Hereditary Angioedema (HAE) Forum

What We Heard Summary Report

Feb 20, 2020

Contents

This What We Heard report has been written to summarize the views shared by participants at the Hereditary Angioedema (HAE) Forum held by Canadian Blood Services. The statements made in this report reflect their experiences, perspectives and ideas, as shared in their own words.

1. Introduction

This report summarizes the key highlights from the Hereditary Angioedema (HAE) Forum held on December 12-13, 2019 in Toronto.

The objectives of the Forum were to:

- Understand the past, current and future anticipated use of HAE products;
- Understand treaters' and patients' experiences with HAE (efficacy, preferred products, etc.);
- Increase, and have a shared, understanding of different perspectives; and
- Identify potential opportunities to improve forecasting and decision-making.

The Forum included a mix of presentations, Q&A, plenary dialogue and small group discussions.

Dr. Isra Levy (Vice-President, Medical Affairs and Innovation) opened the Forum by emphasizing the importance of hearing from the diversity of perspectives in the room and having a dialogue to help build common understanding that will inform future decision-making.

2. Forum Participants

The Forum brought together 20 stakeholders representing a diversity of perspectives, including:

- Patients representatives from HAE Canada and AOHQuebec;
- Treaters/physicians and researchers from across Canada, including Ontario, Quebec, Newfoundland and Labrador, Nova Scotia, and Manitoba; and
- Health systems/policy, including representatives from the Canadian Agency for Drugs and Technologies in Health (CADTH) and the National Advisory Committee on Blood and Blood Products (NAC).

One provincial representative attended as an observer from the funder perspective. Members of Canadian Blood Services' Medical Affairs and Innovation and Public Affairs (Stakeholder Engagement) teams also attended.

A third-party facilitator and note-taker from Hill+Knowlton Strategies attended the Forum to help guide participants through the two-day agenda, ensure a productive dialogue and capture participants' discussions.

3. Summary of Discussion

Throughout the discussion, participants discussed various HAE therapies, including:

Name	Generic name and description	Canadian Blood Services or drug stream
Berinert	C1-inh concentrate	Canadian Blood Services
Cinryze	C1-inh concentrate	Canadian Blood Services
Haegarda	C1-inh concentrate	Canadian Blood Services
Takhzyro	Lanadelumab, kallikrein inhibitor	Drug stream
Firazyr	Icatibant, B2 bradykinin receptor receptor antagonist	Drug stream
Cyclomen	Danazol, androgen	Drug stream

3.1 Product Selection Process

To help set the context for the Forum, Dr. Sylvain Grenier (Director, Plasma Protein Products Program) began by discussing the new interim process for selecting which products are added to Canadian Blood Services' formulary.

Questions and comments about the review process and access to specific treatments were raised by participants throughout the presentation and subsequent discussion, including:

- **Outlining the review process for Haegarda and lanadelumab:**
- **Haegarda:** Dr. Grenier explained that Haegarda (identical to Berinert but labelled for prophylactic, subcutaneous use) went through a brand review, followed by a business impact assessment. The review was successful and Haegarda is now in the process of being added to the formulary, which involves Canadian Blood Services' current negotiations to bring Haegarda to Canada in 2020. The time needed for branding and marketing in Canada could potentially delay access.
- **Lanadelumab:** As the provinces/territories deemed that lanadelumab does not fall within Canadian Blood Services' mandate, it will not be on the organization's formulary. As a result, it went through CADTH's Common Drug Review (CDR) process for public drug plans. The Canadian Drug Expert Committee (CDEC) has since recommended that includes several criteria for use. The pan-Canadian Pharmaceutical Alliance (pCPA) will now begin price negotiations (expected in 2020). Following this, each province/territory will determine whether lanadelumab is listed with a negotiated price, criteria, etc.

- **Comparing access to Haegarda in Quebec to the rest of Canada:** One patient representative noted that Haegarda will be available in Quebec as of January 2020 and asked what the timeline would be for the rest of Canada. Dr. Grenier mentioned an anticipated timeline of May/June 2020. As in Quebec, Haegarda will be listed without limitations.

- **Advertising for clinician and patient input:** Dr. Grenier said the new review process, which is based on the CDR process, includes specific ways for CADTH to collect input from clinicians and patients.

- **Clarifying Canadian Blood Services' position on Haegarda vs. Berinert:** Dr. Grenier said Canadian Blood Services will determine what type of inventory it needs to support patients.

3.2 HAE Context-Setting and Emerging Systems Issues

For additional context to help inform the dialogue, Dr. Kathryn Webert (Medical Director and Special Advisor, Plasma Derived Products) provided information on the various HAE treatments available now and those anticipated in the future, and data reflecting the significant growth in demand for HAE therapies and the impact of that on healthcare budgets and global trends.

