CADTH

CADTH COMMON DRUG REVIEW

Patient Input

Vortioxetine Hydrobromide (Trintellix)
Lundbeck Canada Inc.
Indication : Major depressive disorder (MDD), adults

CADTH received patient input from:
Canadian Mental Health Association, National and Alberta Division
Hope and Me-Mood Disorders Association of Canada
Mood Disorders Society of Canada
Stigma-Free Society

May 23, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Trintellix (vortioxetine hydrobromide) Depression, Major Depressive Disorder
Name of the Patient Group	Canadian Mental Health Association, National and Canadian Mental Health Association, Alberta Division
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Founded in 1918, the Canadian Mental Health Association (CMHA) is the most established, most extensive community mental health organization in Canada. Through a presence in more than 330 communities across every province, CMHA provides advocacy and resources that help to prevent mental health problems and illnesses, support recovery and resilience, and enable all Canadians to flourish and thrive. Website: www.cmha.ca

CMHA Alberta is a recognizable and reliable organization where Albertans find compassionate support, responsible care and accessible resources. For more than 60 years in Alberta, CMHA has focused on recovery and support for Albertans impacted by mental illness. We stand with people living in the community as they achieve their wellness goals. Hundreds of CMHA staff and volunteers engage clients in activity and navigation within the complex matrix of mental health services. Website: https://alberta.cmha.ca

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

CMHA National – Data Sources

Recruitment of participants was attempted through various means: via psychiatrists and general practitioners in British Columbia and Ontario who have prescribed Trintellix to their patients; via the National Council of Persons with Lived Experience – a committee that aims to increase participation and involvement of people living with mental conditions within CMHA; and other patients living with depression or major depressive disorder (MDD) in the United States.

The summary patient perspectives submitted here were gathered through two methods during May 2019: (1) semi-structured phone interviews, and (2) online questionnaires. Phone interviews and online questionnaires were conducted with adults living with depression or MDD. The interview guides and online questionnaires were developed based on the requirements, instructions, and advice for providing patient input to the CADTH Common Drug Review (CDR). All participating adult patients were given the option to choose between either the phone interview or online questionnaire and were required to complete an informed consent form, which described the CADTH CDR process. Phone interviews, which lasted approximately 30-60 minutes, were audio recorded with participants' permission, and audio files were transcribed at CMHA National.

CMHA Alberta – Data Sources

CMHA Alberta Division conducted a survey and follow up focus groups on the topic of depression that is unresolved after the use of two or more antidepressant agents. The survey was composed of 11 questions that required approximately 10 minutes to complete. The aim was to understand the impact of depression on everyday life and explore people's experience with medication and other treatment options. Participants were Albertan adults (18+) who identified as someone with depression and had tried, or are trying, two or more antidepressant medications but have continuous or unresolved depressive symptoms (a formal diagnosis was not required). The survey was disseminated through an online social media campaign, e-blasts, word-of-mouth through stakeholders such as the CMHA regions in Alberta, psychologists, and mental health networks in the province. A volunteer steering committee made up of three doctors, two volunteers with lived experience, and a consultant from EXEP consulting helped design and disseminate the survey, ensuring information was accurate and well-articulated.

The project also included five focus groups – two in Calgary (October 11 and 12, 2018), two in Edmonton (October 18 and 19, 2018) and one in Red Deer (October 15, 2018) (n = 9). Each focus group lasted approximately 1.5 hours. The focus groups were held at accessible locations in three Albertan cities: Edmonton, Red Deer, and Calgary. To increase internal validity, participants were offered an opportunity to provide feedback on the results.

The synthesis integrates both quantitative and qualitative responses to provide a fuller picture of the experience of living with unresolved depression.

Participating Patients Profile

CMHA National obtained two testimonials (1 phone interview; 1 online questionnaire) provided by adult patients living with depression:

- One patient (male, 67 years) resides in Massachusetts, USA and had no experience with Trintellix, hereinafter referred to as P1. He is diagnosed with long-term treatment-resistant depression.
- One patient (female, 32 years) resides in Ontario, Canada and has experience with Trintellix for her depression, hereinafter referred to as P2. She also has experience living with anxiety.

CMHA Alberta had 16 individuals fully complete the survey and 5 partially complete the survey. Participants were aged from 22 to 62, approximately half of whom received a diagnosis of

depression over ten years ago (43.8%, n=7/16). CMHA Alberta also had a total of 9 focus group participants.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Before diagnosis, participants reported 'negative coping' strategies like self-harm, alcohol abuse, abusing pain medications and doing drugs. Some individuals noted they cried a lot and isolated themselves. For example, P1 has been living with treatment-resistant depression since young adulthood. At the age of 18, P1 initiated alcohol and drug consumption. P1 seemed to suggest that his substance use was sought as a coping mechanism to alleviate his depressive symptoms that reverted after months of abstinence.

> P1: "I think I was treating my depression with the drugs and the alcohol so after I got sober, I would say maybe a year in, the first year of sobriety was wonderful, wonderful really and it was great to just be off of that treadmill and I think I started suffering from a certain level of depression and it would go up and down."

Not only did the depressive symptoms return during P1's months of abstinence, they also persisted during his years of substance use.

> P1: "I can remember back in my drinking days specific instances of being so depressed and kind of retreat to the bed for a couple of days and not want to go out or do anything. Very overwhelming."

When participants were asked how depression impacts their life, one participant said, "how does it not?" Other participants echoed this with specific references to sleep, appetite, mood, relationships, exercise, work and the ability to do the activities they used to enjoy. Another participant emphasized even the tasks of daily life -getting out of bed, getting ready, preparing meals, tidying the house – 'can be insurmountable.' Participants also reported feeling apathetic and spoke of a "darkness" they felt was always present. In the pre-survey, participants unanimously reported experiencing feeling tired or having little energy; little interest or pleasure in doing things; feeling down, apathetic or hopeless; trouble falling or staying asleep or sleeping too much; difficulty concentrating; and poor appetite or overeating. All but one participant also reported 'feeling bad about yourself – or having feelings of failure, letting yourself or others down.'

> P1: "I would classify my depression it was kind of like crushing in the morning like getting out of bed was a chore and life didn't feel worth living but I never believed I would commit suicide."
>
> P2: "When I go through a bad depressive episode, there are times when I won't leave my bed other than to walk my dogs and had had to take days off work. It has caused me to lose friends and affected my personal and familial relationships. I had terrible mood swings, I was extremely emotional and often times had social anxiety or felt reclusive. I would cancel plans regularly because I could not bring myself to get out of bed."

As the participants described further, their depression was accompanied by suicidal thoughts, not attempts, particularly when their depressive symptoms were compounded with life- and/or work-related stress.

P1: “I would classify my depression it was kind of like crushing in the morning like getting out of bed was a chore and life didn’t feel worth living but I never believed I would commit suicide [...] If I went into the doctor today and he told me that I have some horrible disease and I’d be dead in two months, I wonder if I would take that as great news or bad news – that kind of thinking.”

P1: “If I went to sleep tonight and never woke up that wouldn’t be terrible news.”

Although some participants’ depressive symptoms also negatively impacted their energy levels, day-to-day activities, and interactions with immediate family members, they consciously hid their struggles from those around them.

P1: “I just had to go through the routine of raising my kid. I had to fake it an awful lot. I would fake it and couldn’t wait till the day ended so I can just go to bed and turn it all off.”

P1: “I was faking it with my kid. I was trying to fill my dad obligations by just faking it and forcing myself to pay attention to [my family].”

