CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**lanadelumab (Takhzyro) for the prevention of hereditary angioedema (HAE) in adolescents and adults**
Name of the Patient Group	**HAE Canada**
Author of the Submission	**HAEC Advocacy Committee and Robert Bick**
Name of the Primary Contact for This Submission	**Daphne Dumbrille, Volunteer Coordinator HAE Canada**
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1. About Your Patient Group

HAE Canada (www.haecanada.net) is committed to creating awareness about HAE and other related angioedema, to help speed the diagnosis of patients, and to enable them to become champions for their own quality of life. We equip patients, caregivers, family members and health care providers with the information, tools and resources they need to ensure that those with HAE and other related angioedema can live healthy and productive lives.

2. Information Gathering

HAE Canada conducted an online survey, offered in English and French, of patients and caregivers from June 2, 2019 to June 11, 2019, to assess the challenges patients and caregivers face as a result of hereditary angioedema. We sought also to gain insight into their experience and expectation with therapies used to treat hereditary angioedema, in particular the treatment under review - lanadelumab (Takhzyro).

A total of 73 Type 1 and 2 HAE patients and caregivers responded to the survey. Seventy-three (73) Canadians responded. Sixty-eight (68) (92%) were individuals living with hereditary angioedema, and 6 (8%) were caregivers. The survey contained the use of free-form commentary, scoring options and limited closed questions. A total of 8 survey respondents indicated that they had used (or are using) lanadelumab (Takhzyro) to treat their hereditary angioedema. Follow-up telephone interviews, using an interview guide, were conducted with four (4) patients who are currently using lanadelumab. This report reflects the results of the survey and patient interviews, as well as insights HAE Canada has garnered from more than a decade of experience in patient support and advocacy related to hereditary angioedema, and previously gathered data from our membership which is outlined in our National Report Card.

3. Disease Experience

Hereditary angioedema (HAE) is a severely debilitating and life-threatening disease. It manifests as unpredictable, recurrent/intermittent edema attacks in different parts of the body including the gastrointestinal tract, upper respiratory tract, extremities and face. Gastrointestinal (GI) attacks are common in HAE, with severe abdominal pain and other GI symptoms. Untreated laryngeal attacks may result in asphyxiation and death. Swelling in other body parts can also significantly interfere with patients' daily pursuits, resulting in severely impaired quality of life.

Patients may still be affected by HAE even after the physical symptoms of an attack abate. For many, the expectation of HAE attacks imposes harsh limits on activities and plans. Due to the unpredictable nature of the disease, many patients experience high levels of distress and anxiety in everyday life, often attributed to: restricted or disrupted social life, anxiety due to fear of future attacks, the concern of HAE being passed to their children, and disruption/interference in educational and career pursuits.

Many patients report that they do not pursue higher education due to HAE, and that they deliberately elect to not seek out certain jobs, and job advancements, due to expected recurrent edema attacks.

In our recent survey, we asked patients and caregivers:

How frequently do you (or the person you care for) experience attacks?

Answer Choices	Responses (N=68)
Never/rarely	10.3% (n=7)
1 or 2 times per year	8.8% (n=6)
3 to 5 times per year	10.3% (n=7)
6 to 11 times per year	20.6% (n=14)
More than once per month	29.4% (n=20)
More than once per week	16.2% (n=11)
Unsure	4.4% (n=3)

On what part of the body have you experienced attacks? *(check all that apply)*

Answer Choices	Answered (n=67)
Gastrointestinal System	89.6% (n=60)
Extremities (limbs, hands, feet)	82.1% (n=55)
Face (facial swelling)	79.1% (n=53)
Upper Airway (lips/tongue, throat/larynx)	71.6% (n=48)
Other (see free-form commentary below)	29.9% (n=20)

Patients had an option to add free-form commentary to the question: ***On what part of the body have you experienced attacks.*** *20 individuals added body locations on which they experienced attacks as follows: Genitals/groin=17, posterior=2, breasts=1, sinus cavity=1, lungs=1, back/shoulders=2, joints=1, full body=1.*