Participants raised the following questions/comments:

- **Tracking increase in usage:** Dr. Webert explained that usage is likely increasing because the number of patients using products is increasing, as is the number of units used per patient. However, Canadian Blood Services currently does not have access to patient-level data and can only track the number of units it issues. She highlighted several factors contributing to increased usage, including greater recognition of HAE, increased recognition of the importance of prophylaxis and transitions in dosage.
    - One participant explained that increased usage is likely related to the higher dosages required with subcutaneous use and that, going forward, models should be changed to track subcutaneous vs. intravenous utilization and to account for the variety of products

available (e.g., introduction of Haegarda). Dr. Webert agreed some variables are not included in the current models and Canadian Blood Services hopes to collaborate with stakeholders to address these gaps.
    - One patient representative noted that an app has already been developed in Quebec, which patients are using to help track this kind of information.

- **Plasma donation requirements:** Dr. Webert noted that, while C1-inh products are plasma-derived, Canadian Blood Services is not concerned about shortages at this time. However, plasma requirements remain an important consideration moving forward as more patients are put on these therapies.

- **Cost implications:** Some participants noted that not all products are priced the same, which should be considered when discussing future costs, especially with Haegarda coming into Canada. One clinician said, "despite units going up, [the increase] may not be parallel to cost."

Following Dr. Webert's presentation, Prof. Nancy Heddle (Director, McMaster Transfusion Research Program), discussed C1-inh trends at four hospitals in Hamilton between 2010-2018, in which there was a significant increase. Prof. Heddle also discussed a new one-year study starting in January 2020 to help support Canadian Blood Services with forecasting/product management, as well as to inform future registry development.

Participants raised the following questions/comments:

- **Increase in type 3 HAE patients:** One clinician mentioned an increase in patients with type 3 HAE and the "very high doses" for these patients as one explanation for increased usage.

- **Scope of new study:** One participant asked whether the new study should involve clinicians from across Canada. Prof. Heddle explained the intention is to keep it at the local level and minimize the need for various Research Ethics Board approvals, similar to the previous study conducted in Hamilton.

- **Rationale for new study/data collection:**
    - Some participants suggested using HAE Canada's data (e.g., National Report Card) which already provides useful information on HAE patients.
    - An HAE Canada representative questioned why a new study is needed, especially if there will still be gaps in tracking patients who are doing well and not being treated/not going to a hospital. HAE Canada is willing to collaborate and partner with Canadian Blood Services and others in this area rather than in collecting more data: "We have all the data you need because we have patients we work with daily."
    - Prof. Heddle acknowledged some of the study's limitations (e.g., not collecting information on patients who don't need the product) and committed to working with others to bring forward key considerations to the study's working group.
    - One participant noted this study is still useful because it could provide a broad perspective on product use across Canada: "You need different snapshots to see what's going on." They noted not all patients are part of HAE Canada (e.g., those who receive one dose post-surgery).

- **Patient confidentiality:** One participant cautioned that patients could potentially be identified in the new study, depending on how data are shared and presented. Prof. Heddle recognized this has been a concern raised by both patients and clinicians.

- **Tracking utilization:** One participant suggested there is a gap in tracking the utilization of blood products compared to products funded through the drug stream, with products funded through public drug plans tracked nationally through the National Prescription Drug Utilization Information

Service (NPDUIS). The need for a database for this purpose was noted, with the expansion of CBDR worth considering (e.g., if there is a recall/notification, they know where all products are).

3.3 Current Clinical / Treatment Practice

For the next discussion, Dr. Stephen Betschel (Staff Clinical Immunologist, St. Michael's Hospital and Associate Professor, University of Toronto) gave a presentation on the clinical features of HAE, care gaps, and how the Canadian/international HAE guidelines can help address those gaps.

Following Dr. Betschel's presentation, participants discussed the following questions/comments:

- **Understanding triggers for HAE attacks:** Dr. Betschel acknowledged there is a general lack of understanding around HAE and its potential triggers, which include stress.

- **Understanding misdiagnosis:** One physician highlighted how patients may be inappropriately started on a C1-inh after an allergic reaction. Another noted that patients with abdominal attacks had been inappropriately treated for appendicitis. Dr. Betschel emphasized the importance of patients seeing specialists who are familiar with HAE and receiving a proper diagnosis.

- **Natural history of HAE:** One participant asked about the natural history of HAE, with a focus on age and gender factors. Dr. Betschel noted that, while there should be no difference between males and females for types 1 and 2, there are more women than men on C1-inh, which may be because more men are able to take oral medications such as danazol. Symptoms of HAE usually become apparent in the first or second decade of life. The life expectancy of individuals with HAE is shortened.

- **Long-term effects of HAE:** Patients and physicians discussed a wide range of long-term effects of HAE. Patient representatives discussed the significant effect on their family, as HAE is a familial condition ("people have told us not to have children"). Treating physicians noted the impact of stress on many HAE patients, with one describing the unpredictability for patients and not being able to "plan anything in life if they have recurrent episodes."

