CADTH

CADTH COMMON DRUG REVIEW

Patient Input

ESKETAMINE HYDROCHLORIDE (TBC)

(Janssen Inc.)

Indication: Major depressive disorder (MDD), adults

CADTH received patient input from:

Canadian Mental Health Association, National, Canadian Mental Health Association, Alberta Division, and Mood Disorders Association of Ontario

Mood Disorders Society of Canada

July 16, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	TBC (esketamine hydrochloride) Major Depressive Disorder
Name of the Patient Group	Canadian Mental Health Association, National; Canadian Mental Health Association, Alberta Division; and Mood Disorders Association of Ontario
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 and one territory, 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

The Mood Disorders Association of Ontario (MDAO) is a community-based mental health organization that supports adults, youth, families, and caregivers who experience mood disorders, early psychosis, and mental health or addictions issues. MDAO offers standards-based peer support, including individual, group and family peer support, along with clinical services and counselling programs to our clients and their caregivers. Our mental health programs and services are developed and supported by a framework of evidence-based

standards, along with a community of practice approach. In addition, MDAO partnered with Sunnybrook Health Sciences Centre, St. Michael's Hospital, and other community mental health organizations to develop, improve and strengthen mental health services across the province. Research and evaluation are essential to MDAO's work which includes partnerships with organizations such as the Ontario Brain Institute (OBI), the Canadian Biomarker Integration Network in Depression (CAN-BIND), the Sunnybrook Collaborative on Research and Education in Youth Bipolar Disorder SCORE-YBD and Collaborative RESearch Team to study psychosocial issues in Bipolar Disorder (CREST.BD). These partnerships demonstrate the effectiveness and impact of MDAO's programs and help facilitate projects through knowledge exchange to fill gaps in the communities we serve. MDAO is a provincially registered charity; registration number is 13097 8570 RR0001. Website: https://www.mooddisorders.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 contacting patients living with depression or major depressive disorder (MDD) in the United States who are either currently participating or have participated in a study of esketamine nasal spray.

The summary of patient perspectives submitted here was gathered through semi-structured phone interviews. Phone interviews were conducted with adults living with depression or MDD. The interview guides 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 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 by MDAO (following the signing of a confidentiality agreement).

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.

MDAO – Data Sources

From April to July 2019, MDAO collected feedback from persons diagnosed with MDD (hereinafter also referred to as patients) and their caregivers through online surveys and phone interviews. The patient survey was composed of 25 questions, while the caregiver survey was composed of 54 questions. The surveys, which were co-developed with CMHA National, required patients and caregivers approximately 10 and 20 minutes, respectively, to complete and each phone interview lasted approximately 30 minutes. The surveys were disseminated by VerticalResponse on June 24, 2019.

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

Participant Profile

CMHA National conducted three phone interviews with adult patients living with long-term treatment-resistant depression. All three patients are currently participating in esketamine studies in Massachusetts, USA. Their demographics are as follows:

- Male, 67 years old, hereinafter referred to as P1.
- Male, 40 years old, hereinafter referred to as P2.
- Female, 70 years old, hereinafter referred to as P3.

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.

MDAO obtained a total of 86 online survey responses:

- 75 online survey responses were collected from persons living with depression, with the vast majority residing in Ontario. Patient respondents were 76% female, 23% male, and 1% other. The majority (97%) were diagnosed more than 2 years ago with a mean age of 53 years old. The highest level of education was 25% postgraduate, 56% university/College, 19% secondary School. One third are working full-time with the remaining working part-time, volunteering, or students. Quotes reported from the open-ended questions in the patient surveys will be indicated with “Patient” followed by a letter to identify different patient responses.
- 11 online survey responses were collected from caregivers of those living with depression. Caregiver respondents were 82% female and 18% male. The majority (64%) spent more than 20 hours per week providing care for their loved one, with 18.2% spending more than 60 hours per week. Quotes reported from the open-ended questions in the caregiver surveys will be indicated with “Caregiver” followed by a letter to identify different caregiver responses.