We asked: ***Do you have regular fear of unpredictable, debilitating attacks?*** Sixty-eight (68) patients responded to the question. 74% (n=50) of patients report having fear of unpredictable, debilitating attacks. We asked those 50 patients: ***If "Yes", how strongly would you rate your fear?*** *("Mild", "Moderate" or "Severe")*. 30% (n=15) report their fear as being "Mild". 62% (n=31) report their fear as being "Moderate", and 8% (n=4) report their fear as being "Severe". We further asked these patients: ***Does your fear of attacks lead to any of the following symptoms/behaviours/feelings****? Please check all that apply:*

Answer Choices	Answered (n=49)
Generalized Anxiety	63% (n=31)
Desire for control over your HAE swells and treatment plans	59% (n=29)
Flashbacks to other times when difficulties occurred administering medications for swells of any kind	49% (n=24)
Sense of powerlessness	41% (n=20)
Mistrust of health care systems and/or treating professionals on your medical team	35% (n=17)
Extreme emotional reactions such as irritability, sadness, or complete terror	33% (n=16)
Difficulty focusing on the present situation due to fears of past HAE swells and/or treatments	28.5% (n=14)
Panic Attacks	8% (n=4)

We asked: *On a scale of 1 - 5* ***please rate how Hereditary Angioedema impacts or limits your life and day-to-day activities****. 1 is "not at all" and 5 is "significant impact".* We had 6 categories as follows:

Rate how Hereditary Angioedema impacts your ***Ability to Travel*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
10pts (15%)	20pts (30%)	11pts (17%)	6pts (9%)	15pts (23%)	4pts (6%)	**2.94**

Rate how Hereditary Angioedema impacts your ***Ability to Exercise*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
18pts (27%)	13pts (20%)	9pts (14%)	11pts (17%)	13pts (20%)	2pts (3%)	**2.81**

Rate how Hereditary Angioedema impacts your ***Ability to Work*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
14pts (21%)	16pts (24%)	10pts (15%)	8pts (12%)	12pts (18%)	**6pts (9%)**	**2.80**

Rate how Hereditary Angioedema impacts your ***Financial Situation*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
26pts (39%)	16pts (24%)	3pts (4.5%)	9pts (14%)	8pts (12%)	4pts (6%)	**2.31**

Rate how Hereditary Angioedema impacts your ***Ability to spend time with family and friends*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
23pts (35%)	18pts (27%)	14pts (21%)	6pts (9%)	4pts (6%)	1pt (1.5%)	**2.23**

Rate how Hereditary Angioedema impacts your **Ability to Conduct Household Chores** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
24pts (36%)	18pts (27%)	12pts (18%)	5pts (8%)	5pts (8%)	2pts (3%)	**2.20**

Patients had an option to add free-form commentary to the question re: **impacts on day-to-day activities**. These are a selection of their comments:

-*"… From the ages of 20-50 I had attacks weekly and it did affect my life adversely. A preventative medicine would have been fantastic when I was younger*."

-*"For the last 3 years I have been given C1 Esteres 1500 injections by a health nurse, weekly. This has made a huge difference to me. There is rarely a flare up since this method has taken place. Prior to this I would have a flare up at least every 3 days."* 6/7/2019 11:17 AM

-*"The veil of anxiety coloured my life every day."*. 6/6/2019 2:31 PM

We asked: ***How has hereditary angioedema affected you psychologically/emotionally?***

Patients said:

"I nearly died from a laryngeal HAE attack which has profoundly changed all levels of my life"

-"*when i was undiagnosed I experienced a lot of pain (abdominal attacks) and with no diagnosis -- no one believed me"*

-*"depending on the location of the attack I have not wanted to go out in public*"

-*"Unrelenting source of stress."*

-*"Chronic anxiety over the unpredictability of this disease."*

-"*Depression, anxiety, feature of future attacks, embarrassment and shame"*

We asked: ***How has hereditary angioedema impacted you financially?*** *(n=65)*

61.54% (n=40) reported HAE caused them to miss time at work or be less productive at work

21.54% (n=14) reported HAE required them to spend out-of-pocket for medical care

9.23% (n=6) reported that HAE has prevented them from securing a job

6.15% (n=4) reported hereditary angioedema has impeded their ability to advance in the workplace

Some patients expounded:

-"Reluctant to advance further due to fear of additional work stressors having a negative impact on my health"

-"Retired now but it was very challenging to meet the demands of work before I stopped."

