue did not allow me to have energy for. But those little things have brought joy into my life. I have since been able to live on my own and finish my degree and I have hope that I can enter the work force part-time, things I didn’t think I would ever be able to do.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

Migraine Canada and Migraine Quebec collaborated on the submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Patient surveys were posted online. The survey from 2018 was managed by a third party vendor (3ALogic) who managed the data collection and collation of the raw survey data however; Migraine Canada assessed the results.

The recent survey launched in May 2021 was managed entirely by Migraine Canada.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Migraine Canada and Migraine Quebec both receive funding from manufacturers for program delivery and resources development. Neither organization receives any funding for time and expense related to gathering data and preparing patient input submissions.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Allergan/Abbvie Canada			√	
Novartis Canada			√	
Eli Lilly Canada			√	
Teva Canada			√	
Miravo Healthcare Canada			√	
Lundbeck Canada			√	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Wendy Gerhart
 Position: Executive Director
 Patient Group: Migraine Canada
 Date: June 28, 2021

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Novartis			x	
Allergan/AbbVie			x	
Eli Lilly		x		
Miravo	x			
Lundbeck			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Louise Houle
 Position: Executive Director
 Patient Group: Migraine Quebec
 Date: June 28, 2021