- **Comprehensive care approach:** One participant called for more funding for comprehensive care clinics, which could provide the social and psychological supports many HAE patients need, adding this has been "missing forever, not just in Canada but internationally."

- **Treatment approach – on-demand/acute vs. prophylactic:** Patients and some physicians discussed the benefits of on-demand and prophylactic treatment, recognizing the type of treatment depends on the patient.
    - One physician, referencing experience treating hemophilia patients, discussed the effectiveness of on-demand treatment if a patient is properly trained in administration and has access to the right treatments.
    - Recognizing the effectiveness of prophylactic treatment, one participant emphasized the importance of funding and access, suggesting patients tend to "hold off and treat too late" because they are aware of the cost of therapies.
    - One treating physician agreed that prophylactic treatment is better when patients can manage it well, as they get fewer attacks over time.
    - One participant highlighted the importance of early treatment of acute attacks, noting that while C1-inh delivered intravenously may start to work within 30 minutes it could still take up to 15 hours for the attack to abate. They suggested some patients use a "hybrid" approach including both intravenous/on-demand treatment and subcutaneous/prophylactic treatment.

- Dr. Betschel highlighted from his experience that patients who have access to acute on-demand therapy also have fewer attacks.

- **Guidelines around oral prophylaxis**: One participant asked about the key considerations for recommending oral prophylaxis, in particular steroids such as danazol.
  - Dr. Betschel explained that danazol is associated with significant safety and side effect issues, such as increasing the risk for liver tumours and stunting children's' growth and cannot be used in pregnancy.
  - Another treating physician expressed uncertainty with danazol's efficacy, as there are some issues with the evidence currently available, but recognized it is the only option in some countries where blood products are not available.
  - A patient representative shared their experience using steroid therapy for 20 years; while these drugs worked well in reducing the number of attacks, one of them had to be stopped when it was removed from the market and another had to be stopped when the patient developed a liver cyst.

- **Impact of accessibility to prophylaxis on system costs:** One participant emphasized that, if patients have access to various prophylactic options, they will only use what they need: for example, "someone will never be on prophylactic C1-inh and prophylactic Takhzyro." This participant believes that providing this type of accessibility will help reduce system costs overall, as there will be fewer phone calls to physicians, ER visits, hospitalizations, etc.

- **Maximizing effective use of products**: Physicians who treat HAE patients underscored the need to focus treatments on "patients who really need it" and "as they are meant to be used," reflecting the importance of building capacity to diagnose patients properly (e.g., in ERs) and conduct follow-up, as well as ensuring access to a variety of treatments as per patients' needs and preferences (e.g., prophylaxis vs. acute treatment). They believe this would help maximize value for money: "I cannot imagine any treater would want to see products used when not indicated. It would impact patients too much and could lead to shortages."

- **Importance of a variety of treatment options:** Patients and physicians agreed that a variety of treatments are needed "so all patients don't have to go on only one medication approved by the province." For example, one patient described their experience of participating in various trials (e.g., Haegarda, lanadelumab), all of which helped to varying degrees in combination with their existing treatments (e.g., Berinert). Others reiterated that "one size does not fit all," noting that certain medications work better for some patients than others (e.g., C1-inh for additional inflammation) and more information/evidence will be available in the future to help inform decisions.

- **Utilization of Haegarda:** One physician suggested most patients using subcutaneous treatments would be switched over to Haegarda.

  A participant asked about the intended dosing of Haegarda by physicians, as the label indicates 60 U/kg but some studies used 40 U/kg. Treating physicians emphasized the need for individualized therapy, noting that each patient is different, and dosage should be adjusted based on response to treatment. One physician explained that patients may start at either dosage, which can then be adjusted up or down by physicians depending on how well it works. While 60 U/kg was the approved dose, evidence has shown little effect when changing dosages for patients. Some physicians agreed with a "step down" strategy, especially for high-risk patients (e.g., preventing laryngeal attacks), but lower-risk patients could use a "step up" strategy, starting at the lower dose and increasing it if their condition worsens.

- **Key considerations for treatment recommendations:** At various points in the discussion, participants discussed key considerations for how patients and physicians would determine the best treatment.
    - In discussing the need for therapy combining preventative and acute treatments, one participant asked whether lanadelumab will become the recommended treatment for preventing acute attacks, or whether more patients will be given icatibant. Dr. Betschel and others noted the key factor is not just patient choice, but what coverage they have. However, it was noted that icatibant may be more convenient for acute treatment because it can be given subcutaneously which may facilitate at home administration.
    - One physician noted that, if "all is equal and the patient could choose," they would prefer something administered less frequently and at home.
    - One patient representative said lanadelumab "is the best medicine for C1-inh normal" and that "you will see the number explode" if it is eligible for coverage. This would then decrease Berinert use and increase access for patients currently taking no treatments.

