

Drug Evaluation  
Questionnaire for Patient and  
Caregiver Associations and Groups

Une production de l'Institut national  
d'excellence en santé  
et en services sociaux (INESSS)

## **Section A – Context and guidelines**

### **Context and objectives of the questionnaire**

INESSS recognizes that patients and caregivers have first-hand knowledge of life with a disease or specific health condition. They can describe the benefits and drawbacks of currently available treatments, which are not always reported in the published literature, and assess new treatments.

This questionnaire was created to help patient and caregiver associations and groups contribute information to the evaluation of a specific drug. Their knowledge on the subject may influence the recommendations of INESSS.

Completing this questionnaire requires significant resources. We are therefore committed to making all contributions available to everyone involved in the evaluation process. Our notice will explain how your answers will be used in developing recommendations.

**Responses to this questionnaire may be published on our website; any personal and financial information that may allow respondents to be identified will be removed.**

### **How to complete the questionnaire**

In this questionnaire, the term “patient” refers to a person who has or had a disease or health condition that requires the prescription of the drug. The term “caregiver” refers to a person who takes care of a patient by providing, for example, care, support and assistance, and includes family members, friends and any other support person.

The first section of the questionnaire concerns information about your patient or caregiver association or group. This information is required so we can get to know the associations that respond to our questionnaire, and their representatives, in the interest of transparency. This section also includes questions about conflicts of interest, since INESSS asks that all participants in the evaluation procedure, whether individuals or organizations, disclose any conflicts of interest they may have in order to ensure an objective and credible procedure. This information will not be used to reject questionnaires or any of the information provided.

The second section of the questionnaire is made up of three major subsections that deal with the impact of the disease, currently available treatments and drugs under study. More specifically, in sections B-2 to B-6, we ask you to describe the difficulties faced by patients and caregivers, experiences with current treatments, expectations of the drug under study and, if you are aware of them, the potential benefits or drawbacks of this drug.

For each of these questions, please think about any existing issues that could be useful for evaluating the drug and making a decision. The issues listed beneath each question are given as examples; these lists are not exhaustive. Identify which issues your association or group thinks are important, and describe any other relevant issue that is not mentioned. Please describe the facts, provide information and summarize the experience of the patient and their family in order to give balanced and specific insight into their perspective. Please specify the source of this information by providing references. For each section of the document, please specify any groups you think should be given particular consideration (e.g., men, women or children; ethnic

groups; people living in a specific region; people with disabilities; subtypes of the disease), and indicate their particular needs or problems.

There is no need to send us scientific articles, as we already have access to this type of information. However, if you have a particular interpretation of specific clinical trials, we would be interested in hearing about it.

If you have any questions about this questionnaire, please write us at:

[plan.commentaires.inscription@inesss.qc.ca](mailto:plan.commentaires.inscription@inesss.qc.ca)

Once you have completed the questionnaire, please send us a digital copy at the above-noted email address, or a hard copy at the following mailing address:

**Institut national d'excellence en santé et en services sociaux (INESSS)**  
**Direction du médicament**  
**2535 Laurier Boulevard, 5th Floor**  
**Québec, Québec G1V 4M3**

## Section B – Feedback about a drug

### 1. Information about the organization and conflict-of-interest declaration

Name of the drug and indication:                      lanadelumab (Takhzyro) for the prevention of hereditary angioedema (HAE) in adolescents and adults

Name of the organization:                              HAE Canada

Website :                                                      <https://www.haecanada.net/>

Name of the respondent to the questionnaire:    Jacquie L.-Badiou, President, HAE Canada Inc

Name of the contact person :                        Daphne Dumbrille, Volunteer Coordinator HAE Canada

Email address :                                            office@haecanada.org

Telephone :                                                613-761-8008

Mailing address :                                        2935 Conroy Rd. Unit #110, Ottawa, K1G 6C6

#### 1.1 Information about the organization

Type of organization (check all that apply):