MDAO also conducted three phone interviews with patients living with depression that were treated intranasally with ketamine in a clinical trial setting. Their demographics are as follows:

- Female, 60 years old, resides in Pennsylvania, USA, hereinafter referred to as P4. She is eligible for and is receiving disability insurance.
- Male, 43 years old, resides in Massachusetts, USA, hereinafter referred to as P5.
- Female, 55 years old, resides in Maryland, USA, hereinafter referred to as P6.

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 and treatment, feedback from patients and caregivers emphasized the negative impact of depression on patients' emotions, quality of life, and ability to do normal daily activities. Patients 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 [then] 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, data from MDAO's online survey responses and all six interviews consistently conveyed negative impacts on daily functions such as going to work, reducing motivation, and becoming socially withdrawn. Other participants echoed this with specific references to sleep, appetite, mood, relationships, exercise, 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. Similarly, and according to data gathered from CMHA Alberta's 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."

> P1: "Things were overwhelming that felt overwhelming to me, that really, you know, weren't overwhelming intellectually and, you know, they weren't overwhelming, they just felt overwhelming."

> P2: "[W]hen things are bad, I'm extremely unmotivated, and uninterested, and, you know, I can't get off the couch, so to speak. […] It severely impacts my ability to work, and enjoy my life, and all that."

> P5: "[Depression] reduced my motivation to do things. It made me feel, overall, less enthusiasm for life. Sometimes emotions can feel overwhelming, in particular

sadness and anxiety. Well, I do feel that depression, as a disorder, can actually impact a person's actual cognitive ability."

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

P1: "I would classify my depression [as] 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 tried to keep 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]."

P3: "Some days are better than others, some months are better than others, but, I try not to let it impact, especially my daughter. My poor husband gets the brunt of it. I try not to let it impact him, but it does."

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 that they 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.

P6: "In the beginning, the stigma definitely kept me from seeking out professionals because I didn't want it on my work record; I didn't want people to know about it; I thought it would hinder my career; it would hinder other people's opinions of me. But that no longer applies. You know, I'll go anywhere or see anybody now, mostly because just how severe my depression got, later in life, that heck-or-high-water I was going to find a way to feel better because it is just insufferable."

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.

Caregivers' online survey responses showed a high burden of care that negatively impacted their physical, mental, and financial health, given the limited availability of supports in the healthcare system. Caregiver responses from the open-ended questions in MDAO's survey noted:

Caregiver A: "The health care system does not always work the way one might think it should and there are now going to be changes that may adversely affect the system."

Caregiver B: "A person without depression truly does NOT know the dark side of it and often can say the slightest thing that turns the depressed off. It's like walking on eggs making sure you respect the individual. It's hard to word it, given the love I have for this person."

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).

Based on currently available treatments in Canada, the vast majority (>90%) of patient respondents to MDAO's online survey have tried medications and psychotherapy to treat their depression. In addition, 37% have tried complementary and alternative treatments and 13% have tried Neurostimulation. Multiple trials of current medications were required prior to improvement in mood, along with the management of side effects such as weight gain and decreased sexual functioning. Patient responses from the open-ended questions in MDAO's survey noted:

Patient A: "It took a long time to find the right medication and level. Terrible side-effects from several e.g. Mirtazapine resulted in extremely rapid weight gain."

Patient B: "Medication trial and error made it very costly. Medication caused weight gain. I was fortunate to have access to excellent care, but I know that is not the same for everyone. I did have travel 2 hours to receive care. ECT

[electroconvulsive therapy] left me with huge memory deficits. I had to live in the hospital for 2 months as my area does not offer this type of treatment or care."

Patient C: "Several of the medications that I tried had negative side effects. It took several trials for me to find one that had the least amount of side effects and the benefits outweighed the side effects. All seemed to affect libido."

Similarly, interviewed patients reported trying multiple treatment options in hopes of managing their disorder, sometimes trying several treatments simultaneously. For example, before initiating the use of TBC, P1 reported having 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. P3 had a similar experience.

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."

P3: "I'm very sensitive to the medication, so they have to put me on very slowly, and then I get up to a, you know, decent dosage and it doesn't work, so I have to then get down very slowly, and I've done this time after time after time over the years, and it's been difficult."

One participant indicated that other forms of mental health care, other than pharmacotherapy, also lacked effectiveness. This included seeking help from mental health professionals.

