

## HAE Canada Input to the Common Drug Review at CADTH for Firazyr (Icatibant)

### Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Firazyr (Icatibant) for acute attacks of Hereditary Angioedema in adults
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Permission is granted to post this submission	Yes

#### 1.1 Submitting Organization

HAE Canada is a national patient organization that provides education and support services for Canadian Hereditary Angioedema (HAE) patients and their families. Founded in 2010, its mission is to partner with physicians, nurses, and other healthcare-related professionals to ensure all HAE patients have access to timely and appropriate treatment to improve their quality of life.

HAE Canada is governed by a national board of directors consisting of three regional directors, three directors-at-large, and one representative each from the physicians' and nurses' groups that treat HAE patients (Canadian Hereditary Angioedema Network and HAE Nurses of Canada). HAE Canada has a membership of 207 people, consisting of 149 patients, 36 family members, and 22 others (primarily friends and healthcare workers). HAE Canada has a very small but dedicated group of volunteers (currently less than 20) who organize regional events, produce educational materials, work with healthcare providers to establish guidelines for a comprehensive standard of care, and provide individual support services to HAE patients.

#### 1.2 Conflict of Interest Declarations

*a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*

As a small patient organization HAE Canada relies on funding from pharmaceutical companies to be able to provide services to its members. Since the organization began 3 ½ years ago, HAE Canada has received unrestricted grants from the following companies: CSL Behring, Viropharma and Shire Canada.

Pharmaceutical funding has been used to cover the start-up and administration expenses of the organization (e.g. legal and accounting fees). The funding has also covered board meetings and teleconferences, meetings with the physicians and nurses who treat HAE, "HAE Updates" (regional

patient meetings), an annual Patient Summit, development of its website and educational materials, and the wages of part-time employees and contract workers (e.g. social worker to assist with patient services). Funding for expenses incurred in relation to information gathering for the patient and caregiver surveys came out of HAE Canada's general budget.

Funding from Shire Canada, the maker of Firazyr, accounted for less than 8% of HAE Canada's revenue since the organization was founded in 2010. To minimize perceived or potential conflict of interest issues, HAE Canada has strict policies regarding interactions with pharmaceutical companies to prevent any control or influence by them on HAE Canada's decision-making or activities.

*a) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

This submission was developed and prepared by HAE Canada volunteers and an independent contractor employed by HAE Canada. None of the aforementioned have a conflict of interest to declare.

## **Section 2 — Condition and Current Therapy Information**

### **2.1 Information Gathering**

Information in this section was obtained from the following sources:

1. A survey of HAE Canada members conducted in February 2014;
2. A telephone focus group consisting of 9 participants from across Canada, all of whom are HAE patients and/or caregivers, conducted in March 2014; and
3. One-to-one conversations with patients conducted by the authors of this document.

The survey of HAE Canada members was conducted via an online survey. Patients were asked a series of questions about themselves, their experience with HAE and current treatment options, as well as their expectations of Firazyr as a treatment. Patients who have obtained Firazyr through the Special Access Program were also asked questions about their experience with Firazyr. Caregivers answered a similar but shorter series of questions. A total of 90 people responded to the survey (63 patients and 27 caregivers) accounting for 48% of HAE Canada's members who are patients and/or caregivers.

The focus group was held by teleconference and consisted of 9 individuals (5 patients, 1 caregiver, and 3 patients who also serve as caregivers for their children). The group was asked a series of questions to obtain a clearer understanding of their experiences; however, the discussion was mostly free flowing allowing participants to provide input where they felt it was most appropriate.

One-on-one conversations were conducted with patients known to have difficulty with current treatment options to obtain a clearer understanding of the issues they face, as well as with 5 patients who have experience using Firazyr. (Four of these patients had a positive experience with Firazyr and 1 had a negative experience).