Participants also spoke about their beliefs in how family, friends, and society view them. They reported being labeled as “broken” or being told to “just go get fixed.” Even when trying to be helpful, family and friends were often a source of stress for the participants. One participant said when family told them "you're doing so well," they thought "no I am just getting better at hiding it." Family, friends or co-workers make comments like "just breathe," "think happy thoughts," or "snap out of it." Participants shared this evokes a sense of frustration, anger and sadness and only further demonstrates to them how much others do not understand what they are going through and are tired of trying to explain what the disease is like for them. Participants described mental illness as a “quiet epidemic” and the healthcare system does not have sufficient supports or treatment options for them and their loved ones.

P2: “I am a very social person, but not being able to get out [of] bed or leave my apartment just kills me. I’ve lost a few of my best friends because of this and because they couldn’t understand what I was going through.”

Dialogue on social supports also included how participants viewed themselves. For instance, “I don’t want to be around me, so how can I expect that of others?” Some individuals noted feelings of self-loathing. Several participants expressed how they have isolated themselves to avoid noise, crowds and social interactions like shopping or going out with friends. Others acknowledged screening phone calls or fabricating addictions or dietary restrictions to avoid attending social events. Participants stated having supportive individuals who were willing to be present or to ‘help with basic daily activities’ would be useful.

Despite campaigns to reduce stigma surrounding mental illness, participants reported feeling they had to hide their condition, particularly at work. Other participants expressed working was not within their ability at the moment, while others said it was essential because of finances or the medical coverage they gained from working.

The most common challenge people articulated about living with depression was related to the financial impact. Those who are not working are struggling to live off savings or disability payments. Individuals who are on a leave of absence from work are technically still employed, which can limit their access to programs, supports and resources from the government. Participants who are working reported pressure to increase hours, stress from feeling the need to hide their condition, adverse impacts from disclosing their illness or concerns, and regression in their ability to cope with depression. The high out-of-pocket treatment costs add to participants’ financial stress. In the survey, 86.7% (n=13/15) reported experiencing financial difficulties since receiving their diagnosis.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Participants reported trying multiple treatment options in hopes of managing their disorder, sometimes trying several treatments simultaneously. Although P1 has had no experience with Trintellix, he has had experience with four other anti-depressants (Prozac, Cymbalta, Luvox, and Wellbutrin), among other available and novel treatments that were associated with side effects and/or lacked effectiveness.

> P1: "I started with Prozac maybe 29, 28, maybe 27 years ago something like that and essentially have been on some kind of anti-depressant since then, maybe except for a break of a couple of months."
>
> P2: "Cipralex worked at first, but then it tapered off and actually made my symptoms worse. Therapy was OK, not something I continued."

P1 acknowledged experiencing benefits after initiating pharmacotherapy for his depressive symptoms. But he also indicated that the side effects were substantial that he opted to discontinue his prescribed treatment, which in turn negatively impacted his experience with depression.

> P1: "The first time I took Prozac it was really pretty powerful, it was very good for a short period of time. But I stopped taking it because it completely squashed my sex drive and I was still a younger man and I was not married and it was like, like I could not stand it. I got off it primarily for that reason because I didn't like the side effects and I kind of sunk back into depression […] It was a hard trade-off for me, a hard trade-off at that point in my life."
>
> P1: "Wellbutrin made me famished at times. I was hungry, unbelievably hungry at times and I kind of figured out after a while that I think it was the Wellbutrin doing that to me. So that may have contributed to stopping that one."

At the time of the phone interview, P1 was on Cymbalta, which seemed not to work as effectively in terms of his overall outlook on life.

> P1: "If I went to sleep tonight and never woke up that wouldn't be terrible news."

Despite anti-depressants' side effects, P2 seemed to prefer pharmacotherapy more than other types of therapy. Furthermore, P1 highlighted the importance of realizing the inevitability of side effects occurring when opting for pharmacotherapy to treat depression.

> P2: "[Trintellix] was the same as Cipralex as it is a pill, but better than therapy as that was very time consuming and emotionally draining."
>
> P1: "You have to be willing to accept the side effects."

Participants also noted there are many barriers to accessing appropriate care in the public system, such as long wait times and appointments which may require substantial travel. Furthermore, provider or system availability and preferences seem to be the core factor in scheduling appointments, instead of when the participant would have preferred or been able to

attend. For example, participants reported limited day-time appointment options and no evening appointments. One essential struggle participants emphasized was difficulty accessing private mental health care services.

Additionally, survey data indicates that 47% of participants (n=7/15) reported a hospital admission for their depression. The amount of total lifetime in the hospital reported ranged from one week to approximately three years – depending on the age of the participant and the timing of their diagnosis. Most participants reported receiving information on treatment options from a family physician (87.5%, n=14), psychiatrist (87.5%, n=14) or a counsellor (68.8%, n=11). All participants had tried some medications. Most individuals reported severe side effects including memory loss, a worsening of symptoms or complications of other conditions that they have (e.g., depression medication increased anxiety issues). For some individuals the medications had no impact. At best, one participant reported their current combination of drugs made them "numb." Medication-related side effects impact the overall quality of life and willingness and ability to seek new treatments. In the survey, the most frequently reported medications were Buproprion (brand: Wellbutrin) and Venlafaxine (brand: Effexor). One participant reported trying up to 23 different prescription drugs with no success. Many said they would be willing to continue to try new medications in the hopes of finding one that works.

The public perception of managing mental illness through walking or exercise has created a new challenge for participants as their family and friends encourage them to exercise as a panacea for depression. Participants spoke of wanting successful treatment solutions, but lamented that there is no magic fix.

Individuals in the focus groups relayed they have tried many treatments with mixed or poor results. Some said they weren't fully aware of the risks and efficacy related to electroconvulsive therapy (ECT) and they felt pressured into it by health care providers. In particular, many participants noted to decline ECT would result in being labeled a "difficult" or "non-compliant" patient. Some participants reported little change to their condition since their diagnosis, which leads to higher levels of suicidal ideation.

Participants revealed the myriad of health care providers they see to try to manage their depression typically do not communicate with one another. As a result of the lack of inter professional communication, there is an increased burden on patients to find and manage their own care team. In the focus groups, participants shared there seem to be different types and varying quality of treatments offered across the province – particularly between rural and urban settings. Some participants shared their health care providers did not seem to be up to date with the latest research on depression and did not have a clear set of recommended treatment options. Many participants have other diagnoses and some reported poor interactions between the treatments for the various conditions. Participants also acknowledged feeling vulnerable and trying to find answers on their own as the treatments they are receiving were not helpful.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

An area worth exploring is the development of new pharmacotherapies that concurrently tackle symptoms of both anxiety and depression. This was highlighted to be necessary for patients like P1 and P2 whose depressive symptoms were coupled with anxiety, and who were concerned with developing an addiction to benzodiazepines.

P1: "I guess a mix of my depression was anxiety, clearly. I guess I wanted to see the anxiety go away. I didn't want to take any benzos or anything being an alcoholic and didn't want to activate any of my addictions."

P1 seemed to suggest a sense of determination to feel better, despite the side effects experienced with prior anti-depressants.

P1: "I wanted to get the gray cloud, just trudging through the day, the faking it to get through the day because I feel so depressed. So I just wanted that to lift an maybe to instead of being locked into my own head to see if I could enjoy aspects of life. You know today is a beautiful day so I wanted to get some joy out of that that instead of walking around feeling weighed down all the time and bleak and hopeless."