3.4 Latest Findings on HAE Treatment

Representatives from CADTH gave a presentation on their evidence review – commissioned by Canadian Blood Services – for discussion. The review included consultation with clinical experts, analysis of utilization trends for C1-inh, economic analysis, and budget impact assessment. This evidence is used by policymakers as they consider long-term funding implications to ensure patient access and efficient use of healthcare resources.

Various questions and comments were raised by participants throughout the presentation, who provided positive feedback on CADTH's work, but noted some concerns, as outlined below.

- **Composition of clinical expert committee:** One participant asked how CADTH chose the four clinical experts to consult as part of this project, as they suggested "you're relying on a small group of opinions which may not present the community of experts." While CADTH recognized this is a limitation of the project, the clinicians are considered well-known experts and were selected in consultation with Canadian Blood Services.

- **Questions around source of data and assumptions:** In reference to the cost-utility analysis, some participants were not familiar with the source for the Quality of Life inputs (i.e., Nordenfelt et al). CADTH explained that the source is a Swedish study, as there are no comparable Canadian data available (which some participants disagreed with). However, one participant highlighted that the Nordenfelt trial "might actually be better data" because it was taken from the general population, not a clinical trial.

  CADTH also recognized issues with some of its assumptions (e.g., patients not discontinuing prophylactic therapies over their lifetime), which may be a limitation of its analyses. However, since the main driver of the results was the cost of drugs, other factors (e.g., variance in attack frequency by treatment) did not have a significant impact on the data: "Even with minor adjustments these results still hold." CADTH agreed it could input new data into its models to reflect the introduction of new therapies as they become available.

- **Clarification on willingness to pay:** Also, in reference to the cost-utility analysis, some participants wondered why the willingness to pay (WTP) threshold "is so wide." CADTH explained that it used a wide range because HAE is a rare disease and there are no set WTP thresholds. When asked about data on patients' WTP, CADTH clarified that the threshold is determined from a payer, not patient, perspective.

- **Caution against "no prophylaxis strategy":** Patient representatives urged that "no prophylaxis" for patients, as outlined in the cost-utility analysis, is not an option: "We feel we're beyond that.

We can't even consider no prophylaxis for HAE patients." However, one physician noted there are some patients who are asymptomatic and wouldn't require prophylactic treatment, and some patients do not want prophylaxis. CADTH explained its methodology was adapted from the Institute for Clinical and Economic Review's (ICER) model and that costs associated with this option were only included to provide comprehensive information.

- **Clarification on new user data:** In reference to the data presented from CADTH's utilization analysis, one participant noted greater clarification is needed to differentiate new and continuous users: "More new users should've resulted in greater continuous users [over time]. It looks like it's lots of one-off treatments and then they didn't use it again." They also suggested considering the age of new users.

- **Data on Canadians diagnosed with HAE:** One participant noted there is often a "huge inflection point" in the utilization data, which could reflect the introduction of new products and prophylactic treatments. They suggested it would be useful to have data on how many Canadians are diagnosed with HAE each year.

- **Need for comprehensive analysis of budget impact:** Some participants expressed concern with the results of the budget impact analysis – specifically that it doesn't include broader health system and societal impacts (e.g., caregiving, missing work days). Some suggested moving any data/content discussing societal impacts to the front section of the report, which will help provide decision-makers with more accurate, comprehensive information: "This is just the health payers perspective, it's not societal."

CADTH acknowledged there are limitations to the study but its analysis reflects the published data available and follows the accepted methodology used to assess and inform decision-makers on all therapies, which helps to ensure equity across disease states. However, some warned that rare diseases are disadvantaged in this process because the data is much more difficult to accumulate. In response, CADTH recognized the need for more flexibility in interpreting this data but said this is still an evidence-based process.

- **Clarification on number of total HAE patients:** Some participants asked whether the data includes patients with all three types of HAE. CADTH explained that a simplified approach was used to determine the total number of patients for its analysis, as it wasn't sure about how the percentage of total HAE patients, but the clinical data was from type 1 and type 2 patients. As a result, some suggested the data is likely underestimating patient numbers.

- **Clarification on number of patients using specific treatments:** In response to one participant's question about how costs were determined for patients using various treatments, CADTH said data on product uptake is not available – rather, the clinical experts consulted for the project provided input.

- **Need for accessible data:** All participants agreed that data accessibility is a significant issue that needs to be addressed. CADTH highlighted the need for a standardized approach for collecting data for blood products (e.g., not just volume but also reason for use), similar to what exists for drug systems. This would help manage the supply and align reimbursement policies between the drugs and blood products streams, which is especially important as participants expressed concern that there could be a shift in access to some products over others. Additionally, one patient representative emphasized the need for a comprehensive data strategy for blood and blood product patients, which will help HAE patients.