### **2.2 Impact of Condition on Patients**

Hereditary Angioedema (HAE) is a rare and potentially life-threatening inherited blood disorder. People with HAE experience attacks of severe swelling that affect various body parts including the hands, feet, face, airway (throat) and internal organs. Swelling of the throat is the most dangerous aspect of HAE because the airway can close quickly and cause death by suffocation. Seventy-three percent of the patients surveyed reported that they have experienced throat swelling at some point in their life, and 9% reported they experience throat swelling frequently. In addition to throat swellings, the most commonly reported swelling symptoms were abdominal swelling (98%), extremity swelling (91%), and



facial swelling (68%). The most commonly reported non-swelling symptoms were pain (98%), nausea (77%), diarrhea (76%), and vomiting (68%).

The severity and frequency of HAE attacks varies greatly from patient to patient, even among affected family members. The patients who responded to the survey described their attacks in a wide range varying from *“uncomfortable, inconvenient, but fairly easily controlled”* to *“severe, frequent and life threatening”*. Some patients reported being asymptomatic for years, while others with extreme cases reported having daily attacks. Attacks typically last three to five days but patients reported that early treatment can significantly reduce the duration and severity of an attack. Patients further reported that attacks fluctuate significantly, both in frequency and severity, thereby introducing a significant element of uncertainty and risk into their daily lives.

Unlike angioedema that is caused by an allergic reaction (e.g. peanuts, bee stings), Hereditary Angioedema is caused by a deficiency in a blood protein that leaves patients vulnerable to attacks at any time. Attacks can occur spontaneously, as well as in response to various triggers such as physical trauma, hormone fluctuations, and stress. Living with unpredictable, extremely painful, and sometimes life-threatening attacks has a significant impact on the day-to-day living and quality of life for both HAE patients and their families. The most common impact of HAE that was cited by patients was stress (98%). In addition, patients reported that HAE has a negative impact on the following facets of their life: travel (89%), work or school productivity (83%), social life (78%), family life (73%), and financial situation (50%). In the words of one patient: *“HAE is something that affects every aspect of my life. Managing HAE requires dedication and effort to ensure that known triggers are minimized to the extent possible and that treatment can be administered as early as possible to lessen the severity of an attack. Every time I leave the house, I have to take my medical supply bag with me, ensure my treatment is always at the proper temperature, and that I have a place to do the required IV infusion.”* Another patient described it this way: *“HAE is described by medical professionals as episodic but there is nothing episodic about living with this disease. I don’t only have to deal with it when I am having an attack. I have to think about it all the time. I have to continually adjust my goals, plans, and dreams every day.”*

The inability of some HAE patients to work in their desired field, or to the capacity they would like, or to be able to meet the demands of school is frustrating. *“I never know for sure that I will be able to function on a given day. I worry about being perceived in the workplace as a malingerer because I have to take more time off for illness than most. I have no energy to take on extra responsibilities that are optional but expected.”* *“When attacks occur I am drained of energy. I’m not able to be the employee I want to be. Even minor attacks make it difficult to use my hands when they are sore and swollen.”* *“I worked full time for 30 years as a high school science teacher. I finally had to take long-term disability because as I got older I found it extremely difficult to summon the energy to work effectively in the aftermath of an abdominal attack”.*

The disruptive nature of HAE attacks also affects social plans and family life. Patients are often faced with the choice of trying to “carry on” through significant pain and embarrassing swellings, sacrificing their own well-being so that the lives of other people aren’t disrupted because of their disorder. One patient commented, *“I never make plans with just one person. I’ll only commit if there are two or more other people involved. That way if I have an attack, I can cancel out of a social event and I don’t have to feel guilty about disappointing others.”* Another patient said, *“I don’t travel because I’ve had very challenging experiences in the past being very sick on a long road trip, on a transatlantic flight, in a foreign country, at a cottage weekend, etc.”*



50% of respondents cited HAE as having a negative impact on their financial situation and for some of those people life is very difficult. For one single mom, trying to live off a small disability insurance cheque creates enormous challenges just to provide the basics for her child. Another patient's disability insurance didn't take effect until after 20 months of unemployment at 55% of her usual salary. *"I had to sacrifice and cut back to be able to sustain. Family members and even a very good co-worker helped out so I didn't have to sell my home."*

While we are very pleased with the response rate of the survey, we recognize the information collected was not population based and can't be considered reflective of the views of all Canadian HAE patients and caregivers. In reviewing the survey results, we noted the data collected on the impact of the condition was more severe than has been reported in previously published literature on the burden of illness for HAE patients in other countries. We believe there are two factors that account for the variances: 1. Having fewer treatment options in Canada compared to other countries significantly hinders management of the disease; and 2. We had a high response rate from patients who reported their HAE symptoms are not well controlled with treatments currently available or prescribed to them.