-"My inability to pay for the medication while being a student has left me on welfare"

-"Caused me to be absent from my job"

Conclusion: The impact of Hereditary angioedema (HAE) goes well beyond its immediate debilitating and life-threatening manifestations. The majority of our recently surveyed patients/caregivers report having regular fear of unpredictable attacks. These patients experience generalized anxiety and stress along with many other emotional and cognitive impacts. HAE also interferes with patients' daily activities, with the disease having substantial negative impact on many patient's ability to work, travel, exercise, do household chores, and socialize with family and friends. HAE inhibits many patients' ability to pursue higher education or job advancements, and negatively affects their personal finances due to sub-optimal employment, interference with employment and costs due to treatment for HAE.

4. Experiences With Currently Available Treatments

Recognizing the burden to patients associated with HAE, including the ever present risk of experiencing a life-threatening laryngeal attack, improved preventative treatments are urgently needed. Further, IV treatments have the effect of requiring patients to expend much time traveling to treatment, and undergoing treatment; especially if they have difficulty doing home infusions. In medical literature, it is stated that despite significant safety measures, there remains the risk of infectious agent transmission with C1-INH inhibitors that are derived from human plasma. Many patients experience, or worry about damage to their veins. Drugs that are for the treatment of acute HAE attacks - that require venous access - pose a serious problem to patients as their ability to precisely and safely self-administer the drug is naturally compromised by the fact that they are having an attack. Some self-administration products require several intricate steps for reconstitution and administration that are challenging to perform during the onset of an attack. These therapies can be particularly unmanageable if a patient is traveling, or in a work environment that hinders the ability to prepare and administer an IV treatment. These barriers amount to amplified risk, and consequently increased fear and anxiety among HAE patients – severely compromising their quality-of-life. HAE patients urgently require improved prophylactic treatments, such as those injected subcutaneously, and therefore easier to administer at home. Patients would also benefit from treatments that have a more convenient and less frequent dosing regimen.

We asked: ***What therapies other than lanadelumab (Takhzyro) have you used to treat your Hereditary Angioedema?*** 59 patients told us what therapies that have used. 50 (85%) patients have used Berinert, 33 (60%) patients have used Firazyr, 8 (14%) patients have used Cinryze, 3 (5%) have used Haegarda.

We asked: *Please rate on a scale of 1 – 5* ***how important it was for you and your physician to be able to make a choice of drug(s) based upon each different drug's known side effects?*** *1 is "not important" and 5 is "very important".*

how important to be able to make a choice of drug(s) based upon each different drug's known side effects? *(n=56)*						
1 (not important)	**2**	**3**	**4**	**5 (Very important)**	**N/A**	**Weighted Average (WA)**
2pts (3.5%)	0pts (0%)	2pts (3.5%)	3pts (5.4%)	43pts (77%)	6pts (21%)	**4.70**

We asked: ***Have you and/or your physician made a choice of drug(s) based on mode of delivery (i.e. IV, subcutaneous etc.)?*** 30pts (52%) had made a choice of drug based on mode of delivery, and 28pts (48%) did not. Patients had an option to add free-form commentary to the

question re: choice based on side effects. From these comments, it is evident that a sizeable number either had no choice, or were not aware there was a choice. Select comments:

-"There is no choice as of now. If i had a choice I would choose a sub-Q option 100%"

-"still waiting for subcutaneous rather than doing an iv twice a week."

-"...Administering this IV at home was impossible without assistance so it required attendance at the emergency department. …. subcutaneous injection is easy to administer. Lanadelumab has dramatically reduced my attack frequency and is also easy to administer."

-"Because of very poor veins and IV drugs going interstitial - we decided that I participate in a Subcutaneous drug trial which i am doing now."

-"At first it was IV but my veins could not take it anymore. I had too change for subcutaneous. I have to give myself the treatment more often."

-"Would like subcutaneous treatment will discuss with Dr at next visit"

-"Giving IVs to yourself can be difficult without any assist and I don't want to hurt my veins for future use."

We asked: ***Have you and/or your physician experienced any challenges or hardships in accessing therapy for your Hereditary Angioedema?*** *(These may be related to cost, length of wait time, distance to travel)*. Fifty-nine (59) pts responded to the question. 18pts (30.5%) reported having challenges in accessing therapy, and 41pts (69.5%) did not. Patients had an option to add free-form commentary to the question re: challenges accessing therapy. Select comments:

-"Length of wait time to get diagnosis (63 years)!!!"