- **Patient collaboration:** HAE Canada representatives urged CADTH to reach out to them for patient input to help inform future projects: “One phone call to a patient organization would have helped you.”

In addition to its presentation on its evidence review, CADTH also responded to some participant feedback on its reimbursement recommendations for lanadelumab that were published in November 2019 for each drug plan’s consideration. **Clarification on “attack characteristics” for coverage criteria:** In reference to approximately “3 attacks within any 4-week period,” some participants noted that patients having such frequent attacks would be on prophylaxis. They asked whether this meant these patients would need to be taken off prophylaxis treatment (“would you need to make the situation worse?”) to qualify for a treatment. CADTH explained there are other implementation considerations (e.g., number of attacks before going on prophylaxis) in addition to these criteria. However, some participants said attacks could be prevented if patients know to use rescue therapies, which means there is “still a grey area” in CADTH’s recommendations.

Some clinicians asked whether the severity or location of an attack is considered, as some patients may have fewer than three attacks per month but suffer one laryngeal attack per year, which is serious and should warrant qualification for prophylaxis. One participant noted that CADTH “chose the mean, but not the range” of attacks in its study. CADTH explained that the expert committee consulted as part of the project also considered the individualized history of the disease. Canadian Blood Services also clarified that CADTH is providing its recommendations to drug plans, which means lanadelumab could be listed in various ways.

3.5 HAE Patient Perspectives

To help inform participants of the patients’ perspectives, representatives from HAE Canada discussed the significant impact of the disease on their lives. Key highlights include:

- **The “success story” of the improvement in care for HAE patients**: Patient and caregiver representatives thanked several of the participants in the room for the care they’ve provided. One patient representative called the current situation for HAE patients a “success story,” particularly in terms of the timely access to HAE specialists and the high quality of clinicians in Canada.

- **The financial impact of HAE on public payers:** HAE patients are high healthcare system users, as attacks frequently result in ER visits, hospitalizations, reliance on ambulance/EMT services – all of which are top drivers of healthcare costs. As a result, newly available treatments for HAE should not be regarded as a “cost” to public payers, but rather an investment that can significantly benefit the health system.

- **The economic and humanistic burden on a family with HAE:** Families who need to care for a child with HAE can incur significant personal costs (e.g., travel, buying a home near an acute care facility, loss of job opportunities), as well as high costs incurred by the healthcare system. These costs were reduced over time through accessibility services, a home infusion program and working with an HAE specialist: “It’s a game changer.”

- **Quality of life:** Patients described their quality of life prior to receiving treatment, in which they previously had no at-home treatment options, relied on ERs during severe attacks and experienced a lack of consistency in treatment overall. Having untreated HAE significantly affected their lives, as they often missed school and work and were unable to plan personal events/commitments. Now these patients have access to a variety of HAE treatment options, which has improved their quality of life.

Several comments and questions were raised following the presentations, including:

- **Factors impacting a patient's decision on specific treatments:** One participant felt it would be helpful for decision-makers to understand why a patient representative "goes between" various treatment options (e.g., subcutaneous vs. intravenous, varying dosages). The patient explained it often depends on how they feel and the estimated time of effect for a treatment, which then determines what they will take and when (e.g., intravenous treatment because it works fast if they think they are having an attack). They added that certain side effects, particularly the risk of fatigue and scarring, can influence patients' decisions. Given the high cost of some treatments (e.g., icatibant), another participant said, "I will take whatever I can get my hands on" to ensure they have access as needed, even if products are expired.

- **Increase physician awareness of identifying HAE:** Given the estimated high proportion of undiagnosed HAE patients, one participant asked whether there is a concerted effort to raise awareness among physicians about how to identify symptoms of HAE. Participants noted various initiatives/ideas, including:
    - Dr. Betschel noted the Canadian Hereditary Angioedema Network (CHAEN) has developed an algorithm tool to help ERs refer patients to specialists.
    - One participant said this has become a priority in Quebec, which has been advanced by facilitating meetings between HAE specialists and physicians and nurses, with a focus on those who may have frequent interaction with potential patients (e.g., ER, gastroenterologists).
    - One participant recommended HAE Canada encourage its members' families to get tested.
    - One participant suggested getting more physicians "to think about bradykinin… when you have that, they will think about what is needed and order it."

- **Support for research:** One HAE Canada representative noted the organization is planning to start a foundation within the next five years to raise money for research.

3.6 Canadian Bleeding Disorder Registry (CBDR)

To conclude Day 1, Dr. Betschel gave a presentation on the CBDR – a national clinical database for patients with bleeding disorders, designed to be used on a daily basis by clinicians. Developed by the Association of Hemophilia Clinic Directors of Canada (AHCDC), the CBDR also includes MyCBDR – a patient and caregiver interface using the same back-end database. Dr. Betschel discussed the database's various features, including clinic patient management, product management, personal health and treatment records, analytics and reporting. The CBDR provides a model that could be used for collecting data and tracking utilization and outcomes for HAE patients.