### 2.3 Patients' Experiences With Current Therapy

Our survey respondents reported experience with the following therapies:

1. Berinert – a C1 Esterase Inhibitor approved by Health Canada in 2010 for acute abdominal or facial attacks of moderate to severe intensity, primarily used as indicated, but sometimes used off-label as a long-term prophylactic treatment to control attacks in patients with frequent and severe HAE attacks. as Also, it is sometimes used off-label as a short-term prophylactic treatment prior to dental treatment, surgery, etc.
2. Danazol – an anabolic steroid not indicated by Health Canada but used off-label as a long-term prophylactic treatment by some patients to control the onset of attacks;
3. Tranexamic Acid (Cyklokapron), an antifibrinolytic agent approved by Health Canada but used by a small number of patients as both a long-term and/or short-term prophylactic option; and
4. Firazyr – the drug currently under review, which has been available to a limited number of Canadian HAE patients under the Special Access Program since 2010.

Fifty-seven percent of patients surveyed agreed or strongly agreed that their current treatment controls their HAE symptoms. The vast majority of these patients (83%) used Berinert and most reported no side effects. Many described Berinert with words such as *"incredible"* and *"life changing"* and proclaimed, *"When Berinert became available I got my life back"* and *"After years of being incapacitated I finally have a full-time job and a social life."* It is important to note that while these patients felt Berinert controlled their symptoms, a number of these patients added the caveat that IV infusion was difficult and commented they need to constantly adjust their activities and plans to ensure they always have access to treatment and a setting where it can be administered. *"Berinert is a very effective treatment for HAE attacks, however, IV infusion presents challenges that are difficult for me to overcome. Not being able to infuse anywhere is a major negative to this product. It's difficult to insert your own IV and then to mix and administer Berinert at a public venue. It's also really hard to travel with Berinert because it has to be temperature controlled."*

Of the 15% of patients surveyed who were neutral on whether their current treatment controlled their symptoms, the majority were also Berinert users (50%). Many of these patients found Berinert to be an effective treatment but stated they selected the option of *"neutral"* on its ability to control their symptoms for the same reasons listed as caveats by the group above. Other patients who were neutral on whether their current treatment controlled their symptoms were patients who use Danazol and felt it controlled their symptoms *"to some degree"* but experienced significant side effects (anxiety,



depression, weight gain, mood swings, low sex drive, excessive hair growth, etc.) that made it difficult to use.

A number of reasons were cited by the 28% of survey respondents who feel their current treatment doesn't control their symptoms. Just as the Berinert patients in the two previous categories reported, many patients in this group commented that the difficulty of not always having a place to administer Berinert in a timely manner compromised the success of their treatment. One patient commented that, *"Infusing Berinert requires controlled settings and life doesn't always accommodate this need. If I am unable to use Berinert at the first sign of an attack, it doesn't work for me, and even a redose at ER failed to resolve restricted airway symptoms."*

Other patients commented on poor vein access making the use of Berinert difficult or impossible. *"I have tiny veins that make inserting an IV very difficult. The ER nurses use a child-sized IV and it still often takes two, and sometimes up to five tries before one of them is finally able to access a vein. Because picc lines and portacaths aren't meant to be placed permanently this is the only option I have right now. If they can't get it I just have to suffer through abdominal attacks, and for laryngeal attacks I have to be intubated."*

For other patients current treatment options (Berinert, Danazol, and Tranexamic Acid) have proven to be only mildly effective or completely ineffective. *"Nothing works well. I'm at my wits end."*

## 2.4 Impact on Caregivers

When asked which aspects of their lives were impacted by being the caregiver for an HAE patient, respondents to the caregiver survey said HAE has a high or very high impact on the following: leisure activities (75%), day-to-day family life (62%), work or school productivity (50%), social life (50%), and financial situation (28%). Because HAE is an inherited disease, many HAE patients are often also caregivers themselves, which magnifies the impact of the illness on a family.

