

CADTH COMMON DRUG REVIEW

# Patient Input

**FREMANEZUMAB (Ajovy)**

(Teva Canada Innovation)

Indication: Migraine

CADTH received patient input from:

**Migraine Canada and Migraine Quebec (joint submission)**

May 20, 2020

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## Patient Input Template for CADTH CDR and pCODR Programs

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|--|--|
| <b>Name of the Drug and Indication</b>                 | <b>Fremanezumab (AJOVY)</b>                    |
| <b>Name of the Patient Group</b>                       | <b>Migraine Canada<br/>Migraine Quebec</b>     |
| <b>Author of the Submission</b>                        | ██████████<br>██████████████████<br>██████████ |
| <b>Name of the Primary Contact for This Submission</b> | ██████████                                     |
| <b>Email</b>   | ██       |
| <b>Telephone Number</b>                                | ██████████                                     |

### 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 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. We leverage traditional and social media channels 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.migraine canada.org](http://www.migraine canada.org)

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

We partnered with these groups for survey diffusion:

Website(French): [www.migraine quebec.com](http://www.migraine quebec.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 gained insights from patients through an on-line survey that was promoted through our 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.

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 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 and to provide context for quantitative elements. A comprehensive 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 are 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. 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 attacks 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 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 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 exhaustion 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:

- “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.”
- “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.”
- “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 2year old daughter but even that's a struggle. When she goes to bed at 8-8:30pm, so do I thus, 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.”
- “Migraines have ruined my life... on a score of 1-10 describing frequency and intensity, mine is a 10 on both counts, with 10 being the most painful and daily frequency.”
- “Having chronic intractable migraine has had devastating effects on my marriage. I am unable to do many things we used to enjoy together and as a result there is distance between us. My husband is usually out

pursuing his interests and I stay home where it is quiet & calm. And of course, there is the financial difficulties caused by my inability to work. Another issue is not being able to keep up with housecleaning, cooking, laundry etc. Also, my migraine has significantly increased my depression which is another negative effect on our relationship.”

- “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.”

We also asked the participants to request input from a loved one about their state. Full answers can be found in the detailed 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.”
- “It’s hard to see my wife in pain all the time, to be around her and be powerless to do anything about it. To see her not enjoy life.”
- “Her migraines have an intimately personal impact on my life because I care so much about her, and I don’t want to see her hurting, and I feel powerless to help. I can offer her things like Advil, ice packs, making the room dark and quiet, but that’s it. It sucks. I just wish there was something more to offer her, so she wasn’t suffering all the time.”
- “I miss my wife and our friendship and intimacy. She goes to bed early leaving me alone at night where I have been playing video games. We feel more like roommates now. I feel so terrible for her because she’s always in pain, but it has left me on my own too.”
- “I watch my wife struggle 20 plus days per month with the pain and disability of migraine. She has tried so hard over the years trying countless medications and seeing the best specialists without much success. I want to be able to explore the world together, make plans, and have her have a fulfilling life both personally and professionally. I am frustrated that I can’t do more to help.”
- “Migraines impact my wife greatly. She has trouble just doing daily house cleaning or cooking meals. She cries a lot when she is in pain or so dizzy, she can’t even go anywhere. She tries to avoid triggers and tries to stay calm, but her migraines still persist. My wife’s migraines affect me because I feel sorry that she is always dizzy or in pain. It hurts me when she cries for days. There are many things we would love to do together, but she hates making plans in case her migraines will ruin them. She needs to try these new drugs! She suffers too many days per month”.
- “I am [REDACTED] husband. I care for her daily and work from home to better be able to accommodate our life. I cook all our meals, do all household chores, and all activities that require any lifting or repetitive movements as that is a trigger for her migraines, She is often bed-ridden for many days at a time and in agony. The drugs she has tried thus far, as well as interventions, have not been significantly helpful. We are exhausted as a couple and constantly in crisis mode.”
- “A lot of extra pressure to be the major breadwinner of the family. A lot of frustration at being helpless to help partner, a lot of frustration at the inefficiencies of the health care system that fail to help migraine patients, a lot of frustration that my wife’s health isn’t better both for her and us and our family.”

- “Watching the person, I love most, the strong man I fell in love with, suffer day after day, in pain, unable to do things he enjoys is unbearable. Seeing how these terrible headaches has stolen his life, our life is just sad. Watching him try treatment after treatment with no real relief is sad. Being unable to vacation, go out to dinner, garden or simply enjoy time with our children and grandchildren because Papa has another headache has made our lives unbearable at times.”