The following questions and comments were raised:

- **Timeline for development/implementation:** Dr. Betschel estimated that, after the development of a business case, re-working the CBDR platform for HAE would take approximately 18 months.

- **Need for funding:** Dr. Betschel and others emphasized the importance of funding for the implementation of this database. Dr. Robert Klaassen (Pediatric Hematologist/Oncologist, CHEO and President, AHCDC) described the AHCDC's experience with funding and implementing the CBDR to demonstrate proof-of-concept over three years, at which point "the PTs and Canadian Blood Services realized its value and funded it." The CBDR now has stable funding and all provinces are using it (except British Columbia which has its own provincial database, iCHIP). Dr. Klaassen urged that funding be in place to support the implementation of an HAE module. One patient representative suggested it may be more difficult to convince governments to fund this for HAE patients, as they are a much smaller group than those affected by hemophilia: "It will be a struggle to get that kind of money because we don't have as many patients."

- **Varied use of database:** Dr. Klaassen said the CBDR is not used optimally by all hemophilia centres, noting that while McMaster University "leads the pack" others only do the bare minimum, "so there is a spectrum." The focus is on getting less-engaged centres to contribute more to the database.

- **Database governance:** One patient representative recommended leveraging HAEi Connect – an online membership database available to all HAE member organizations globally – and other existing resources/collaborations: "We have huge things out there that wouldn't cost anything to use." Both Dr. Betschel and Dr. Klaassen noted the governance of an HAE database would belong to the HAE community – AHCDC only wants to help in implementing what it has already set up with CBDR. Additionally, HAEi Connect has been considered and some issues have been raised around the type of data it collects ("it's not a real-time registry… it wouldn't provide much of the data we need in Canada to inform treatments"), as well as its significant cost implications and potential data transfer issues that could arise.

- **Privacy concerns:** Given the low prevalence of HAE in Canada, one participant asked whether results from a registry/database could be published without risking patient confidentiality. Dr. Klaassen noted that, although the data would be aggregated, there are sometimes challenges with the sub-analysis for hemophilia patients, which is addressed by conducting privacy analyses and getting consent from patients before they go on the registry.

- **Patient engagement:** One patient representative expressed the need to engage HAE Canada in the development and implementation of database, noting that there are "too many other patient groups speaking on our behalf." Dr. Betschel emphasized that patient input will be critical moving forward, citing the continued collaboration between HAE Canada and CHAEN. Dr. Klaassen shared a similar sentiment in terms of the Canadian Hemophilia Society's ongoing support for the AHCDC's work and the CBDR.

3.7 Our Common Understanding: Considerations and Opportunities for Moving Forward

Informed by the context-setting presentations and discussion from Day 1, participants then focused on considerations and opportunities for moving forward. Following a round of individual reflection, participants collaborated in multi-disciplinary groups to share their perspectives and ideas. All considerations and opportunities were then discussed and further informed in plenary. A dot-mocracy exercise helped identify the group's collective priorities, as each participant had the opportunity to vote on their top ideas.

Top ideas

1. HAE patient registry and database (24 votes) • Similar ideas included: **National data strategy**	
Description	An HAE patient registry would help document and provide data on the uptake of products and patient outcomes, while a database would help ensure all patients are captured (including those doing well and not actively regularly receiving treatments). Both a registry and database are needed to help ensure information is available and used, particularly to help Canadian Blood Services forecast demand. Some participants recognized this is a long-term solution that requires time to build, which means an interim solution is also needed to collect utilization data.

	In addition to building a registry, a comprehensive data strategy for all blood and blood products is also needed, which would help HAE patients.
Key considerations and opportunities	• Provides access to better data, such as patient information, available inventory and product location • Supports patient engagement and accountability • Addresses broad information gaps (e.g., cost of drugs/treatment, research needs) • Supports better patient care
Limitations	• Privacy legislation/requirements, especially navigating the specific requirements for different jurisdictions • Funding • Resources for ongoing maintenance • Further fracturing of existing registries/databases (e.g., MyCBDR) • "Imperfect information" from a lack of published data to help inform decision-making
Supports needed for success	• Strong governance, which requires engaging a diversity of perspectives "so everyone is at the table" • Balancing accessibility to and privacy of data, especially to help ensure transparency/accountability of decision-makers • Patient engagement

Other discussion points	• Who is responsible for creating the registry?
	  ○ One participant asked about CBS' role in developing the registry as a national project, while another suggested the Canadian Institute of Health Information (CIHI) could be involved to leverage existing databases that could then be used to develop a separate HAE module.
	• Who is not currently represented in the room? Who needs to be involved at the hospital level?
	  ○ Participants highlighted the importance of engaging nurses ("they are the ones that will make the thing work"). Future discussions should include representation from specialist nurses, as there is already a group who treat HAE and meets 2-3 times a year.
	  ○ Blood banks should also be involved.