-"travel time is 45 minutes to a hospital"

-"Drug shortages"

-"Long hospital wait times before in home therapy"

-"cost is unbearable and wait time can sometimes be lengthy"

-"Costs as I'm currently a student and the medication will only be covered under Ontario works insurance"

Conclusion: Many patients find the treatment schedule for current treatments to be onerous, and disrupting. They also find administering IV treatments at home to be difficult and uncomfortable with some patients reporting damage to their veins, or concern about damage to their veins after years of treatment.

5. Improved Outcomes

Patients continue to seek treatments that better control attacks while offering greater convenience and ease of use. Treatments that eliminate or substantially reduce attacks compared to existing treatments are of critical importance to patients as each edema attack can be severely debilitating and in many cases life-threatening. Greater control of attacks would also ameliorate the ever present anxiety and fear many patients experience due to unpredictable attacks, and reduce the negative impact on a patient's ability to work, pursue education, travel, exercise, do household chores, and socialize with family and friends.

We asked: ***If you were to consider taking a new therapy for your hereditary angioedema please rate the following on a scale of 1 - 5. 1 is "not important" and 5 is "extremely important".*** We had 5 categories as follows:

Improved management/reduction in attacks of edema (swelling) *n=57*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
1pt (1.75%)	0pts (0%)	2pts (3.5%)	7pts (12.3%)	47pts (82.5%)	**0pts (0%)**	**4.74**
No direct cost to user/patient *n=58*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
2pts (3.5%)	1pt (1.7%)	1pt (1.7%)	2pts (3.5%)	52pts (90%)	**0pt (0%)**	**4.74**
Option to administer prophylactically before known triggers (eg. traveling, dental procedures etc.) *n=56*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)

1pt (1.8%)	1pt (1.8%)	2pts (3.6%)	7pts (12.5%)	44pts (78.6%)	**1pt (1.8%)**	**4.67**
Easier mode of delivery as a subcutaneous option *(vs. IV) n=58*						
1 (not important)	**2**	**3**	**4**	**5 (extremely important)**	**N/A**	**Weighted Average (WA)**
2pts (3.5%)	1pt (1.7%)	3pts (5%)	7pts (12%)	44pts (76%)	**1pts (1.7%)**	**4.58**
A more convenient dosing interval/less frequent dosing *n=58*						
1 (not important)	**2**	**3**	**4**	**5 (extremely important)**	**N/A**	**Weighted Average (WA)**
5pts (8.6%)	2pts (3.5%)	5pts (8.6%)	8pts (13.8%)	38pts (65.5%)	**0pts (0%)**	**4.24**

Conclusion: Of critical importance to patients are therapies with improved efficacy in preventing attacks. Additionally patients are seeking treatments that provide an easier mode of delivery (vs IV), have no direct cost to the patients, can be administered prophylactically before known triggers such as traveling or dental procedures, and have fewer side effects.

6. Experience With Drug Under Review

A total of 8 survey respondents indicated that they had used (or are using) lanadelumab (Takhzyro) to treat their hereditary angioedema. Follow-up telephone interviews were conducted with four (4) of these patients. The following data and data interpretation is based on the survey results and in-person interviews with these patients.

We asked patients who have reported experience with Lanadelumab: ***How long have you been on Lanadelumab (Takhzyro)?*** Two patients have been on treatment for 1-6 months, and 6 patients have been on treatment for more than 2 years, and accessed lanadelumab through a clinical trial.

We asked: ***Based on personal experience with lanadelumab, how would you rate its effectiveness in prevention of attacks of hereditary angioedema?*** *1 is "not effective" and 5 is "extremely effective".*

How would you rate Takhzyro's effectiveness in prevention of attacks of hereditary angioedema? *n=8*						
1 (not effective)	**2**	**3**	**4**	**5 (extremely effective)**	**N/A**	**Weighted Average (WA)**
0pt (0%)	0pt (0%)	1pt (12.5%)	1pt (12.5%)	6pts (75%)	**0pt (0%)**	**4.63**

We asked: ***Based on your personal experience with lanadelumab (Takhzyro), how would you rate its side effects?*** *1 is "completely intolerable" and 5 is "very tolerable".*

How would you rate Takhzyro's side effects? *(n=7)*						
1 (completely intolerable)	**2**	**3**	**4**	**5 (very tolerable)**	**N/A**	**Weighted Average (WA)**
0pt (0%)	0pt (0%)	0pt (0%)	0pt (0%)	6pts (86%)	1pt (14%)	**5.00**

We asked ***If you did experience side effects that were particularly difficult to tolerate, please describe the side effects and your experience***. No patients reported side effects that were difficult to tolerate.