P1 indicated that if such improvements were incorporated in the development of new treatments for depression, that his quality of life and sense of purpose would be greatly enhanced.

P1: "I could probably be a better father, be a better husband, be more hopeful about the future [...] I wanted to lift the weight off my shoulder."

Furthermore, and based on the data gathered by CMHA Alberta, the following areas for improvement were identified:

- Better System Coverage. There are limited treatment options through the public system. Barriers to receiving these treatments include wait times, appointment scheduling and service locations. Nearly all participants (86.7%) reported experiencing financial difficulties since their diagnosis. In the focus groups, high out-of-pocket treatment costs and gaps in social funding support were the main reasons identified for financial distress. Expanding the publicly-funded treatment options would reduce the out-of-pocket expense and improve participants' supports.
- Better System Integration. Participants remarked they are being forced to manage their care and ensure information gets to each of their care providers. Participants reported poor or no communication between their health care team and felt like this is another burden on them. They also noted there are differences in the breadth, depth and availability of treatment options offered across the province and some providers do not have current information about the disease.
- Resources. Participants noted there is limited information, tools or support for both patients and their caregivers and social supports. In the pre-focus group survey, participants indicated a preference for receiving health information on websites (93.8%), through webinars and public education events (43.8% each) and in pamphlets or podcasts (37.5% each). For many, the flexibility of the virtual options means they are more likely to participate. Participants spoke of how family and friends don't know what support is helpful and therefore ask the participant what they need or step away from the relationship. Better education and communication resources for individuals who have a loved one living with depression could help improve the progressive isolation often experienced by Albertans living with unresolved depression.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

P2 was prescribed Trintellix (5-10 mg) for depression by her psychiatrist and has been on the medication for six months. Overall, and compared to other treatments the patient has received in the past (i.e. Cipralex), the patient reported positive experiences with Trintellix, including no difficulties accessing and receiving the treatment. What seems to be unique with Trintellix is its capacity to alleviate P2's symptoms of anxiety as well.

> P2: "Since starting Trintellix my life has turned around and my symptoms are infinitely better [...] I call it the miracle drug and have told multiple friends to ask their doctors about it because of how well it works. My moods are easier to control – when I would get upset or in a bad mood it would often last for hours or days. Now I am able to shake it off fairly quickly. [...] The benefits have made my life so much better and have improved my relationships."

> P2: "I am extremely social and don't have any more social anxiety and am not afraid to go out and meet people in my personal life and at work."

Nevertheless, and as with other anti-depressants currently available in the Canadian market, Trintellix comes with its share of side effects.

> P2: "The only side effects I had were upset stomach but it is mitigated by eating food with the pill."

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid forr testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

N/A

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

CMHA National hopes to ensure the drug review process, specifically for mental health drugs, involves explicit communication and transparency with mental health patient organizations. This is of particular significance to CMHA along with other mental health patient organizations, given that approximately only half of Canadians living with MDD receive adequate formal care. According to the Canadian Health Policy Institute, 76.2% of mental health drug submissions have been rejected between 2004 and 2015, compared to 48.5% of non-mental health drug submissions. That being said, CMHA recognizes that the drug review process also considers data from clinical trials, and that the evidence base for the safety and efficacy of antidepressant medications that is generated from clinical trials can be improved by funding a greater number of independent trials and by expanding the inclusion criteria within the trials to include patients who would receive treatment in routine practice settings. Therefore, CMHA emphasizes the need for more standardized controls for the ethics and procedures governing clinical trials for mental health drugs. In turn, higher quality clinical evidence is likely to be produced, which may likely increase the efficiency of the drug review process for mental health drugs.

Furthermore, more than 930,000 Albertans consult physicians for addiction and mental health-related concerns each year and more than 500,000 Albertans fill antidepressant prescriptions in the course of their treatment. The experiences shared by the focus group participants have added depth to our understanding of the challenges faced by Albertans who are impacted by depression wherein existing treatment options have not provided relief.

While the number of participants in the focus groups conducted by CMHA Alberta was relatively small, the feedback is remarkably unified concerning impacts related to the quality of life, economic challenges, systemic barriers and resource limitations. The extent of the agreement is perhaps the most alarming discovery of this study. Failed drug treatments can create personal jeopardy and relational challenges that are difficult to overcome.

There is also a need for continued advocacy efforts for equity in publicly-funded supports related to health, including mental health. Affordable, equitable and timely access to the full spectrum of psychological support is critical for individuals when medication alone does not resolve depression.

It is pivotal to improve information sharing between health care providers, community supports and the matrix of systems individuals with depression are required to access over the course of their illness. Continuity of care can help decrease patients stress associated repeating traumatic experiences again and again with each new provider. Support systems that consider the needs of the whole person and not just individual segments are essential examples of ways that integration and enhanced information-sharing would benefit individuals living with major depression.

Providing education and support to families on what it means to have depression or live with someone suffering from major depression disorder is crucial to enhancing the quality of life of the individual. It is also vital to ensure appropriate care for caregivers as this may improve the quality of lives of Albertans living with depression and their loved ones.

Finally, we recognize individuals living with depression report an overall lack of resources and options to support their recovery and inform themselves and their families. Virtual and in-person supports are required to create a diversity of pathways for learning about depression and building information and resource pathways which are accessible to individuals, families and communities.

The wisdom and bravery of the focus group participants have begun to shed light on the acute needs of Albertans living with major depressive disorder that is unresolved with existing treatment options. Some of these identified approaches may exist elsewhere in Canada or the world and require dedicated implementation support to bring them to Alberta. Others need multi-sectoral collaborative efforts to overcome bias and stigma, entrenched clinical practice and other systems-level challenges. This project has acutely focused attention on the challenges that impact the quality of life of Albertans with unresolved depression and the importance of a comprehensive approach to addressing them.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

N/A

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Global Public Affairs assisted CMHA National by providing the contact information for the psychiatrists and general practitioners in British Columbia and Ontario. Global Public Affairs is a privately held strategic communications and government advocacy consultancy organization based in Toronto.

Additionally, Janssen Scientific Affairs (Janssen) is one of CMHA National's funders. Janssen assisted by providing patient contacts, upon their consent. One of Janssen's patient contacts consented to share with us their experiences with MDD. This patient has never been prescribed Trintellix, although has experience with other anti-depressants currently available in the market, as well as experimental treatment.

Janssen also funded CMHA Alberta's Major Depressive Disorder Project, which involved a survey and focus groups held with Albertan adults (18+) who identified as someone with depression.

CMHA, Alberta Division is also grateful to the volunteer steering committee, Dr. Toba Oluboka, Dr. Vincent Agyapong, and Dr. Adam Abba-Aji, for their clinical contributions, expertise and support. We thank EXEP Consulting and Dr. Lisa Petermann who conducted the focus groups, analyzed the data, wrote the final report and who extended her knowledge and time to ensure accurate representation of comments provided by the participants. We thank our volunteer advisory team, Tim Hay and Ron Campbell, who continuously provide the voice of lived experience to our work and helped develop the focus group tools used to obtain the data.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Lundbeck Canada Inc. provided CMHA National financial payment				Yes
Janssen Pharmaceutical Companies of Johnson & Johnson provided CMHA Alberta financial payment			Yes	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Dina Bayoumy
Position: National Research Analyst
Patient Group: Canadian Mental Health Association – National
Date: June 20, 2019

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Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	
Name of the Patient Group	**Hope and Me-Mood Disorders Association of Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

• About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

MDAO is a community-based mental health services provider with more than 35-year history. It supports adults, youth, families, and caregivers, province-wide, who experience mood disorders, early psychosis, and multiple mental health or addictions issues, all through increasingly sophisticated and standards-based peer support, and including individual, group, and family peer support. Our peer support facilitators are, for the most part, volunteers, and all have the lived experience that is, the personal knowledge about mental illness gained through direct, first-hand experience or experience supporting a loved one, family member or a friend. All are highly trained, and working within a framework of guidelines, evidence-based standards, and a community of practice approach.