P3: "I've tried therapy. I actually went to a counsellor who I thought was very helpful, and now that I don't go to her any more, I actually realize she made things worse by bringing up [and] making me re-live things in my life that were not pleasant and I maybe had, pushed way back, and now they're in the forefront and I didn't really need to remember them. And I've seen countless therapists, and I don't find any – and I see a psycho-pharmacologist and I don't find any of them particularly helpful."

P1 acknowledged experiencing benefits after initiating pharmacotherapy to treat his depressive symptoms. Patients' experiences with side effects seem substantial, which negatively impacts their adherence with prescribed treatment. For example, and as a result of experienced side effects, P1 opted to discontinue his prescribed treatment, P5 indicated that the side effects exacerbated his depressive symptoms, and P2 was motivated to change their prescribed treatment.

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."

P2: "I mean, everything sort-of works to a degree. It's not as if, like, something doesn't work at all, but, the various drugs have various side effects. Sometimes I wouldn't like the side effects, sometimes I didn't feel like, you know, it was accomplishing what I needed it to…you know, so that's the motivation to go and, and sort of, try something else."

P2: “A couple of [available treatments] I’ve tried have made me nauseous, like, the first few days. In fact, I think Lexapro was one of them. So, that’s happened, but then that goes away after you’re sort-of, you know, you’re on-boarded to the medication. And, I’ve experienced some sexual side effects from some of them. Those are the two standouts. The sexual side effects caused me to try something different. […] Switching treatments for me was a voluntary, you know, proactive decision.”

P3: “Headaches from some of them, upset stomachs from some of them. Seroquel I just couldn’t take because it put me right to sleep and I couldn’t function at all.”

P5: “I have been on medications that really diminish libido and sexual function, and it’s a problem, I guess, that I can tend to sort of be depressed about.”

For P3, although the experienced side effects negatively impacted her quality of life, they were not the sole reason she opted to discontinue her prescribed treatment. Rather, it was the lack of effectiveness of the treatment.

P3: “I test [side effects] out, hoping that, you know, they will lessen and that the medication might kick in, but once the medication didn’t kick in I didn’t want to deal with the side effects.

P1 highlighted the importance of realizing the inevitability of side effects occurring when opting for pharmacotherapy to treat depression.

P1: “You have to be willing to accept the side effects.”

Participants were asked about their overall experience with currently available treatments for MDD. It seemed that available treatments for MDD do have a positive impact on a patient’s quality of life and level of satisfaction, as long as the experienced side effects are transient.

P2: “I mean, they’re better than nothing, certainly.”

P2: “I mind if [side effects] are going to affect my quality of life, like, on an ongoing basis.”

Participants also noted there are many barriers to accessing appropriate, professional mental health 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 that participants emphasized was difficulty accessing private mental health care services. Interviewed patients reported the following barriers with available forms of mental health care services:

P2: “I’ll seek out cognitive behavioural therapy but, you know, finding the right person to do that with is challenging and, not just from a[n] availability standpoint, but, you know, from a personality standpoint.”

For P2, the challenge seemed to be identifying and having access to a “compatible” clinician to re-fill his prescriptions. However, obtaining the medication “once the prescription is written” did not seem to be an issue.

P2: “The most difficult part of [receiving available treatments], historically, has been, you know, keeping up with appointments, you know, for a doctor to continue prescribing. I mean, I had a doctor that I was going to see for a while, and then she lost the practise, and then I had to try to find somebody else, and, you know, it’s difficult to find a compatible provider, I think and, you know, so you end up going through a few people who you don’t really like very much, but you have to because you have to get a prescription, and it’s, you know, that whole process is

probably the most difficult. […] So that was de-motivating, and, you know, made it difficult to keep up with appointments."

Surveyed patients and caregivers reported the following barriers to accessing mental health care:

Patient D: "Wait times for appointments is excruciating when you are suffering and costs [are] financially impossible for counselling."

Patient E: "I have not had luck finding a psychiatrist who would see me long-term."

Caregiver C: "My daughter needs a psychiatrist, and none are available unless she is in severe crisis and only for those short periods of time. We live in central Toronto."