- ☒ **Association:** Group of persons brought together with a common interest, other than that of making profits to be shared among its members, whose activities promote the study, defense and development of the economic, social or moral interests of its members (Registraire des entreprises, Gouvernement du Québec)
- ☐ **Group of persons:** Any aggregation, other than an association, which joins two or more persons who share a common interest (pecuniary or not). (Registraire des entreprises, Gouvernement du Québec)
- ☐ **Non-profit legal person:** Group of individuals that engages in non-profit activities (Registraire des entreprises, Gouvernement du Québec)
- ☐ **Community organization subsidized by the MSSS:** Group of persons from the community that is supported by the community and mobilized around shared objectives in the field of health care and social services, and which is subsidized through the Programme de soutien aux organismes communautaires of the Ministère de la santé et des services sociaux (MSSS) of Québec
- ☐ **Registered charitable organization:** Charitable organization registered with the Canada Revenue Agency or Revenu Québec
- ☐ **Public foundation:** Foundation operated for charitable purposes; the majority of its administrators or other managers deal with each other at arm's length (Ministère du Travail, de l'Emploi et de la Solidarité sociale)
- ☐ **Private foundation :** Foundation in which more than half of the administrators are related persons or have a non-arm's length relationship, and for which over 50% of the funding comes from a single person or group of persons that have a non-arm's length relationship (Ministère du Travail, de l'Emploi et de la Solidarité sociale)

- ☐ **Mixed association or group:** Association or group that brings together patients and professionals
- ☐ **Group of associations:** Union, federation, coalition or any other type of group of associations, community organizations, groups of persons, charitable organizations, etc.
- ☐ Other, please specify:

#### Jurisdiction

- ☒ National
- ☐ Provincial
- ☐ Regional
- ☐ Other, please specify:

#### Mandate/role (check all that apply)

- ☒ Defense of members' rights and promotion of their interests
- ☒ Improvement of access to new treatments
- ☒ Support for individuals
- ☒ Research funding
- ☒ Research promotion and support
- ☐ Training
- ☒ Information and awareness campaigns
- ☐ Other, please specify:

Describe the make-up of the main branches of your organization, and give the names of managers and their titles.

*For example:*

- *Organization chart (provide a reference to the organization's website, where applicable)*
- *Main branches, units, departments, etc.*
- *Board of directors (BOD), where applicable*

HAE Canada ([www.haecanada.net](http://www.haecanada.net)) is committed to creating awareness about HAE and other angioedema, to speed diagnosis of patients, and to enable them to become champions for their own quality of life. Our membership consists of patients with HAE and other angioedema, along with caregivers. HAE Canada has one dedicated employee (Daphne Dumbrille) with other specialized support contracted as needed and is operated by a volunteer Board of Directors: Jacquie Badiou (Pres), Richard Badiou (Treasurer), Tina McGrath (VP and Ontario Regional

Director), Kari Feere (Atlantic Regional Director), Anne Rowe (Director at Large), Lorraine Coumont (Pacific Director)

Describe your members.

*For example:*

- *Number and types of members*
- *Regions served*
- *Demographic data*

HAE Canada currently has 473 members from across all provinces comprised of 334 patients, and 139 caregivers. HAE also has a Child and Youth Associate program where we provide customized information and advocacy support to individuals under the age of 18 that join our Associate program. HAE Canada also has a medical advisory committee which provides HAE Canada with scientific advice on matters regarding the treatment information we provide to patients and issues regarding treatment access advocacy.

### *1.2. Conflict-of-interest declaration*

A conflict of interest arises when a person is in a situation in which, objectively, their judgment in a particular role may be or appear to be influenced by other considerations, whether personal, financial or professional. A conflict of interest may be real, potential or apparent. Organizations may also have financial or reputational interests that are in conflict with their obligations under their mission or mandate.

Please list all the companies or organizations that have provided you with resources (financial, human, material or other services, including consulting, communications, representation or research) in the last two years AND that have an interest in the drug under evaluation. Your list should not be limited to the manufacturer of the drug under evaluation but also include any organization involved directly or indirectly with this drug.

Reminder: This information is not used to reject questionnaires or any information provided.

### **Organizations**

HAE Canada solicits and receives unrestricted educational grants from certain manufacturers of treatments for HAE including:

Takeda

Amounts

[REDACTED]

### **Organizations**

CSL Behring

Amounts

[REDACTED]

## **Organizations**

BioCyst

Amounts



## **Organizations**

Amounts

Has your organization, or one of its managers, ever published or publicly expressed (e.g., in a press release, media interview, online) a clear opinion about the treatment under evaluation? If so, of what nature ? Reminder: This information is not used to reject questionnaires or any information provided.