We asked***: What are the side effects that you have experienced with lanadelumab (Takhzyro)?*** *Rate them on a scale of 1 - 5. 1 is "completely intolerable" and 5 is "very tolerable".* Eight (8) pts answered. We provided six side effects to rate*: Blood clots, Allergic reactions (including hives, chest tightness, wheezing, difficulty breathing, faintness, facial swelling and fast heartbeat), Nausea/vomiting, Increased severity of the pain associated with HAE, Headache, Pain at injection site.* Eight (8) patients experienced "*pain at injection site*" with 6 patients rating it "5-very tolerable" and 2 patients rating it "4" for a weighted average of 4.75. Two patients (2), reported "*headache*", both rating it "5-very tolerable" for a weighted average of 5.0. There was no reported experience with the other listed side effects.

We asked: *On a scale of 1-5* ***how would you rate your quality of life while taking lanadelumab (Takhzyro)?*** *1 is "low/seriously impacted", and 5 is "high/normal living".*

how would you rate your quality of life while taking lanadelumab *n=8*						
1 (low/seriously impacted)	2	3	4	5 (high/normal living)	N/A	Weighted Average (WA)
0pts (0%)	0pts (0%)	1pt (12.5%)	1pt (12.5%)	6pts (75%)	0pts (0%)	**4.63**

We asked: ***Is there anything else about lanadelumab (Takhzyro) that you would like us to know and include?***

-"I would like to stress the effectiveness of this product. It has taken away the stresses of my living with HAE."

-"It is the best. I now have a better quality of life since taking this. I can travel freely, as I had a lot of trouble with my veins and had to go to the hospital every week. And now I give my own injection. I absolutely love it."

-"This is an extremely effective product. I am very concerned about future access to this very effective product"

We asked: ***How has lanadelumab (Takhzyro) changed, or how is it expected to change, your long-term health and well-being?***

-"Expected to reduce attacks by 92% (?) and has reduced my attacks by 100%."

-"I have vein issues so have difficulties with some of the other treatments. I no longer have to go to the emergency room when treating my HAE. It has reduced my stress. I am no longer worried about having attacks because I have not had any since using this product. I am in a job that requires me to be there in person on a daily basis. Now I am able to meet my time commitments without delay."

-"It means not having to go to the hospital every week for a couple of hours"

-"I have had no attacks while using this product. I have gone from weekly attacks, requiring treatments, to no attacks while using this treatment."

We asked: ***Can you tell us about your story and why access to lanadelumab (Takhzyro) and future therapies are so important to you?***

-"This drug is a life saver. I am so much happier with my day to day life taking this drug. I feel SO much stress and fear lifted off of my shoulders... I rarely worry about having an attack or worry about not being able to participate or do certain things that would normally cause a swell."

-"As I said, I no longer have visits to the ER for treatments. This would take up much of my time. I have a very demanding job in which I need to meet many personal commitments. Many HAE sufferers would benefit greatly from this treatment. It absolutely works. I believe we owe it to the next generation to provide them with this treatment. No more hiding away and suffering. I have not had any throat swells or any other swells since taking this product."

-"Other medications were not giving me a full week without having a swell. But with Takhzyro it is one injection every 2 weeks. No side effects, no swelling. It is the best and I feel..... Normal"

-"Myself and two of my children have HAE and we are awaiting on test results regarding my very young grandchild. I have not had throat swells yet but one of my children has. This is a life threatening disorder and can be very debilitating. Using Lanadelumab reduces the costs associated with HAE treatments. (Lost work time, emergency room visits and lost productive time). These attacks can be very disfiguring which can be very difficult on young people having attacks."