MDAO served over 275,000 people province-wide and anchoring 33 peer support affiliates across Ontario with a range of training and networking supports. MDAO peer supporters have the lived experience, are knowledgeable, empathetic, trained, and supportive people who ‘get it’ and convey hope. MDAO works to honour others’ experiences and strives to understand their needs. Our Ontario-wide evidence-based programming is pivotal in fostering resiliency, promoting self-care, instilling empowerment, and building hope. MDAO’s work and the cost efficiency of its programs would not be possible without the contribution of over 310 volunteers who annually, on average, bank over 16,000 volunteer hours across the province.

In addition to peer support, MDAO has a decade of counselling expertise in the Toronto area, starting with early psychosis counselling, and deepening in the last five years to include time-focused professional clinical knowledge in the Toronto area to help individuals and families. At the time of writing, MDAO is the only Toronto area community-based mental health services provider offering peer and clinical services four evenings a week, in addition to regular daytime hours, to enhance accessibility for clients.

MDAO’s counselling programs provide support to individuals experiencing mental health challenges related to mood and addiction issues, as well as help to family members/supporters.

The Early Psychosis Intervention Program helps youth in the early stages of developing psychosis, providing them with a full range of services to help them maintain their goals at work, at school, and within their social networks. The program, which specializes in psychosis and mood disorders, also works closely with individuals' families, providing them with education and supportive counselling.

We also collaborate with St. Michael's Hospital, Sunnybrook Hospital, and Community Mental Organizations around Ontario to develop more effective community mental health services models to improve and strengthen mental health services delivery.

Research and evaluation are essential to our work. We have established several partnerships with research institutions and organizations. Our research partners include Canadian Biomarker Integration Network in Depression (CAN-BIND), the Canadian Network of Mood and Anxiety Treatment (CANMAT) and the Ontario Brain Institute (OBI) and The Collaborative RESearch Team to study psychosocial issues in Bipolar Disorder (CREST.BD).

MDAO nominated Dr. Erin Michalak and CREST BD for the 2018 CIHR Gold Leaf Prize for Transformation in Patient Engagement Award, and they were selected.

We will continue to enhance these research partnerships and develop new ones to demonstrate the effectiveness of our programs and to facilitate projects through knowledge transfer activities that fill gaps in the communities we serve.

We are a regional member of the Canadians for Equitable Access to Depression Medication (CEADM) where we want all Canadians to have access to all depression medications.

For more information about Hope and Me – MDAO, please visit https://www.mooddisorders.ca/

• Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

We gathered information through personal experience between April 12, 2019, and April 30, 2019. Information through a Patient Survey for patients receiving TRINTELLIX across Ontario, with five people responding. Three female and two males, three were working part-time and two fulltime. The ages ranged from 27 to 55 years old with one individual at age 64.

The level of education arranged from two with Secondary school and three with University/College

We also conducted two individual interviews with patients in the Toronto area. Both were female ages 35 and 42. They both worked full time. All individuals were diagnosed with depression for more than two years, both with University /College education. All obtained the drug through Private Payer Insurance.

• Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Individuals with Major Depressive Disorder (MDD) often exhibit impairments in cognitive function, including executive function, processing speed, concentration/attention, learning, and memory (National Academies of Sciences, Engineering, and Medicine, 2015)

Indeed, among working adults with MDD, measures of cognitive dysfunction may be a greater determinant of presenteeism/absenteeism than is the total depression severity score (McIntyre et al., 2015b).

Major depressive disorder (MDD) is a common, chronic and disabling disease. Our experience in supporting group participants and clients across the province is that MDD is highly complex and individualized where there can be over 227 possible combinations of symptoms affecting emotion, cognition and physical health, which affects every person in a different way. Therefore, there is no size fits for all approach treatment. Patients with treatment resistant depression report they experience sadness, loss interest to do things that they use to give them pleasure, difficulty concentrating, lack of energy, persistent low mood, irritability and not able to laugh and smile. This not only impacts them but their families and workplace as well.

Self- stigma is something that impacts individuals and therefore, they isolated themselves from the outside world, family and friends, unable to work and provide self-care and care for their family. This has negative impacts on their children because they cannot provide care for them.

Unfortunately, many with severe MDD are unable to work, leaving them without private

Insurance – a severe inequity in our system. Cognitive function impairments would be important to control so that people could be able to work and feel productive.

- **Experiences With Currently Available Treatments**

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

In our experience Depression is a complex condition which is tackled best through a holistic viewpoint. The current treatments for depression are just as complex as the sources of this illness. Medications, peer support, psychotherapy, cognitive behavioral therapy, and nutritional psychiatry are all options to tackle the disease.

Medications

Canadian guidelines recommend antidepressants as first-line treatments for MDD. Guidelines also recognize high unmet need due to incomplete response, tolerability issues, and challenging persistence with current therapies. MDD is highly complex and individualized where there can be over 227 possible combinations of symptoms affecting emotion, cognition, and physical health, which changes every person differently. Having greater choice of antidepressants will help people find the antidepressant that works for them. The trial and error prescription of medications leaves many people frustrated and confused; however, then they find the right drug it will make all the difference to their quality of life. We believe in both the medical and non-medical model for people to heal and recover. In working with our clients, they need to be able to find a drug that will provide a direct benefit on cognitive symptoms and functioning, independent of its effect on depressive mood, which can aid in functional recovery and enable individuals through their self-determination find the right non-medical treatment. For those with private insurance, medications are often covered shortly after federal approval from Health Canada. Unfortunately, many with severe MDD are unable to work, leaving them without private insurance – a severe inequity in our current system**.**

Peer Support

- We have been offering peer support for over thirty-five years. Research provides evidence supporting the peer recovery model. The benefits are vast. The positive impact starts with the individual, ripples through families, workplaces, and communities, reducing costs across the entire healthcare system. Depression can isolate people from their family and friends. Discussing symptoms and emotional reality with a non-judgmental trained peer support worker can do wonders for someone's outlook. It's vital to have a peer support worker who demonstrates empathetic behaviors and has the self-awareness to be respectful and fully engaged. Our evidence-based peer support programming is pivotal in fostering resiliency, promoting self-care, instilling empowerment and building hope. Managing stress and understand the importance of a plan which is fundamental to maintaining good mental health to accomplish goals.
- Research shows that peer support across various disorders leads to statistically significant decreases in symptoms similar to professional psychotherapy. Mental Health Commission of Canada (MHCC), Making the Case for Peer Support, September 2010

Psychotherapy

Psychotherapy is an evidence based process which through our experience is useful for individuals with depression. It is about understanding the thoughts, emotions, and behaviors which exacerbate depression while working to build coping techniques and problem-solving skills.

- There are advantages to using antidepressant medications such as Trintellix, as they may work faster than psychotherapy, is more widely available, and is more effective, particularly for severe symptoms.
- Trintellix is recommended in the 2016 CANMAT guidelines as first-line treatment of major depression disorder with particular benefit in persons with cognition issues and in reducing medication related sexual dysfunctions.

