

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Erenumab
Name of the Patient Group	Migraine Canada Migraine Quebec
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1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Migraine Canada is a national 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. Our work is carried out by our volunteer Board of Directors, consisting of patients and healthcare professionals.

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 1,000 members of our Facebook page and by playing a role with various other online groups. We leverage traditional and social media to empower patients to share stories and experiences in order 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/>

We partnered with these groups for survey diffusion:

Website(French): www.migrainequebec.com

Partage Migraine Québec (French, private)

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

Migraine Warriors Calgary (English, private):

<https://www.facebook.com/groups/355353438279969/>

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Answer

We wanted to provide input from a wide number of patients and therefore, we used an online survey method. The survey was designed and analyzed by the volunteer Board members of Migraine Canada. It was promoted on our Facebook community, shared on Migraine Canada's Twitter account and through migraine clinics in Canada. The survey was open online from June 4th to July 4th, 2018. A total of 597 patients participated in the survey.

Table 1: Demographics of survey participants

Age	0-25	26-39	40-54	55-69	70+
% of the population	5	34	46	14	1
Gender	Female	Male			
	93	7			
Headache frequency	1-6/month	7-14/month	15+/month		
%	26	32	42		
Work status	Full time	50	Short term disability		6
	Part time	10	Long term disability		16
	Homemaker	4	Other		7
	Retired	7			

The majority of the 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.

We have included patients' quotes to ensure their voices are captured in this report and to provide context for quantitative elements. A report capturing all patient comments is also available for review.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Answer

Migraines are not just headaches but a neurological disease. Migraines 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 but 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.

Migraine is usually categorized according to particular 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 interactions 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. Cognition is not normal during a migraine, with slowed thinking, lack of focus, and difficulty reading and speaking. This would disrupt most activities involving a computer or interacting with other people. A controlled migraine attack can be brief, but uncontrolled attacks may last multiple days in a row.

15% of migraine patients 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 of those 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.

The quality of life of migraine patients is also lowered during the interictal state. Survey respondents indicated in their comments that they fear the next attack, and have difficulty planning ahead. Migraine sufferers end up dreading potential triggers and limiting their activities (personal and professional) to either avoid an attack or avoid blame for having to cancel an activity.

Migraine has a huge impact on the family. 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. Full comments can be found 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:

- “Made the decision long ago to not have any relationship or children because I believed that it wouldn’t be fair to either one. I also did not want it on my conscience that my child would be crippled with migraine.”
- “We hesitate to make plans and often have to cancel and stay home. My husband sometimes needs to come from work and finish the tasks I did not get to during the day. And take care of the kids. Sometimes he needs to miss work to watch the kids or find other childcare.”
- “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.”
- “I have missed major family functions much to my disappointment and the family. I was forced to take early retirement due to my sick time with migraines. My grandkids and great grandkids know when I have one. They know they have to be quiet and the older ones know not to wear perfumes or cologne as it will worsen the head. When my husband was alive he would sleep on the couch so as not to disturb me in bed.”

We also asked the participants to request input from a loved one about their state. Full answers can be found in the full report. 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. Survey feedback captured by loved ones include:

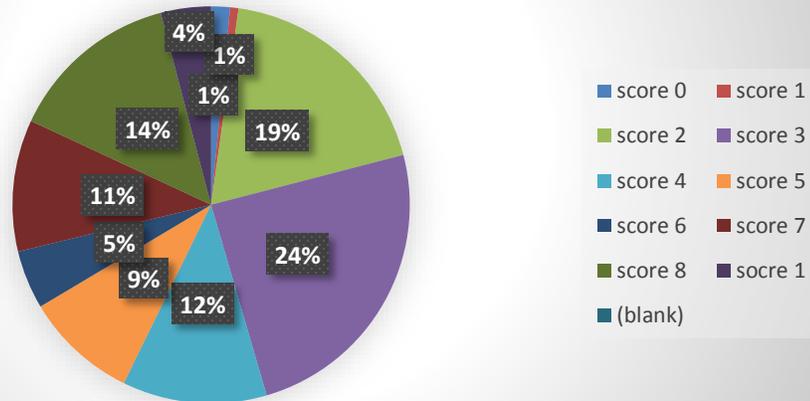
- “I wish I had my old life back with my normal fun mom who can do anything and everything and is always happy.”
- “My wife and I do miss out on time together because she has to go to sleep. I’ve had to go to family functions without her and many times take the children to all activities and school because she just can’t.”
- “We do not do fun things because mommy can’t do it.”

Migraine has a huge impact at work.

Survey results clearly demonstrate the impact of migraines of ability to work. On an 8-degree scale (see graphic), 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 child care and home-making activities) on 1-2 days per month
- score 4: I miss work (including child care and home-making activities) on 3-4 days per month
- score 5: I miss work (including child care 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 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.”

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Answer

In this 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. 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 erenumab.

The efficacy of currently available treatments is completely insufficient. 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.

Side effects are a major problem and cause for discontinuation of preventive medications. Indeed, among participants who had tried preventives, 68% had experienced a side effect leading to the discontinuation of the drug. 25% did report side effects that were tolerable, and only 7% said they did not have side effects. Somnolence (76%) and weight gain (54%), dizziness (58%), gastrointestinal upset (45%), mood difficulties (44%) and cognitive difficulties (53%) were the most commonly reported side effects. 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.

A comment reflective of patient feedback is:

- “My neurologist is trying to get me see at the CHUM Headache clinic (university center headache specialty clinic), but it is a long and frustrating process.”

5. Improved Outcomes

CADTH is interested in patients’ views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Answer

We asked specifically what would be a meaningful, successful outcome for a preventive therapy. 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. 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.”

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

Answer

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.

Only seven survey respondents had been involved in one of the erenumab clinical trials. Two stopped before the end of the study, five completed the study. Only two patients knew that

they had received erenumab. One patient responded 50%, and the second patient responded 75%. None reported side effects.

One patient who received erenumab sent us this comment:

- “It gave me my life back for 15 months, I didn't worry about having meds with me or if I was going to have to cancel plans. I lived.”

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

- “I don't like having to take a pill every single day in order to prevent a few migraines per month. If it was a once per month medication, even injectable, would be more acceptable in my opinion.”
- “I'm beyond thrilled that there is something finally on the market soon that is designed for migraine sufferers. Me personally I do not care how I have to receive the medication orally or through injection I am just over the moon that this is designed specifically for migraines that in itself makes me happy.”

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

Answer

There is no companion test for migraine diagnosis or erenumab prescription.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Answer

We have a significant concern that the new biologic treatments for migraine will not be reimbursed in part because migraine is stigmatized and unrecognized. 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.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, 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.

No.

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.

Our patient survey was posted online by our webmaster Jonathan Guay from 3aLogic. He also collected and collated our raw survey data however, Migraine Canada assessed the results.

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.

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 Canada via Canadian Headache Society			√	

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: Beth Kidd

Position: Director, Board of Directors

Patient Group: Migraine Canada

Date: August 24, 2018