### **Opinion published or publicly expressed**

Poster

Real world data of Canadians living with Hereditary Angioedema (HAE): Attributes of new medications.

Presented at The Canadian Society of Allergy and Clinical Immunology (CSACI) Annual Scientific Meeting (Montreal-October 2019) and at the 2019 GLOBAL FORUM FOR HEREDITARY ANGIOEDEMA (Berlin- November 2019)

The data presented in the aforementioned poster is also presented in this submission.

Reference (if applicable)

<https://www.haecanada.net/real-world-data-attributes-of-new-medications/>

### **Opinion published or publicly expressed**

November 22, 2019 - HAE Quotation for Takeda News Release: TAKHZYRO® (lanadelumab injection) receives positive recommendation from CADTH's Canadian Drug Expert Committee (CDEC) for the routine prevention of hereditary angioedema (HAE) attacks

"We are hopeful that CADTH's positive recommendation will provide Canadians living with HAE access to a new and useful therapy to help bridge the gap in care", said Jacquie Badiou, President, Hereditary Angioedema (HAE) Canada. "HAE not only affects patients physically but can have detrimental impacts on one's quality of life due to the debilitating and unpredictable nature of the disease which is why new options are important."

Reference (if applicable)

**Opinion published or publicly expressed**

Reference (if applicable)

**Opinion published or publicly expressed**

Reference (if applicable)

Does your association or any of its managers have any other conflicts of interest to disclose?

☐

Yes

☒

No

If so, of what nature ?

*For example:*

- *Personal benefits received from a manufacturer or organization with an interest in the INESSS evaluation (donation, gifts, promotional items, trips, services, shares, call options, etc.)*
- *Activities funded by a manufacturer or organization with an interest in the INESSS evaluation (research grant or scholarship, consultant fees, conference participation or organization, committee, salary, etc.)*
- *Support for the association from a manufacturer or organization with an interest in the INESSS evaluation*
- *Affiliation*
- *Personal or business relationship with a manufacturer or other interest group*

**1.3 Information on the method, help received and sources of information used to complete the questionnaire, if applicable**

Indicate whether you received help to complete this questionnaire, and, if so, specify what kind of help, who provided it and in what capacity.

HAE Canada retained the services of a Health Policy Consultant (Robert Bick) to assist our organization in the designing of patient research instruments, data analysis and reporting.



Indicate the nature of the information and the method used to complete the questionnaire.

*For example:*

- *Number of participants*
- *Method used: solicitation of members; investigation online or elsewhere; comments on social media, in working groups or discussion groups; testimonials; analysis of calls to a telephone help line; medical files; conversations with patients or family members of patients during clinical trials; stories told by patients or their families; etc.*
- *References*

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 including eight (8) respondents from Quebec. 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 (including 1 from Quebec) 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 input submission 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. (National Report Card Available at this link: <https://www.haecanada.net/real-world-data/>)

## **2. Impact of the disease or health condition**

2.1. How does the disease or health condition treated by the drug under evaluation affect patients' quality of life? Which aspects cause the most difficulty?

*For example:*

- *Primary symptoms to control*
- *Impact on daily activities and domestic life*
- *Need for assistance in daily life*
- *Impact on social life and relationships*
- *Family balance*
- *Intimate relationships, sexual issues*

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)

We also asked patients and caregivers: How frequently do you (or the person you care for) experience attacks? 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 also 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 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 categories as follows:

#### 1. Rate how Hereditary Angioedema impacts your Ability to Travel

1 (not at all)	10pts (15%)	
2	20pts (30%)	
3	11pts (17%)	
4	6pts (9%)	
5 (significant impact)	15pts (23%)	
N/A	4pts (6%)	Weighted Average (WA) = 2.94

2. Rate how Hereditary Angioedema impacts your Ability to Exercise.

1 (not at all)	18pts (27%)	
2	13pts (20%)	
3	9pts (14%)	
4	11pts (17%)	
5 (significant impact)	13pts (20%)	
N/A	2pts (3%)	Weighted Average (WA) = 2.81

