

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

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: Belzutifan
Name of the organization: Canadian VHL Alliance
Website : www.CVHLA.ca
Name of the respondent to the questionnaire: Stephen Parrott
Name of the contact person : Stephen Parrott
Email address : SParrott@ValueBasedPlanning.com
Telephone : 289-314-3047
Mailing address : 1215 Bayly St. Suite 1407, Pickering Ontario,
L1W 1L7

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

Hi there, our board of Directors are:

Stephen Parrott (Chair)

Renee Tsang (Treasurer)

Patty Milburn (Secretary)

Jess Pearson

Susan Anson

Nicky Harder

Describe your members.

For example:

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

Our members are from across Canada. In the past we have been focused on raising money for Research, but with the recent symposium, the new drug Belzutifan, more time from board members and greater opportunity to really make a difference, we are expanding our activities. We hope to work more with Gail Ouellette and the Regroupement québécois des maladies orphelines more in the future.

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

Merck Canada

Amounts

\$15,000 to sponsor the 2022 International VHL Medical Symposium - Here is a link to the presentation videos
(<https://www.youtube.com/playlist?list=PLprmGjNfymhGecYsqeg0GKS0gC9x0rwdP>).

The 2022 VHL International Medical virtual Symposium brought together 56 researchers, medical professionals and patients from all over the globe to discuss the latest in VHL research and treatment. Celebrated researcher Marston Linehan, MD of the National Institutes of Health participated extensively and we had a video presentation by Nobel laureate Gregg L. Semenza, MD, PhD.

Many of the presentations were re-packaged and published in the "Endocrine Pathology Journal" titled - Abstracts of the 15th International VHL Medic/Research Symposium.

The symposium was accredited by Canadian Association of Genetic Counsellors (CAGC) for Continuing Education Credits (CEC) Credits.

Organizations

No others.

Amounts

Organizations

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

No

Reference (if applicable)

Opinion published or publicly expressed

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.

I have been working with the following national organizations on a submission to CADTH due Feb. 21st, 2023. These organizations also support the drug's reimbursement in Quebec:

- Gail Ouellette and the Regroupement québécois des maladies orphelines
- Kidney Cancer Canada (KCC),
- Canadian Organization for Rare Disorders (CORD),

In the process of this work we circulated a survey to VHL patients and caregivers and received 121 responses. 7 of these responses came from people identifying as living in Quebec.

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*

Within my capacity as Chair of the Canadian VHL Alliance, I am worked with Kidney Cancer Canada and Pancreatic Cancer Canada to send the survey out to their patients and caregivers. We also asked the US based not for profit organization the VHL Alliance to send the survey out to their Canadian based patients. Based on these efforts we received 121 responses to the survey, including 7 from Quebec residents. We used these surveys to answer the questions below.

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*

Overall, living with VHL is a constant struggle. From the fear of having additional tumours, the symptoms these tumours cause, the surgeries to remove the tumours, and the after effect of living without a significant part or all of an organ, or multiple organs, is very challenging.

My two daughters have VHL and both of them have had their two adrenal glands removed. Without adrenal glands they must take hydrocortisone to replace cortisol and Florinef to decrease the potassium in their bodies. If the medications do not work sufficiently, for a few reasons, this opens them to episodes of low blood pressure that can lead to life threatening situations.

In our survey we asked patients, (on a scale of 1-5, 1 is "not at all" and 5 is "significant impact"), rate how your symptoms associated with VHL impact or limit your day-to-day activities an 45% of them said it was a impact 4 or 5, in other words a large impact.

In another part of the survey we asked patients to let us know how living with the disease and the associated surgeries have impacted your ability to work or your quality of life, including spending time with loved ones.

Here is a selection of what they said:

- Cannot work, speech is slurred cannot eat, can't walk weak
- I was on dialysis for 6 yrs,
- Confined to wheelchair following brain surgery. Needs fulltime personal care. Low quality of life.
- "I'm no longer working", was said by many.
- I am on disability now since 2017. In my case it is progressing more fast
- I had to sell my business and retire at 50.
- Have to take days off of work and not able to lift more then 10lbs
- limited my ability to work and affected my balance.
- 2 hours is my limit if at all with my pain mgmt and nerve damage.... I'm a recluse most of the time. I was paralyzed on the left after a two part brain surgery So much more but too much to type.
- My 1st husband left me as I was sick & I passed this disease to both our children, so he remarried a "healthy" lady & got a "healthy" child who didn't require surgeries every few years. He doesn't like hospitals or sick people. I have now passed this on to both my daughters & 1 grandchild who are now going through all the same issues & surgeries...We VHL Warriors need something other than surgeries & invasive procedures throughout our lives to slow or stop the growth of these tumors. My first surgery was at age 6 & my last one so far was at age 69. Each time I go under anesthesia it is one more step towards anesthetic dementia.