*"We're retired now and would like to travel during this stage of our life but that isn't an option."*

*"Proximity to medical attention is always a forefront consideration for any activity. Before planning a family outing for my wife and daughter, I quietly research treatment facilities and plan the day's events carefully, always being mindful of where we could safely treat an attack if necessary."*

*"There is a lot of uncertainty. It's hard to plan things because we never know when she will be sick or how sick she will be. I have to take time off work to look after her. We often have to cancel plans."*

# Section 3 — Information about the Drug Being Reviewed

## 3.1 Information Gathering

Information gathered for this section is the same as in 2.1.

## 3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

- a) Patients with no experience using Firazyr expressed the following expectations of it as a treatment option:
  1. That Firazyr may be an option in emergency situations. *"I would like to have it on hand as an 'epi-pen' idea for my child who has HAE. I would use it in an emergency situation where we need to buy time."* *"Inserting my own IV can be difficult at any time but when a severe attack comes on quickly, my veins start to collapse and I become weak and lightheaded and putting in my own*

*IV is impossible. Having Firazyr on hand for those times would give me peace of mind that's hard to describe."*

2. That Firazyr may be a possible treatment for those patients for which other treatment options are ineffective. *"No one seems to know what will or won't work for me. Berinert is somewhat successful but I have to take it in extremely high doses (2000 units per day). My doctor thinks a bradykinin blocker might be the answer."*
3. That Firazyr, a subcutaneous injection, would make treatment feasible for patients with poor vein access. *"I know Berinert works for me but not being able to access a vein makes it useless for most attacks."* While almost all patients expressed a desire for a treatment with an easier mode of delivery than IV infusion, the need for Firazyr as a treatment option was described as "imperative" by many with poor vein access.
4. That Firazyr would be more portable (i.e. doesn't need to be temperature controlled and can be administered in situations where it may be difficult or impossible to do IV infusion). *"HAE attacks don't wait for you to be in a safe and controlled environment that allows for early treatment. Having access to a treatment that could be easily self-administered would alleviate so much stress."* Another patient commented, *"With Firazyr I would hope to be able to feel the freedom to travel and to travel safely. It would be no different than someone with diabetes being able to fly with their insulin instead of without it."*

- b) The following are comments from patients who have experience using Firazyr as part of a manufacturer's compassionate supply through the Special Access Program:

*"I have the experience of using this drug in emergency situations. It works. I firmly believe it has saved my life by giving me time to get to an ER for further intervention. Since I have had access to Firazyr I have not needed intubation."*

*"Firazyr slowed my attack but did not take it away completely. It obviously won't work for all of us but I think it should be an option for those that it does work for, especially for emergencies."*

*"The first time I was given Firazyr was when I had been intubated for a week. After I was discharged from the ICU and I needed to give myself Firazyr for the first time, I remember 30 minutes later that it was like a curtain was raised and I knew I was coming out of the attack. What a difference. Having Firazyr to treat my attacks allowed me to return to work, I was given a promotion, and my life became more stable."*

*"For the first time since being diagnosed with this awful disease, I feel like I finally have control over my life again and that HAE is not controlling it. I feel safe knowing that I have a 'lifesaver' with me at all times. I want everybody with HAE to feel that sense of safety and control over their own lives. My quality of life has increased and I hope to be able to go back to work. That would not be possible if it wasn't for Firazyr."*

#### **Section 4 — Additional Information**

A number of patients who received Firazyr through the Special Access Program but were eventually cut off due to lack of funding expressed extreme frustration about finally having a treatment that works and then having it stopped due to their inability to pay for it. One of these patients summed up the frustration by saying, *"To have a treatment that works taken away because a patient can't afford it is inhumane. My life is back to being hell since Firazyr was taken away from me. I desperately want my life back. I want to get back to work and be able to care for my family again."*