3. Rate how Hereditary Angioedema impacts your Ability to Work.

1 (not at all)	14pts (21%)	
2	16pts (24%)	
3	10pts (15%)	
4	8pts (12%)	
5 (significant impact)	12pts (18%)	
N/A	6pts (9%)	Weighted Average (WA) = 2.80

4. Rate how Hereditary Angioedema impacts your Financial Situation.

1 (not at all)	26pts (39%)	
2	16pts (24%)	
3	3pts (4.5%)	
4	9pts (14%)	
5 (significant impact)	8pts (12%)	
N/A	4pts (6%)	Weighted Average (WA) = 2.31

6. Rate how Hereditary Angioedema impacts your Ability to Conduct Household Chores.

1 (not at all)	24pts (36%)	
2	18pts (27%)	
3	12pts (18%)	
4	5pts (8%)	
5 (significant impact)	5pts (8%)	
N/A	2pts (3%)	Weighted Average (WA) = 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=64)

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, and do household chores. 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.

## 2.2 How does the disease or health condition affect patients' families and friends?

*For example:*

- Emotional/psychological effects
- Family balance
- Intimate relationships, sexual life

We asked: On a scale of 1 - 5 please rate how Hereditary Angioedema impacts or limits your Ability to Spend time with Family and Friends. 1 is "not at all" and 5 is "significant impact".

1 (not at all)	23pts (35%)	
2	18pts (27%)	
3	14pts (21%)	
4	6pts (9%)	
5 (significant impact)	4pts (6%)	
N/A	1pts (1.5%)	Weighted Average (WA) = 2.23

Beyond interfering with many functional aspects of a person's life, HAE also interferes with patients' leisure activities and relationships, with the disease having substantial negative impact on many patient's ability to socialize and interact with family and friends.

## 3. Experience with currently available treatments (other than the one under evaluation)

3.1. To what extent do the patients, with the help of their families, where applicable, manage their health condition with current treatments? Treatment refers to any form of intervention, such as drugs, rehabilitation, psychological support or hospital procedures. If no treatment is available, this should be stated.

*For example, list the main treatments used and their effects in terms of:*

- Procedure for administering/taking the treatment (frequency, treatment at home or at the hospital, access, route of administration)
- Difficulties taking a drug as prescribed (swallowing, use of a device, schedule, etc.)
- Specific actions involved in current medications (tablets, injections, checkup, review of dosage and frequency, etc.)
- Required consultations and complementary examinations (checkup, biological and X-ray exams), related treatment (kinesitherapy, psychiatry), need for hospitalization or other treatments
- Effectiveness for controlling or diminishing the most difficult aspects of the disease
- Adverse effects, specifying the effects that are acceptable and those that are most difficult to tolerate
- Control or reduction of symptoms (primary benefits and adverse effects of this drug, etc.)
- Impacts on daily life and domestic activities
- Impacts on personal and social life and relationships (work interruptions, changes in physical appearance, difficulty getting around, etc.)

- *Concerns regarding long-term use of the existing treatment*
- *Ease of access*

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 precisely and safely self-administer the drug is naturally compromised by the fact that they are having an attack. Some self-administration products require sterile environments along with 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".

1 (not important)	2pts (3.5%)	
2	0pts (0%)	
3	2pts (3.5%)	
4	3pts (5.4%)	
5 (very important)	43pts (77%)	
N/A	6pts (21%)	Weighted Average (WA) = 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 to 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”

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. HAE Canada also recognizes that C1-INH inhibitors are derived from human plasma, with inherent risk of infectious agent transmission and supply interruptions / shortages.

### 3.2 What are the main expectations patients and their families have for the new treatment?

*For example:*

- *Expectations of effectiveness for relieving certain symptoms*



- *Expectations with regard to adverse effects*
- *Expectations with regard to other characteristics of the treatment*
- *Expectations with regard to access*
- *Deficiencies the ideal drug should address*
- *Alternative to current treatments*

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:

1. Improved management/reduction in attacks of edema (swelling) n=57

1 (not important)	1pts (1.75%)	
2	0pts (0%)	
3	2pts (3.5%)	
4	7pts (12.3%)	
5 (extremely important)	47pts (82.5%)	
N/A	0pts (0%)	Weighted Average (WA) = 4.74