Answers from Quebec residents included:

- First surgery, 1997, they were able to return to work (office work) within 4 months. Second & third surgeries, 2017 as well as SRS radiation: a good 5 months to return to somewhat normal, and they were able to travel 7 months later. In both cases, no effect on spending time with loved ones.
- Luckily it went well, had to take time off work (1 month), now i am back with several follow ups with doctors.
- cerebellum: loss of balance; multiples surgeries in the brain cause hydro-cephalia; multiples surgeries in spinal cord: loss of sensibility of legs, feet and left arm and thorax, the obligation to take cortisone after the ablation of both adrenal glands cause me many problems with many years of use. Psychological depression. I can't access the new Belzutifan drug even if I have only one eye left and I have an hemangioblastoma sitting in the middle of my brain, on my right optic nerve that they can't remove because it is too dangerous for my vision, on my right

eye, the only eye I have. My doctor here in Québec, Dr -----, Centre de cancérologie Hôpital Enfant-Jésus, is not able to access Belzutifan for me. I am discouraged not to be able to access the drug. Because it will benefit me not becoming blind.

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 Caregivers to: Please let us know how surgeries have impacted your ability to work or your quality of life, including spending time with loved ones.

Answers from Quebec residents included:

- It has impacted my daughter's life. I retired to help her.

Here is a selection of what other Canadian caregivers said:

- My dad and grandfather died at a young age because of vhl... so far I have been blessed with good recoveries but that is bound to change as the years go by.
- I was a caregiver for someone who passed on because of VHL tumors. The patient was confined to a wheelchair because of the loss of use of her legs. All of her personal needs had to be taken care of by a caregiver. She was responsive when spoken to but could not follow along in conversation well enough to make her own decisions about what to say.
- The person I cared for became blind and paralyzed. She had no quality of life
- Took her vision, then her ability to walk, eventually paraplegic.
- The results of surgery impacted the patient and made him bedridden, and took away his ability to swallow, walk. Needed to use oxygen. Inability to speak clearly. Fighting pneumonia frequently. Needed all-around care.
- He can't work now due to VHL complications
- The surgeries always impact the time we get to spend together because he's away for surgery and then trying to recover at home. It has impacted the time we spend with him because he is so sick. He is away so much for medical reasons he's missing out on so much family time. And as for work, he is not at all able to work. He has been sitting at home for the last year too sick for work.

- It has forced me to take a lot of time off work over the years to have surgery and recover, which in turn has deterred me from going further in school or taken a more serious role at my current jobs.

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*

Currently the main method of treatment is surgery. Dr. Maryam Soleimani (maryam.soleimani@bccancer.bc.ca), who is the CVHLA Medical Advisor, noted that "There are currently no definitive curative treatment options for VHL, nor any which reverse the course of the disease. This is because the current management strategy does not target the underlying pathophysiology of disease, and prevent the recurrent nature of tumour development.

Of the 112 individuals who answered the question, 95.85% reported surgeries to removal VHL cysts and tumors.

Where have you had VHL-related cysts and tumors? 112 individuals provided data for this question. 87 individuals reported multiple tumor sites ranging from 2 to 8 sites. Based on the data collected, the average patient had tumors in 2.8 "sites". However, many patients reported more than one tumor in one location/site. The sites reported included: kidney, pancreas, eyes/retina, epididymis, adrenal glands, endolymphatic sac, spine, brain/brainstem/cerebellum, neck, breast, inner ear, choroid arteries, jugular vein, lungs, duodenum, and groin. Patients reported not only having tumors resected, but in various cases having a whole kidney or lung removed.

We asked: How many surgeries have you (or the patient you care for) had with respect to the removal of VHL cysts and tumors? 98 individuals provide data that we were able to use. Unfortunately, numerous patients had so many surgeries that they reported comments like: “don’t know”, “multiple”, “too many to remember”, or “lost count”. Of the 98 individuals that provided usable numeric responses, there were a total of 520 surgeries reported, with 18 individuals (18.4%) reporting 10 or more surgeries. The average number of surgeries reported = 5.3. Some patients emphasized that the reported number was “so far” indicating that more surgeries were anticipated.