Patient Interviews: Interviews were conducted with four patients that have experience with lanadelumab. The following are quotes from those patients:

Quotes from Interview with LA: *"I used to have one attack every 3 to 4 days. Since starting Takhzyro I have been "Attack Free" (approximately 2 years). My attacks were in various places: Hands, feet, posterior, intestines/internal. These attacks have caused me to lose employment....not*

seek employment, and not get hired. When employed, before treatment, these attacks would cause me to not be able to go to work or work efficiently. The stress of work would causes attacks, and the attacks cause stress."

"My life has changed dramatically --no more attacks! I finally took a trip to the Caribbean. Traveling has always been a worry. I have never previously gone on a recreational vacation/trip. It simply was not something I could previously consider. I now have (much) less stress in social circumstances. I can plan recreation and visits with little to no worry."

"I am not the only one that is sick in my family. I am the only one on this study that has access to Takhzyro (and doing so well). Insurance and coverage are a big concern. This product is life changing."

Quotes from Interview with JD: (re: Takhzyro) *"It's amazing and truly a miracle. I think everyone in Canada should have the opportunity to use this drug. It has changed my quality of life and significantly decreased my attacks"*

"I am still having about one attack per month, but when not on any treatment, I have approximately 4 attacks or more per month. I typically have throat swelling or abdominal swelling with nausea and vomiting. As a kid I was sick all the time. I was only diagnosed as young adult. Missed half of school days. In post secondary it was a challenge, missing classes."

"*We need subQ and oral medications because patients with this disease react/respond differently to different medications. We need choice for patients so they can find the treatment that best treats their disease. IV medications were a miracle, but after long term use, the veins get damaged. With Takhzyro, the dosing schedule is a great thing especially for those with needle hesitancy."*

Quotes from Interview with KU: "*I've been virtually 100% attack free since starting the clinical trial for Takhzyro in June 2016. ….That is truly life altering in a major way."*

"I do not think of HAE while on this treatment. I am like a person that doesn't have the disease when I am on this medication. I can live my life like anyone else."

-Before receiving Takhzyro: - high attack frequency of 20 to 30 episodes annually with about 50% being debilitating abdominal episodes (uncontrolled internal swelling). Pain is excruciating. Cannot eat, cannot drink water. Vomiting is constant. Takes two days at minimum to recover. Even acute treatment of abdominal attacks left me ill and in need of a day or two of recovery time.

Quotes from Interview with KM: *"The ease of use is important. A highly efficacious treatment. Much improved Quality of Life for me. This is potentially life-saving. My attacks are typically abdominal, but attacks can threaten life...so to be able to prevent the life-threatening manifestations of HAE, this is an important new treatment. My cousin's daughter was in ICU for a couple of weeks because of laryngeal swelling. There is endless suffering that comes with this disease.*"

"We need to do more to educate health care workers to properly identify and diagnose and treat HAE and to differentiate between Type 1/2 and the allergic form (and all other allergies)."

Conclusion: HAE patients require a variety of treatment options to address a range of unmet needs including: improvement in prevention of attacks, improvement in the acute management of HAE, and more convenient methods/modalities of self-administration (vs. IV). Different treatment options are vital to ensure patients have options when they are faced with drug shortages, with both oral and injectable treatments; which is currently a reality and potentially will be in the future. Lanadelumab is an extremely important addition to treatment options for HAE, and will greatly improve quality-of-life for many patients**.** Patients with experience with this treatment report better, and in many cases complete, control of attacks. Patients also report greatly improved quality of life afforded through much reduced attack-fearing anxiety, easier mode of treatment administration, and reduced dosing frequency. Lanadelumab is a superior drug treatment that affords patients desperately needed efficacy, while reducing the burden of disease related to treatment modality and frequency.

Appendix: Patient Group Conflict of Interest Declaration

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

   HAE Canada used regular and contracted employee assistance (R. Bick) to conduct research and complete this 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 collection and analysis of data was accomplished through the use of HAE Canada's SurveyMonkey subscription which includes an online survey platform along with tools for data analysis, sample selection, bias elimination, and data representation. Both regular and contracted staff participated in data collection and analysis efforts.

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
Takeda (formally Shire)				X
CSL Behring				X
BioCryst			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: Jacquie Badiou.
Position: President, on behalf of the HAE Canada Board of Directors
Patient Group: HAE Canada
Date: June 19, 2019