2. Cognitive Behavioral Therapy

Cognitive behavioral therapy operates from the perspective where emotions, thoughts, and actions are connected. Negative concepts and habits can trap individuals in a cycle of depression.

- We have found that Cognitive behavioral therapy (CBT) is a partnership with a mental health professional who works with the client to examine their mental, emotional, and physical habits to identify how specific self-beliefs contribute to their depression.
- Collectively they should successfully locate negative cycles and work to undo them.

3. Dialectical Behavioral Therapy

Dialectical behavioral therapy (DBT) is a by-product of cognitive behavioral therapy. DBT is used to treat borderline personality disorders, and we have found that it's also useful for people with depression who intensely experience emotions.

- The primary goal of DBT is to teach the client how to deal with stress while managing their emotions and enhancing their interpersonal relationships.
- Dialectical behavioral therapy combines mindfulness and helps the client accept who they are while allowing them to appreciate themselves**.**

4, Exercise

Exercise isn't a strategy for depression by itself, but the impact of regular activity does play an important role in helping fight the disease.

- Clients can find it difficult when depressed to find the energy to start being active. However, for individuals with mild to moderate depression physical exercise can help lift their mood, provide more energy, and help prevent depressive symptoms.
- The key is choosing an activity they enjoy.

5. Self-Care

Our client's with Depression can find it difficult to perform even the most routine of tasks, like brushing their teeth or getting out of bed.

- Self-care means making room for themselves. Sleep, healthy eating, and staying active are all components of utilizing self-care to combat depression. This can be very difficult to achieve.

6. Nutrition

Food alone isn't going to neutralize all the symptoms of depression; in our experience it does give people the best chance for success. If clients are eating high fat, greasy, sugary fast food, then it will be challenging to have the balance needed to fight depression.

- A healthy diet is the best bet for optimizing fuel sources. Of course, having access to healthy food can be expensive for people on a fixed income when they are unable to work due their depression.

7. Creative Outlets

Many of our clients find that writing their thoughts and feelings in a journal is therapeutic. Listening to music and using humour has both emotional and physical benefits which can alleviate the symptoms of depression.

- We have been offering a recovery program for over ten years called Laughing Like Crazy. It is a 16-week program that teaches participants how to develop a stand-up comedy routine based on their experiences with mental health issues and the mental health system. The group combines the benefits of peer support with the physical, social, and emotional benefits of laughter, as well as the challenge of public speaking and performance. Program graduates perform their routines for three hundred people in the public, creating a positive dialogue about depression and other mood disorders in the community.

• Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

[redacted] and [redacted] (current Hope and Me-MDAO clients)

[redacted] is a 47-year-old married woman with two children. She works as a bookkeeper at a small landscaping company. Her husband [redacted] is a custodian. [redacted] has struggled with MDD for over a decade. His numerous episodes over the past ten years have resulted in many medical leaves from work as well as considerable strain on their marriage and financial situation. [redacted] found this to be very stressful and began to feel his confidence eroding. Both "thinking on his feet" and having to respond quickly was quite threatening. His inability to focus and feeling like he was in a fog continually. Eventually, he found it difficult to go to work and began taking more and more time off, often staying in bed with the covers pulled over his head. When he was at work, he has aggressive and lashed out at the people. It became necessary for him to take a long-term leave. He is struggling with finding the right medication that would work for him. They have two children both in high school and with finances being tight [redacted] is worried about how the family will afford to send them to University.

The improvements that patients and caregivers like to see in a new treatment that is not achieved in currently available treatments are as follows:

With a staggering 227 combinations of symptoms that affect individuals emotional, cognitive and physical health. A broader range of choice of medications addresses all three facets, bringing with them a greater probability of recovery. If those choices aren't available to those who rely on the public drug plan system, then the chances of successful treatment are considerably slimmer.

1. **Choice:** A broader range of choice of depression medications that address the following :
    a. Emotional, cognitive and the physical health.
    b. The wish is to bring greater probability of recovery so they can return to work and remove the financial burden
2. **Accessibility:**
    - If the broader ranges of depression medications aren't available to those who rely on the public drug plan system, then the chances of successful treatment are considerably slimmer.
3. **Psychotherapy:**

    a. Changing the OHIP system to allow psychotherapy to be purchased under OHIP, therefore making it free to all individuals.

How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements?

a. There are advantages to using antidepressant medications such as Trintellix, as they may work faster than psychotherapy, is more widely available, and is more effective, particularly for severe symptoms. Trintellix has demonstrated a unique and direct benefit on cognitive symptoms and function, independent of its effect on depressive mood, which can aid in functional recovery.

b. Interventions that can improve cognitive function in individuals with MDD could be expected to improve psychosocial outcomes and, possibly, workplace functioning and public safety, which could reduce health-related costs and expenditures.

c. If [redacted] was able to access this drug within the public drug plan system he would be able to improve his cognitive symptoms which would enable him to return to work. The family's quality of life would improve as well. The financial burden would be lifted and the functioning on the family unit would improve.

What trade-offs do patients, families, and caregivers consider when choosing therapy?

- Some of the trade-offs that patient consider when choosing therapy is cost. If the therapy is expensive, in some cases they choose between paying for rent or food or therapy.
- The ease of access to obtaining the therapy is also a consideration and a trade-off.
- Making a trade-off between a small improvement and a large out-of-pocket expense.
- Tolerability issues and challenging persistence with current therapies

- **Experience With Drug Under Review**

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

How did patients have access to the drug under review?

Trintellix has been available on the Canadian market for about 4 years and has been used by thousands of patients who had access to a private insurance.
Many private plans in Canada do cover innovative treatments for depression – while this is positive it must be balanced by the recognition that only those patients who have high quality drug plans through their work have had access.

Compared to any previous therapies patients have used, what were the benefits experienced?

Several clinical trials and indirect comparisons have established that TRINTELLIX™ offers similar level of efficacy to other antidepressants.

How did the benefits impact the lives of patients, caregivers, and families?

TRINTELLIX™ has a more beneficial profile in sexual dysfunction and weight gain than comparators – contrary events that are known to impact adherence and the best option for recovery. Patients indicated that the fog was lifted and they felt hopeful. Other patients talked about the fact that they could do computer work and were able to focus on a task and completed it within a reasonable time frame.

What were the disadvantages?

TRINTELLIX™ is well-tolerated; most adverse events are at control level, except nausea, which is the only frequent adverse event about 23%. In most cases, it is typically mild and temporary.

Was the drug easier to use than previous therapies? If so, how?

Individuals with Major Depressive Disorder (MDD) often exhibit impairments in cognitive function, including processing speed, concentration, learning, and memory. TRINTELLIX™ significantly improved cognition, independent of depressive symptoms and therefore represents an important treatment for MDD-related cognitive dysfunction.

Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

TRINTELLIX™ maintains tolerability in elderly patients and in the longer-term, with treatment withdrawal rates below that of active references/comparators.

• Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

• Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

The CHOICE-D Guide

This evidence-based tool aims to raise awareness and knowledge about depression treatment options. This guide was written by people affected with depression for people living with depression, including patients, caregivers and peer support workers. All information was adapted from the CANMAT 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder.

This guide is an easy to understand and there has been over 5000 downloads of the CHOICE-D guide across the world including, Canada, USA, UK, France, Germany, Spain, Ukraine, India and Australia. Online versions of the CHOICE-D Guide are available at this link, http://bit.ly/guidinghope, and will soon include French and Chinese versions of the document. By increasing access to this information, this guide empowers the public to engage in shared decision-making with healthcare professionals to take an active role in their care.