We asked patients to: Please let us know how surgeries have impacted your ability to work or your quality of life, including spending time with loved ones. Here is a selection of what they said:

Patients

- Surgeries and threat of surgeries has made everyday a struggle. Some physically as the surgeries have limited my ability to do the things I once enjoyed like running and sports. Some mentally as the fear of surgery or possible surgery has effected every life decision I have ever made.
- Surgery on the brain stem tumours removed “affected” tumours. It took away their ability to swallow, walk, breathe without oxygen, speak clearly.
- The surgeries have impacted my work, quality of life and including spending time with loved ones quite a bit. I have struggled with pain on a daily basis and it is hard to be active.
- As a mother they severely impact my ability to care for my son. Weeks of time taken away where I can’t care for him. As I heal, I can do more but I’m not the mom I was before. I haven’t been able to work in 2 years.
- Because the surgery location is a cerebellar tumour, there were many concerns about the side effects and whether I would be able to live again after the surgery..... I had to quit the company repeatedly due to symptoms and treatment. This results in hardship financially and mentally.
- I have had spinal cord surgery three times, all in the lumbar spine. With each surgery the scar tissue becomes more extensive.... causes pain and issues with sensation and strength. The doctors say the tumours are like salt and pepper all over the cord, from top to bottom. I’m terrified they will grow and require more surgery. I can’t keep doing this ...
- I started a new job seven months ago and I hate having to tell them I’m going to need time off for surgery. I wasn’t even done my probation when I had to take time off to go for medical appointments and tests and I’m scared I will lose my job over this. Already been passed over for interesting projects because they know I’m going to be taking time off. VHL sucks.

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*

Based on the patient feedback and the data from the clinical trials, belzutifan stops the growth of VHL tumours and in many cases reduces the size of the tumours. This means that surgeries are avoided, the pressure and symptoms that tumours cause on adjacent organs diminishes and the effect of the disease is significantly reduced or removed.

The data from the clinical trials for belzutifan shows a significant reduction in the numbers of surgeries needed for VHL patients that were given the drug. Specifically, I would point to minute 21, of the following video from our 2022 International VHL Medical Symposium: (<https://www.youtube.com/watch?v=RUhOCg916Wg&list=PLprmGjNfymhGecYsqeg0GKS0gC9xOrwdP&index=10&t=33s>)

The graph displayed on screen, and is attached to this email, represents the number of surgeries before and after patients started on belzutifan. You can see a huge reduction in the number of surgeries and the associated suffering the surgeries inflict on people with VHL. Another significant element of a reduction in surgeries, is the affect on a life after surgery without a critical organ (e.g. pancreas, adrenal glands, kidney etc.) or worse a portion of the brain or spine. At best, the post surgery life of a VHL patients involves a slightly reduced the quality of life, at worst, if life goes on after the procedure, VHL patients cannot work nor care for one's self.

In our survey, we asked "If you were to consider taking a new therapy for your VHL disease, please rate the following on a scale of 1 - 5. 1 is "not important" and 5 is "extremely important" we asked: 1) Improvement to your physical condition such as decreasing the size of (or stabilizing) the tumour(s), reducing pain, improving your breathing? 89 people answered, 93% said it is either a 4 or a 5, meaning very important. 2) we asked if the new therapy offered the "Opportunity to avoid surgery(s) for the removal of VHL related cysts/tumours", 88 answered and 96% said this was either a 4 or 5, so Extremely Important!

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)*

In our survey, 19 individuals reported having had experience with belzutifan to treat VHL disease.

We asked patients who had used belzutifan: 1) "Based on personal experience with belzutifan, how would you rate its effectiveness in controlling your VHL disease?" (1 is "not effective" and 5 is "extremely effective"). 100% of the patients with experience said it was a 3, 4 or 5. 2) Based on your personal experience with belzutifan, overall how would you rate its side effects? (1 is "completely intolerable" and 5 is "very tolerable".) 100% said it was a 3, 4 or 5; 33% said it was a 3

We further asked: Is there anything else about belzutifan that you would like us to know and include? Here are what respondents said:

- Very hopeful this drug will help all VHL patients
- Hoping for great results for vhl patients.
- We have never had a normal scan until now.
- This medication is life saving in more ways than one, access is vital, and should be granted to those with vascular tumours beyond just RCCs, as it has been proven to be incredibly effective at controlling and reducing the size of CNS tumours of the brain, spine and eyes, and endocrine tumours like pheochromocytomas, and pNETs as well.

We further asked: How has belzutifan changed, or how is it expected to change, your long-term health and well-being?

- No more surgeries and long life expectancy.
- Shrinking tumours
- So far it has lessened tumor size.
- I am hoping for less surgery's and a longer life then my predecessors
- We hope that it helps to give him more quality of life with less surgeries and hopefully less tumours
- Hoping to not have as many surgeries as I have had in the past. Hoping for longer life expectancy.
- If it can prevent more surgeries this is a major improvement to well being as neurosurgeon has said no more surgeries as possible. Progression of tumours will result in full loss of bodily functions.

-Peace.

-Slow or stop the growth of VHL Kidney tumors specifically & hopefully the neuro-endocrine tumors associated with VHL in my pancreas, adrenal gland & brain & paragangliomas .

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. Please support VHL patients in their quest for a normal life, free of debilitating tumours and the loss of life sustaining organs.
2. VHL patients and their loved ones want to work and contribute to our society. Belzutifan will allow them the opportunity to work.
3. Surgeries to remove tumours should not be our only option to address VHL tumours!
- 4.
- 5.

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.