2. Coordination of blood products, drug formularies, policymakers and funders (19 votes) • Similar ideas included: **Equal access to blood product/drug products, Coverage under different formularies, Increase awareness of changes in funding environment/process**	
Description	Greater coordination is needed among health system stakeholders to ensure equal access to products (e.g., lanadelumab) for HAE patients across Canada. This could be supported by providing full coverage through Canadian Blood Services rather than having some products covered through Canadian Blood Services and some products covered through drug plans, as access can differ greatly depending on a patient's location, availability of product, etc. In terms of formulary management, this involves increasing awareness of potential changes to the funding environment, outlining steps that can be taken

	to "work within new systems," and identifying and improving information gaps (i.e., setting up new databases).
Key considerations and opportunities	• Ensures equal access to treatment across provinces • Facilitates better communications between different stakeholders/levels • Equalizes treatment plans by streamlining access • Supports system sustainability by ensuring that one group/system has oversight of all treatments for a given condition; this allows for robust utilization monitoring to inform decision-making
Limitations	• Securing buy-in/participation from all provinces to ensure equitable access and affordability
Supports needed for success	• Support from funders/provinces and territories
Other discussion points	• Appreciation for what Canadian Blood Services has done as a national organization ("Canadian Blood Services is actually doing this quite well… when I go international we have to be so proud of what we've done")

Additional ideas

3. **National nursing support program** (9 votes): This is about "inviting nurses into the circle of care," with a focus on providing the support needed to collect data for a national registry and monitor for HAE patients (less on day-to-day practice). For example, nurses could interact with patients and check in with prescribers, which would help them keep a closer eye on dosing strategies and adjust if needed. Additionally, this would help those who don't have access to larger clinics in hospitals.

4. **Consensus among providers/payers/patients on treatment plans** (8 votes): It would be helpful to have patient involvement in the development of consensus guidelines and treatment algorithms, particularly around the rationale for a patient "to move from one step of care to another" (e.g., product selection, dose). The goal is not to restrict access to any specific treatment, but to provide guidance for the optimal, judicious utilization of products without impacting patient care, especially given the current fiscal environment.

5. **Comprehensive multi-disciplinary clinics for HAE treatment/Equal access to social worker resources** (7 votes): Similar to the model for hemophilia treatment centres, these facilities would include nurses – who would play an instrumental role in helping to coordinate complex care needs ("currently this falls on us [physicians] in our free time"), optimize patient outcomes, and facilitate participation in a registry. Some suggested this could "replace industry-sponsored infusion clinics." Additionally, an existing provincial renal program could be considered as a model. Building on the discussion comparing supports available for hemophilia patients, participants also highlighted the value of HAE patients having access to social workers.

6. **Development of HAE Standards of Care:** This could help ensure the consistent treatment of HAE patients across the country by outlining the minimum requirements for clinical care, similar to what the AHCDC has developed for hemophilia patients. However, some patients and physicians said these standards have already been developed and implemented with some success: "Now we have good specialists and distinct centres of excellence." However, the ongoing challenge is that some treatment centres have not secured the funding needed to

implement the standards, which has led to some inequity in care across the country.

7. **Address distribution issues:** Some participants discussed the challenges facing blood banks in distributing products, as they have to follow strict standards and regulations, don't have capacity to store products for long periods of time, are "not built to provide customer service," and are not sufficiently compensated for additional work. As a result, some smaller blood banks are refusing the carry products like Berinert and are directing patients to hospitals instead. Some physicians discussed how access to products has been managed differently in other provinces, such as organizing pick-ups through labs and clinics (e.g., Manitoba). However, this means there is unequal access across provinces. There was some discussion of distributing these products through pharmacies.

Before closing this discussion, the HAE Canada representatives reflected on the considerations and opportunities and highlighted the following points:

- **HAE Canada's success:** Over time, HAE Canada has had much success in helping to identify patients, and the Centres of Excellence have helped patients navigate the healthcare system to get the care they need: "Before it was a nightmare. I can say in the past year we haven't found anyone who had an unnecessary surgery or was addicted to morphine. Now the people we find are newly symptomatic and people are seen [by a specialist] within a week. That's a celebration."
- **Focus on labs:** One patient representative agreed with the need to pursue opportunities with labs, which have the capacity (as opposed to blood banks) and are well positioned to help with distribution ("they see people all the time").
- **Buy-in/engagement with registry:** In terms of developing and implementing a national HAE registry, one patient representative emphasized the importance of getting physicians, patients (through HAE Canada's membership) and nurses on board.

3.8 Next Steps and Reflections

In discussing the next steps following the Forum, participants discussed:

- **Planning future meetings and including more/new members to continue this work**
- **The possibility of having similar meetings for other rare diseases requiring blood products** (HAE Canada expressed interest in participating)
- **Various responsibilities for moving this work forward:** The next meeting should include reporting on progress.