This project is a partnership between Hope + Me - Mood Disorders Association of Ontario (MDAO), Canadian Network for Mood and Anxiety Treatment (CANMAT), Canadian Biomarker Integration Network in Depression (CAN-BIND) and the Ontario Brain Institute (OBI). The guide includes information about medications, psychological treatments, brain stimulation treatments and complementary & alternative treatments.
A quick summary is included to help a person decide on treatments in partnership with their healthcare provider. There are advantages to using antidepressant medications such as Trintellix, as they may work faster than psychotherapy, is more widely available, and is more effective, particularly for severe symptoms. Trintellix is recommended in the 2016 CANMAT guidelines as first-line treatment of major depression disorder with particular benefit in persons with cognition issues and in reducing medication related sexual dysfunctions.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

No, we did not receive help form outside our patient group to complete the submission

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No, we did not receive help from outside our patient group to collect or analyse data used

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Lundbeck Canada Inc 21/04/2016	X			
Lundbeck Canada Inc 11/12/2018	x			
Canadian Biomarker Integration Network in Depression (CAN-BIND) 22/12/2018		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Ann Marie Mac Donald
Position: Executive Director/CEO
Patient Group: Hope and Me -MDAO
Date: May 29th, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Trintellix (vortioxetine hydrobromide)**
Name of the Patient Group	**Mood Disorders Society of Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

The Mood Disorders Society of Canada (MDSC) has evolved to become one of Canada's best-connected mental health NGOs with a demonstrated track record for forging and maintaining meaningful and sustained partnerships with the public, private and non-profit sectors throughout Canada.

The Mood Disorders Society of Canada has grown out of the vision and drive of a number of mental health consumer leaders from across Canada who in 1995 saw the need for a broad-based structure to bring consumers of mental health services together and who believe that consumers have a key role to play with regard to education and advocacy at the national level.

It was formally launched and incorporated in 2001 with the overall objective of providing people with mood disorders with a strong, cohesive voice at the national level to improve access to treatment, inform research, and shape program development and government policies with the goal of improving the quality of life for people affected by mood disorders.

The MDSC's overall objective is to provide people with mood disorders with a strong, cohesive voice at the national level by:

- Raising awareness that mood disorders are treatable medical issues and working towards eliminating barriers to full community participation in reducing discrimination and stigma, involving members of the public, government and treatment/service providers.
- Building a national clearinghouse of information and resources related to mood disorders.
- Advocating for the creation of adequate and accessible stigma-free programs for Canadians living with or suffering from mental illness.
- Ensuring that the voices of consumers and family members are accurately understood and communicated on issues of national importance by building on existing networks and alliances.

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include when the data were gathered; if data were gathered in Canada or elsewhere; demographics of the respondents; and how many patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Information used to compile this submission was gathered via the following:

The information presented in this submission is from extensive direct discussions with patients with Major Depressive Disorders (MDD) over the years, including focus groups, meetings and online discussions. Our opinions also include input provided to us by numerous family members/ caregivers as well.

A national online survey distributed between March 3rd and 22nd 2018; The primary objective of the Mood Disorder Society of Canada's 2018 Treatment Resistant Depression Study was to identify priority issues and improvements or changes to the Canadian mental health care system that need to be addressed with relation to treatment resistant depression (TRD). More specifically, this study sought to gain a better understanding of the issues and concerns among Canadians who are currently living with depression.

MDSC is proud of the very large number of dedicated followers and client base our organization has with more than 50,000 social media followers. We have extensive website visitors as well, our depressionhurts.ca website alone has 500 visitors per day, we also have our mdsc.ca website which is extremely active, along with our national mental health campaign, Defeat Depression, which holds mental health fundraising walks from coast to coast with over 20,000 people taking part. We also have a national online discussion support chat line that has over 2,500 discussion threads and over 32,000 posts.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

The mental, emotional and physical impact MDD can have on a patient is very serious and can become devastating to the individual and their families.

The MDSC 2018 survey received one hundred and nineteen completed surveys were received. Of these respondents 51% stated experiencing more than 10 bouts of depression, 63% indicated having to visit the emergency department due to their illness, 19% had to be hospitalized with stays varying from 11 to 30 days. 3 out of 4 also stated having to be treated for anxiety.

In a Canadian community health survey: mental health (2012), 4.7 percent of Canadians met the criteria for a major depressive episode.

Number of Canadians 15 years or older who, in the past 12-month period, reported symptoms consistent with either a major depressive episode, bipolar disorder, a generalized anxiety disorder or alcohol/drug abuse: 2.8 million.

Here at MDSC, we hear from patients or family members on a daily basis. Many share their personal stories of living with Major Depressive Disorder, and the struggles and challenges they have in finding the road to recovery and wellness maintenance. We hear from mothers who they themselves are becoming ill while caring for their children. The huge stress and anxiety that they are living with on a daily basis is directly affecting their health and welfare. We know that MDD is an illness that impacts people in ways that can be different. We also know that treatment and wellness maintenance is very individualized. What works for one person may not work for the person down the road and vice versa. With millions of Canadians living with depression, it is very obvious that new treatment options must be provided. The evidence provided by our survey clearly shows there is a great need.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Our MDSC national survey showed 69% of respondents have been dealing with their depression for more than 11 years. With an incredible 49% of the respondents indicated they were not doing well with their symptoms.

Respondents were asked to indicate the frequency with which they experienced nine (9) problems over the last two weeks.

• At the time of the survey, feeling tired/having little energy, sleeping problems (either falling/staying asleep or oversleeping), and feeling bad about oneself were problems being experienced by at least one-half of respondents most of the time (i.e., daily or more than half the days), while slightly fewer were bothered to this same frequency due to having little interest/pleasure in doing things, poor appetite/overeating, feeling down/depressed/hopeless and trouble concentrating.

• Thoughts of suicide/self-harm and noticeable slowing of movement/speech were notably less common; however, more than one in ten reported experiencing each of these problems most of the time, while a notable minority experienced each of these problems several days during a two-week time period.

Those experiencing TRD have taken a wide-variety of anti-depressant drug medications to treat their depression. Respondents most commonly report having taken Wellbutrin and Effexor/Effexor XR, followed by Celexa, Prozac, Zoloft, Cipralex and Paxil at one point during their treatment. Specific medications are generally used for less than five years. While medication order varies, Prozac and Celexa are most commonly identified as being initial treatments. Alternatively, Effexor/Effexor XR and Wellbutrin are most commonly prescribed as replacement or supplementary treatments, and both are most commonly identified as being part of respondents'

current drug treatment. Compared to the past, far fewer report taking Ativan, Seroquel, Lithium, Risperdal, Xanax, Valium and Zyprexa.

MDSC is very familiar with private health care coverage for mental illness medications, We are quite aware of how many private plans cover new treatments for depression – It is our position that this coverage leads to quicker recovery and wellness maintenance for the patient. This of course leads to other significant benefits, such as quicker return to work for the patient (a great benefit to the employer), lower negative long-term impact on the families of the patient.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

The most significant challenge to accessing this treatment is that unless a person has, through their employer, a quality drug plan, they will not have access to the new treatments that could work best for them. This barrier to equal access is detrimental to the wellbeing of Canadians.

Patients, families and caregivers believe strongly that access to treatment should not be limited to those only with private drug plan coverage, while those who work for employers who do not have drug coverage do not get access to the best medication for their individual illness. Our position is that accessing the best medications to treat mental illness should be fully equitable for all those who suffer. With one in five people suffering from a mental illness, patients need choice. Choice offers hope.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

7. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

No.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No.