2. No direct cost to user/patient n=58

1 (not important)	2pts (3.5%)	
2	1pts (1.7%)	
3	1pts (1.7%)	
4	2pts (3.5%)	
5 (extremely important)	52pts (90%)	
N/A	0pts (0%)	Weighted Average (WA) = 4.74

3. Option to administer prophylactically before known triggers (eg. traveling, dental procedures etc.) n=56

1 (not important)	1pts (1.8%)	
2	1pts (1.8%)	
3	2pts (3.6%)	
4	7pts (12.5%)	
5 (extremely important)	44pts (78.6%)	
N/A	1pts (1.8%)	Weighted Average (WA) = 4.67

4. Easier mode of delivery as a subcutaneous option (vs. IV) n=58

1 (not important)	2pts (3.5%)	
2	1pts (1.7%)	
3	3pts (5%)	
4	7pts (12%)	
5 (extremely important)	44pts (76%)	
N/A	1pts (1.7%)	Weighted Average (WA) = 4.58

5. A more convenient dosing interval/less frequent dosing n=58

1 (not important)	5pts (8.6%)	
2	2pts (3.5%)	
3	5pts (8.6%)	
4	8pts (13.8%)	
5 (extremely important)	38pts (65.5%)	
N/A	0pts (0%)	Weighted Average (WA) = 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.

#### 4. Experience with the drug under study

4.1. For those who have tried the drug under study, what effects did it have (positive or negative)? What differences did using this drug make in their lives?

*For example, in terms of:*

- *Benefits and drawbacks compared to currently available treatments*
- *Ease of use or observance (procedures for administering/taking the treatment, use of the drug as prescribed)*
- *Effectiveness, quality of life (e.g., improvement of symptoms)*
- *Adverse effects (e.g., aggravation of symptoms)*
- *Effects on daily life and domestic activities*
- *Effects on personal or social life or relationships (e.g., financial impact)*

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". (n=8)

1 (not effective)	0pts (0%)	
2	0pts (0%)	
3	1pts (12.5%)	
4	1pts (12.5%)	
5 (extremely effective)	6pts (75%)	
N/A	0pts (0%)	Weighted Average (WA) = 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". (n=7)

1 (not effective)	0pts (0%)	
2	0pts (0%)	
3	0pts (0%)	
4	0pts (0%)	
5 (extremely effective)	6pts (86%)	
N/A	1pts (14%)	Weighted Average (WA) = 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". (n=8)

1 (low/seriously impacted)	0pts (0%)	
2	0pts (0%)	
3	1pts (12.5%)	
4	1pts (12.5%)	
5 (high/normal living)	6pts (75%)	
N/A	0pts (14%)	Weighted Average (WA) = 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: HAE Canada conducted interviews with four patients that have experience with lanadelumab. The following are quotes from those patients:

Quotes from Interview with (Quebec Resident)█: “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 █ (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 [REDACTED]: “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 [REDACTED]: “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 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). Lanadelumab is an extremely important addition to treatment armamentarium 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.

## **5. Additional information**

Please provide any additional information that may be useful for the drug evaluation.

*For example:*

- *Ethical or social issues, relationship conflicts with family members or health care professionals*

## **6. Key points**

In a maximum of five statements, list the most important elements of your responses to this questionnaire. These statements will be quoted and highlighted in the evaluation of the drug.

1. Hereditary angioedema (HAE) is a severely debilitating and life-threatening disease
2. For many, the expectation of HAE attacks imposes harsh limits on activities and plans.
3. Administering IV treatments at home is difficult and uncomfortable with some patients reporting damage to their veins, or concern about damage to their veins after years of treatment.
4. Patients require therapies with improved efficacy in preventing attacks with an easier mode of delivery.
5. Lanadelumab is a superior drug treatment that affords patients desperately needed efficacy, while reducing the burden of disease related to treatment modality and frequency.

### **INESSS thanks you for your participation!**

This questionnaire was based on the “Questionnaire de recueil du point de vue des patients et usagers pour l’évaluation d’un médicament” (2016), by the French National Authority for Health, and the “Patient Input Template for CADTH CDR and pCODR Programs” (2017), by the Canadian Agency for Drugs and Technologies in Health.