At the end of the Forum, all participants shared their reflections on the two days of discussion.

- **Highlighting common ground:** Many participants appreciated the shared issues, perspectives and ideas that emerged from the discussion, especially with the diversity of stakeholders in the room: "It's interesting to see that we all came to the same conclusions."
- **Developing a deeper, more complex understanding of the issues:** Several participants felt the Forum was very informative and appreciated having the opportunity to learn from others. This has helped them build both a broader and deeper understanding of the various issues which they will share with their colleagues/networks.
- **Maintaining ongoing dialogue and collaboration with a diversity of key stakeholders:** Participants highlighted the importance of all stakeholders continuing to work together: "We should continue having meetings like this. It's the only way to bring all sides to the same table and to truly understand perspectives."
- **Engaging provinces and territories in a national approach:** Given the importance of funding, more provinces and territories (e.g., formulary committees) need to be involved in this conversation: "Everything happens within provinces and territories… they need to understand what's happening at the national level."

- **Establishing stronger connections:** Some participants described feeling more connected to others as a result of the Forum, which has helped to build the foundation for further collaboration.
- **Engaging other key perspectives:** Canadian Blood Services needs to ensure that no one "feels left out" of the conversation, including nurses and other clinicians and patients.
- **Ensuring ongoing collaboration with HAE Canada**

In closing, Dr. Levy expressed gratitude to participants for their time and contributions, emphasizing that Canadian Blood Services' goal was to help facilitate dialogue among stakeholders to help better understand the diversity of viewpoints. In his perspective, the Forum helped validate many assumptions and challenges, while also highlighting some new insights shared by participants.

He commended the high level of engagement from all participants and said a "What We Heard" summary report would be shared, along with a participant contact list for those interested.

Appendix: Participant List

Provincial representatives

Brian Bertelsen, Department of Health and Wellness Senior Policy Lead at National Blood Portfolio Unit

National Advisory Committee on Blood and Blood Products (NAC)

Dr. Katerina Pavenski, Head of the Division of Transfusion Medicine, St. Michael's Hospital

HAE patient representatives

Jacquie Badiou, President, HAE Canada

Richard Badiou, Director, HAE Canada

Anne Rowe, Director, HAE Canada

Tamara Armoogan, Director, HAE Canada

Charles St-Pierre, Président, HAE/AOH Québec

Physicians

Dr. Stephen D Betschel, HBSc, MD, FRCPC, FAAAAI, Associate Professor of Medicine Department of Internal Medicine, University of Toronto, Division of Clinical Immunology and Allergy, St. Michael's Hospital

Dr. Robert Klaassen, MD, FRCPC, Investigator, CHEO Research Institute, Pediatric Hematologist / Oncologist, CHEO Associate Professor, Department of Pediatrics, Faculty of Medicine, University of Ottawa

Dr. Gina Lacuesta, MD, FRCPC, Assistant Professor, Division of General Internal Medicine, Department of Medicine, Dalhousie University, Allergy &Clinical Immunology, QEII Health Sciences Centre

Dr. Andrew O'Keefe, MD, FRCPC, NL Allergy & Immunology (private practice)

Dr. Jacques Hébert, MD, FRCPC, Allergie et Immunologie, CHU de Québec

Professor Nancy Heddle, Research Director McMaster Centre for Transfusion Research

Dr. Paul Keith, MD FRCPC, Associate Professor**,** Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University

Dr. Rozita Borici-Mazi, Associate Professor, Division of Allergy & Immunology, Department of Medicine & Pediatrics, Queen's University

CADTH participants

Amanda Allard, Manager, Clinical Research, Pharmaceutical Reviews

Michel Boucher, Program Development Officer, Pharmaceutical Reviews

Estefania Ruiz-Vargas, Health Economist, Evidence Standards

Tessa Cornelissen, Health Economics Research Officer, Evidence Standards

Canadian Blood Services participants

Dr. Isra Levy, Vice-President, Medical Affairs & Innovation, Office of VP Medical Affairs & Innovation

Dr. Kathryn Webert, Director, Medical & Special Advisor – Plasma, Office of VP Medical, Affairs and Innovation

Dr. Sylvain Grenier, Director, Plasma Protein Products, Formulary, Medical Affairs and Innovation

Dr. Sarah Jennings, Manager, Utilization Evaluation, Formulary, Medical Affairs and Innovation

Lindy McIntyre, Director, Government Relations, Public Affairs

Ellis Westwood, Director, Stakeholder Engagement, Public Affairs

Stephanie Kelly, Senior Manager, Stakeholder Engagement, Public Affairs

Christy Simpson, FFS – Bioethics Consultant – Legal Services
Christine Mastroianni, Coordinator, Strategy Planning & Integration