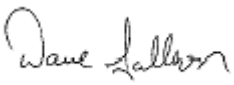
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Janssen Inc				X
Pfizer Canada				X
Lundbeck Inc				X

Our millions of dollars of funding comes primary from non-pharmaceutical companies. We emphasize that none of our positions are influenced in any manner whatsoever by this sector.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Dave Gallson



Position: National Executive Director
Patient Group: Mood Disorders Society of Canada
Date: April 17th, 2019

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Trintellex**
Name of the Patient Group	**Stigma-Free Society**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Stigma-Free Society https://stigmafreesociety.com/

The Stigma-Free Society is committed to combating stigma of all kinds. The Charity's Vision and Mission foster programs that cultivate, encourage, and educate diverse communities to be inclusive and compassionate through awareness and understanding through education, support and leadership. Our Society helps people achieve personal empowerment by providing peer support for youth and adults and raising awareness through education in schools and the community.

The Society's goal is to create **AWARENESS** of the various stigmas that exist in the world, develop an **UNDERSTANDING** of the challenges that numerous people face and encourage all people to foster **ACCEPTANCE** of themselves and others

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

The Stigma-Free Society administered CADTH's patient input survey from Survey Monkey starting on April 18, 2019 and ending on May 21,2019. It is extremely difficult to find survey respondents that have been administered the drug Trintellex. Only one out of 20 respondents had been administered the drug in question. There were 20 respondents in question, but they did not answer every question. However, the additional questions in the survey did provide more insight into the people's views of living with mental illness.

All survey respondents are Canadian and residing in Victoria and Metro Vancouver, B.C. The 20 respondents identified as 5 male, 14 female and 1 non-binary person. As for education for the 20 respondents: 4 have secondary school, 14 have university/college and 2 post-graduate education.

As for their employment situation: Full-time 6, Part-time 9, Student 3, Volunteer 4, and None of the Above 2.

Andrea Paquette, President attempted to promote the survey on social media, but was accused that the survey was only a means to promote Trintellex and this individual pointed out that advertising for psychiatric medication is illegal in Canada. The Stigma-Free Society is a registered Canadian Charity and we cannot be seen to be promoting any type of medication, so the President decided to keep the CADTH survey within the parameters of people with lived experience who have come into contact with the Society and trust our motives, which is for obtaining authentic patient input.

As suggested by the primary contact for this submission, the survey was shared with additional organizations such as:

BCSS (Schizophrenia Society)
BPC (Better PharmaCare Coalition)
Bad Gut Society
BCMD BC Mood Disorder

There was an increase of 0% in survey responses.

Dr. Wei Song, Principal, Canadian Psychiatric Association and Advisor to the Stigma-Free Society was contacted and the President requested assistance in seeking out potential participants for the survey, but he was unfortunately unavailable. If the CADTH Patient Input shared with the Stigma-Free Society had a longer timeframe then it may have been possible to gather more respondents.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Major Depressive Disorder (MDD) - progression and treatment goals

Relevant Survey Findings indicated that 16 of the respondents identified as having MDD and 2 caregivers shared their experiences on the survey. One respondent identified as being diagnosed less than a year ago, while all others were diagnosed for 2+ years.

The disease experience includes stigma of the medication from a societal view and also self-stigma where someone with lived experience and often taking medication is ashamed of their situation.

The patient input survey posed the question:

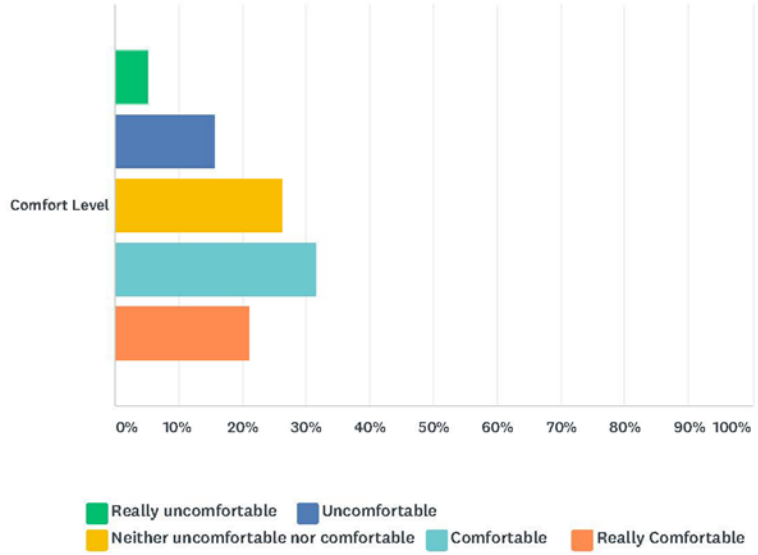
Do you feel that the stigma of depression inhibits your ability to get help for your disease?

- ☐ I am not inhibited by stigma in getting helped
- ☐ No
- ☐ Sometimes I feel embarrassed to tell my job I need to go to the hospital or that I was in the hospital. It's also hard talking to my school if I miss a day due to mental health.
- ☐ No. I have tried various treatments. People have encouraged me to get help. Not the other way around.
- ☐ Somewhat. Although attitudes are changing.
- ☐ It used to, no more. My support network has been very good with reducing shame

- [ ] Yes. Fearing judgement from work/employers
- [ ] Yes, because I didn't feel comfortable talking to a doctor about it. However, getting help was easier once I was in university, because I felt like the stigma on campus was lower than in society in general.
- [ ] No
- [ ] No
- [ ] I feel taken seriously when it comes to mental health but not with physical. Doctors think im exaggerating physical pain because of my mental health
- [ ] Not sure
- [ ] I don’t notice the stigma, I talk about it and people listen I find most people either know someone who has depression or have been depressed at some point
- [ ] I think that some caregivers, like psychiatrists, sometimes don't believe us & this can result in misdiagnosis.
- [ ] Not at all.
- [ ] No
- [ ] Sometimes. I had issues with employment due to stigma.
- [ ] Yes nobody takes you seriously. If you go into the ER for a heart pain and feel you are having a heart attack, people assume that you are having a mental illness 'episode'

Q5 On the scale below, how comfortable are you with sharing the fact that you live with depression with others?

Answered: 19 Skipped: 1



	REALLY UNCOMFORTABLE	UNCOMFORTABLE	NEITHER UNCOMFORTABLE NOR COMFORTABLE	COMFORTABLE	REALLY COMFORTABLE	TOTAL	WEIGHTED AVERAGE
Comfort Level	5.26% 1	15.79% 3	26.32% 5	31.58% 6	21.05% 4	19	3.47

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

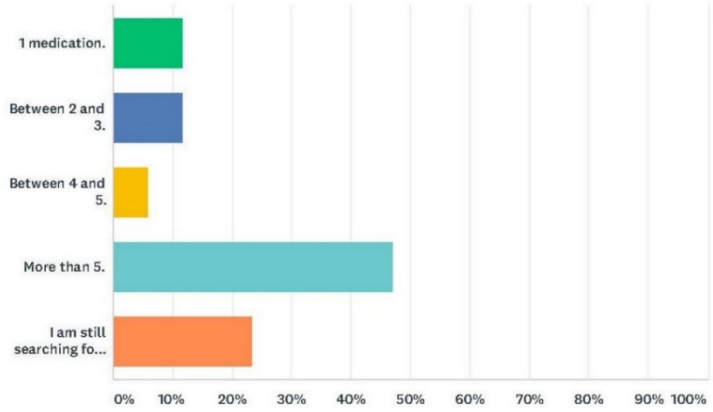
Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

From analyzing the data, it is apparent that one of the most significant factors that impact a person's life is the difficulty in finding a medication that works for the person with lived experience and quite often people are on 5+ medications. This is problematic because one never knows what side-effects are coming from which medication. Although, a medication 'cocktail' is often effective, it is not ideal for this reasoning.