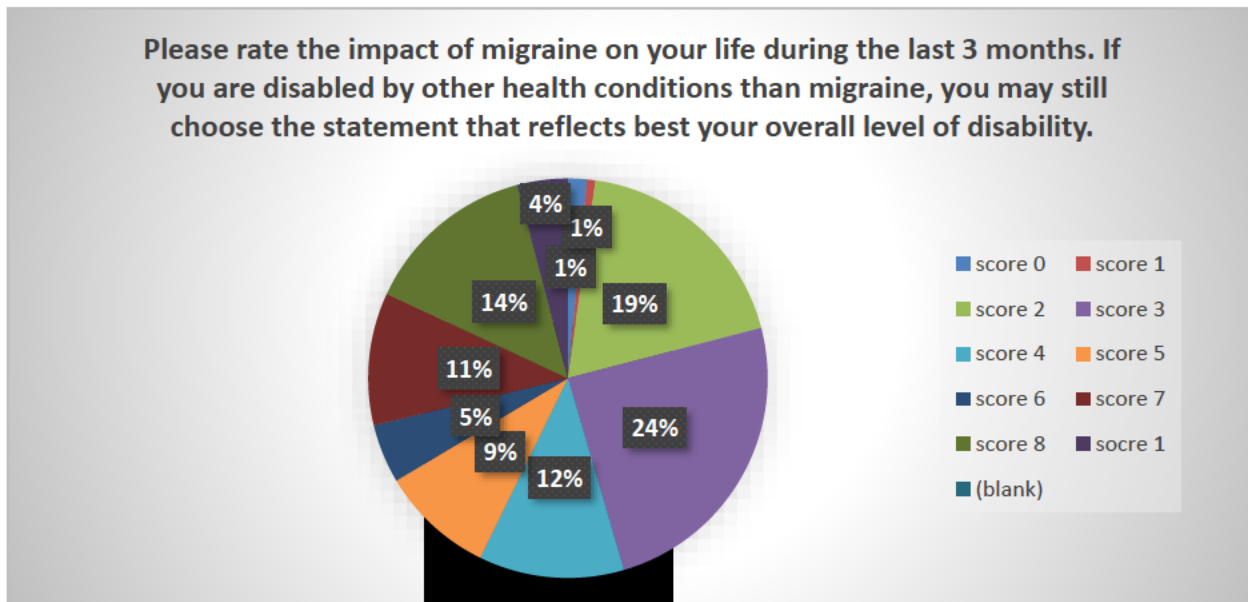
### Migraine has a huge impact at work.

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».



### 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 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

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 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.

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 fremanezumab.

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.

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.”

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.

## 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 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."

## 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.

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."
- "If I had access to a preventive that I could take only once monthly, I would be thrilled."
- "I would just love to be able to stop having to take so many pills. I take at least 2 boxes (12 pills) worth of GD-Eletriptan, plus countless amounts of Advil, Tylenol, etc. per month. I know this is not good for me, but right now, it's my only option. I would absolutely love to end this by only need a monthly injection."
- "Something that brings the frequency of the migraines down to manageable level (would be overjoyed with it coming down to one a week) and helps to stop the full migraine attack including predominantly/aura and postdrome symptoms. Triptans (when they work) stop the pain but I normally still get the fatigue, concentration and focus issues so still stuck on the couch for a day or so. This constant low energy affects my life as much as the bad pain."
- "When I am in a cycle of 18 - 20+ attacks per months I would be delighted with a 50% decrease in frequency with a monthly injection."

## 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?

**Answer** - There is no companion test for migraine diagnosis or fremanezumab 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 are concerned 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.

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 fremanezumab 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 fremanezumab would only be applicable for the 20% minority of migraine sufferers, 15% are high frequency episodic (8-14 monthly migraine days) & 5% are chronic ( $\geq 15$  monthly migraine days).

We've included some direct quotes below:

- "A migraine preventative that would be able to decrease the severity and frequency of my migraines by at least 70% would be my idea of a good outcome. Of course, I would prefer 100%! If I was able to manage well enough to go back to work and lead a fairly normal life outside of work as well, it would be amazing."
- "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."
- "That would allow me to be able to go to work regularly and spend some time with my family and friends and be able to tolerate less pain every day."
- "Although I prefer a tablet daily over an injection monthly (for comfort and just I feel that medication spread out daily vs. injection once a month might be safer), if it works - I would totally do it. I have suffered, my family has suffered - I am willing and have tried EVERYTHING out there, so will try this. (can't be worse than nerve blocks!) If a once a month injection/patch can reduce the severity/frequency of my migraines by even half, I would consider that to be a success. Not to have to miss as many family/social activities and just feel generally more "well" would be a gift."
- "A good preventative would be one that allows me to have a decrease in migraines. This would allow me to be a more productive member of society."

## 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 |                                |                   | √                  |                       |
| Novartis 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: May 20, 2020

## Appendix: Patient Group Conflict of Interest Declaration

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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 worked together 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.

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

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|                      | \$0 to 5,000                   | \$5,001 to 10,000 | \$10,001 to 50,000 | In Excess of \$50,000 |
| Allergan             |                                |                   | X                  |                       |
| Novartis             |                                |                   |                    | X                     |
| Aralez / Nuvo Pharma |                                |                   | X                  |                       |
| Eli Lilly Canada     |                                |                   | X                  |                       |
| Teva Canada          |                                |                   | 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: Marzieh Egtesadi  
 Position: Board Member  
 Patient Group: Migraine Quebec  
 Date: June 11, 2020