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 Bupropion (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 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?

When evaluating new therapies, feedback from surveyed patients and caregivers focused on the importance of a more rapid treatment response compared to current treatments. This is of critical importance for persons with suicidal ideation and persons with MDD. Such concerns were also echoed by interviewed patients.

> P6: "Immediate response. Something that will alleviate the crisis of depression whether that's suicidal ideation, whether that's mental anguish, whether it's debilitating lethargy, it's something that'll work immediately, and by immediately I mean anything that's quicker than, "let's wait six weeks and see if this medication works." I think both patients and caregivers are really looking for something that can address the urgency of a depressive crisis."

P2 also indicated a preference for a treatment option that is "infrequent", "more effective" than currently available treatments, "least invasive", and "least expensive". This implies that although a treatment's mechanism is of importance to MDD patients, cost is also an important determinant of treatment accessibility. In terms of perceived sense of enhanced effectiveness, P2 described it as follows:

> P2: "I see 'more effective' as in, you know, I don't want to feel like I'm struggling with it all the time. It would be nice just to, just start to be normal."

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 whose depressive symptoms were coupled with anxiety, and who was 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 and 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."

Nevertheless, some patients feel strongly about specific side effects, to the extent that they would be willing to terminate their prescribed treatment.

> P5: "Weight gain - I'll be honest with you: it's important to me. That is one of the side effects that I would rate as being more of a concern to me. And there are a lot of side effects. That one in particular is a consideration."

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?

All six US-based adult patients interviewed were being treated with esketamine intranasally in controlled clinical trial settings in the US. Overall, all participants consistently reported that they experienced relatively instantaneous improvement in their depressive symptoms and cognitive functioning in comparison to traditional treatments.

> P1: "The immediateness, it was kind of stunning, and it was like, I mean if I characterized it, it's not like I was all of a sudden, you know, skipping though the days, it wasn't like oh my god, everything's perfect, but it just turned. […] If you describe it, it went from, you know, like, eighty down to a twenty."

P5: “So I’ve had counselling all along, and what’s changed is the Esketamine has really reduced the symptoms of depression. And as the depression has gotten better, it’s also really kind of made me realize (a) how bad it was, and (b) that I could actually expect some additional improvements that were, that I didn’t realize, were related to the depression.”

P5: “When I first started taking [esketamine], it was completely unconventional. I can’t compare it to any other therapy. There’s nothing else like it. With pills, as you know, one is always told that you’ve got to give it plenty of time. Except of course the more, more risky mornings that I have to get up on time and you’d think that would be a health risk. This is entirely different from [esketamine’s] effects [that] were noticed very quickly. And it’s using the tags, I didn’t find anything unconquerable about taking the drug.”

The most common side effects were unpleasant taste, short term dissociation, headache and dizziness. Patients indicated that the aforementioned side effects, which one participant described as “a bit of a hangover”, diminished within a few hours of receiving treatment.

P2: “I don’t feel like there are side effects aside from, you know, a very short-term disorientation and, you know, maybe medium-term, you know, sort-of lack of coordination. But, after that, there’s no side effects that I’m experiencing.”

P5: “The side effects with the Esketamine is very, very short-term. The immediate effects of the Esketamine drug are just following the dosing. After I self-administer the nasal spray, it starts to take effect very, very quickly, and so it has a slight tranquilizing effect. There’s very, very mild hallucination. There’s some, also, you know, kind of mild dissociations happening because the drug sort of gets you to a kind of relaxed state where you’re mostly in your head and you’re not really actively engaged. And so, for probably about an hour, one feels a little bit lethargic and dissociative, and then it’s over. Depending on the time of dosing I personally, if I dose in the morning, usually in two hours I’m fine and back to normal baseline. If I dose later in the day, I might be a little bit more tired for the rest of the day.”

P5: “There’s nothing very terribly unpleasant about the experience except, of course, the taste of the compound. The nasal spray will go in and there’s usually a little bit of post-nasal drip that comes with the dosing, and it’s a terrible taste. It’s a synthetic, sour taste.”

P6: “I’ve seen people from the clinic after an hour be lucid and clear and back to themselves and they get up and they walk out and they’re fine.”