See below for survey summary.

Q3 Approximately how many different antidepressant medications have you tried before finding the right one that works for you?

Answered: 17 Skipped: 3



ANSWER CHOICES	RESPONSES	
1 medication.	11.76%	2
Between 2 and 3.	11.76%	2
Between 4 and 5.	5.88%	1
More than 5.	47.06%	8
I am still searching for the right medication for me.	23.53%	4
Total Respondents: 17		

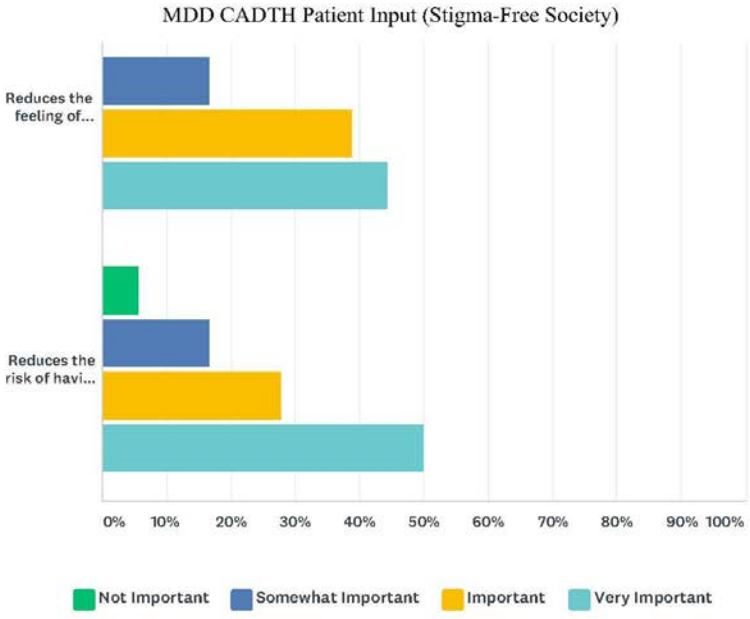
Q4 PLEASE SPECIFY WHICH TREATMENT(S) YOU HAVE TRIED AND THE REASON WHY YOU HAVE DISCONTINUED THIS/THESE TREATMENT(S).

- Multiple SSRI's and SSNI's which caused weight gain and issues with sex. I have used anti-psychotics with better results, but struggle with weight gain. I only use medication when I am struggling with depression and use mood stabilizers a daily basison
- Venlaxafine, Olanzapine, Quetiapine. Venlax made me manic, Olanz made me too cathertic and sluggish, Quetia seems to be working more or less.
- Counselling, dbt therapy, medications. Stopped counselling because I moved and haven't found another . Stopped dbt for the same reason. Still take meds
- Group therapy (CBT, social anxiety workshop, toast masters). Councillors. Medication. Phycologists. Valentus Clinic. Diet. Naturopath. Exercise. I discontinued most of these except for medication because I did not get the results I desired.
- I have not discontinued treatment aside from medications that were not effective
- Mindfulness CBT/ Talk therapy, psychotropic medications. The former as still in practice, the latter is not(it didnt have enough positives to justify the impact it had)
- I tried yoga and it was working for me as because of lack of time management I discontinued
- DBT & CBT
- Celexa, effexor, trazedone, wellbutrin, abilify. Discontinued because they did not significantly impact my depression.
- I haven’t discontinued any
- Mood Stabilizers, Anti-Depressants, and Psychotherapy
- Many just didnt work until lithium
- I don’t know the names of all the different ones that I have tried but each and every time I switched away from them it was because they weren’t conducive to the life I want to lead. They either turned me into too much of a mental zombie, impacted my sleep cycle or prevented me from legally being able to do my job
- mood-stabilizers(still on), ECT(only when hospitalized), anti-psychotics(don't work), anti-depressants(still trying)
- Quetiapine / Ativan for anxiety. My psychiatrist is now considering transitioning to antidepressants.
- I have tried over 30 different medications that had bad side effects, pooped out or didn't work.
- Anti convulsant Lamictal for depression. Stopped welbutrin because of mania side-effects

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Q7 When considering a medication, please rate how important it is to you that the medication: (see below)



	NOT IMPORTANT	SOMEWHAT IMPORTANT	IMPORTANT	VERY IMPORTANT	TOTAL	WEIGHTED AVERAGE
Minimizes weight gain	0.00% 0	33.33% 6	38.89% 7	27.78% 5	18	2.94
Minimizes sexuak problems (sex drive, intimacy, sexual functioning)	5.56% 1	33.33% 6	27.78% 5	33.33% 6	18	2.89
Reduces the feeling of anxiety	5.56% 1	5.56% 1	44.44% 8	44.44% 8	18	3.28
Reduces the feeling of being too tired or slowed down	0.00% 0	16.67% 3	38.89% 7	44.44% 8	18	3.28
Reduces the risk of having trouble concentrating	5.56% 1	16.67% 3	27.78% 5	50.00% 9	18	3.22

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

One out of 20 people with lived experience of MDD responded to the Stigma-Free Society's survey about having been prescribed Trintellex in the past. This individual was interviewed personally by the President of SFS. The person with lived experience had access to the drug through samples when they attended to the Emergency Psychiatric Hospital. She returned home to take the drug Trintellex for 3 months.

The patient attests to having a very negative experience with the drug in question. They did not identify any benefits, but attested that the most significant disadvantage was the excessive nausea that they experienced for the entire 3 months on the medication. The patient stated that she vomited every morning for the entire 3 months and even more 1 month after being weened off the medication. Eventually the nausea stopped as she and her doctor decided to end the administration of Trintellex. Their psychiatrist advised strategies before deciding to cease the medication and recommended the administration of the drug at different times of the day and with or without food. There was no success and the patient states that out of the approximate 30 medications that they have tried for their mental illness, Trintellex is rated as being in the top 5 of the worst.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

A: N/A

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

None at this time.

See Appendix A Attached

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

   Andrea Paquette had discussions with Stephen Filbey from WestPAR Consultancy Inc. who first made me aware of the CADTH Patient Input opportunity. Up to that point, Andrea was not aware of the CADTH patient input process or opportunity with Trintellix. After looking into it further on your own, the Society decided it was important for people with lived experience to have a voice and decided to participate in the CADTH Patient Input process.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   An online patient survey was deemed to be the most efficient and most useful direct patient input process. After approving a final survey, the Society found it did not have the skill set or personnel available at the time to set the survey up online. SFS reached out to WestPAR for assistance who then provided the Society with the survey to set up in Survey Monkey on its behalf. WestPAR's involvement ended at this point. The survey results and information were processed internally by SFS.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Lundbeck Canada		X		
Otsuka Pharmaceuticals		X		

Refer to Stigma-Free Society Annual Reports for names of the Society's Funders at: https://stigmafreesociety.com/annual-reports/

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.
Name: Andrea Paquette
Position: President
Patient Group: Stigma-Free Society Contacts
Date: May 21, 2019