Despite the temporary side effects, interviewed patients seemed to notice a significant improvement in mood and overall functioning. These improvements were also recognized by others in participants’ lives. Together, these benefits counterbalanced the inconveniences participants associated with accessing esketamine (e.g., long drive to clinical trial site; short-term side effects).

P1: “I think it’s had a positive impact on my family life, [be]cause I can be more attentive, and better around the house, and not so stuck in my own head.”

P2: “My girlfriend certainly noticed a change when I started taking [esketamine], so, you know, just a change in my mood, in my, sort-of, participation in, you know, things, and, you know, I’ve certainly had a lot more good days since I’ve started taking it than, than not.”

P5: “Yeah, well, I mean, one of the big things I keep mentioning is that . . . I’m currently in grad school, and I think, in grad school alongside coming through this

trial, and I keep thinking to myself that it's very fortunate that my depression has lifted, because I'm required to a lot more reading and writing at this point in my life than I've done in a very long time. And I am able to do so without, I don't know, the procrastination that I would experience when I was more depressed. I actually feel like my cognitive functioning [has become] better. I feel more productive. Better able to concentrate. Oh, and in other little things, that I did not necessarily know were related to depression, I've now sort-of comfortably woven it into depression. Like the quality of my sleep has improved. I have a more full range of emotions. And one very big benefit is that I am on a much lower dosage of the SSRI [selective serotonin reuptake inhibitor], so some of the more negative side effects that came with that have been lessened."

P6: "My mood has been pretty stable. That was the first thing that really responded to the esketamine. And it was the more physical, long-term, depressive symptoms that have taken longer to smooth out. So, I'm not as reactive as I used to be, I'm not as volatile or vulnerable to emotional stresses."

P6: "So, my mood, and my ability to be social, my ability to be optimistic, all those things almost immediately changed for the better, but more of the physiological symptoms of depression took longer to resolve, but even knowing that, if none of those other depressive symptoms resolved, and just my mood and suicidal ideation allayed, I would even testify then that it is worth it, absolutely worth it, without hesitation."

Reiterating participants' concern with treatment cost, and despite the reported immediate benefits, esketamine clinical trial participants seemed to be concerned about cost beyond their participation in the clinical trial.

P2: "Talking about Esketamine for a moment, it happens that I'm getting it, you know, at no charge because I'm on a trial but, you know, I'm well aware that outside of the trial it's going to be an incredibly expensive treatment. So, you know, if I can't afford it, then I can't afford it. But, you know, the difference between twenty and forty dollars is not going to be an issue to me. The difference between forty dollars and two thousand dollars, it's, you know, that's a big deal." Another concern that emerged was in relation to the long-term effects of esketamine use, which are currently under study.

P2: "I'm curious about long-term effects which are, you know, still being studied. In fact, I'm, you know, a participant in one of those studies, so, I'm not, like, really worried about it? But, you know, there are still some questions there, and when the FDA was reviewing the drug in March, you know, those were some of the objections that were raised."

Despite the immediate enhancements in mood and other MDD symptoms among participants receiving esketamine treatment, this treatment option does not seem to permanently cure depressive symptoms.

P1: "Since I'm probably a year-and- a-half into [esketamine treatment], and I'm on a two-week schedule, so, do I still feel depresse? Yeah, I do, [although] nowhere near the level that I was before when I started the treatment, but, you know, I'm still aware of it, so I don't want to say it's like this panacea, like, it's just everything goes away. It's just, I feel better."

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.

N/A

8. Anything Else?

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

Together, the Canadian Mental Health Association (CMHA) and Hope + Me – Mood Disorders Association of Ontario believe that affordable, equitable and timely access to a full spectrum of reasonably priced psychological support is critical for individuals when medication alone does not resolve depression. We also believe in equitable access to a wide range of safe and effective medications for people who access medication as part of their treatment plan. Equity in access is vital, given that many Canadians who experience several mental illnesses experience high rates of poverty and unemployment that preclude them from private coverage. Further, it is pivotal to reduce siloing by improving 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.

Hope + Me – Mood Disorders Association of Ontario maintains that access to the best medications should not be only available in private drug plan coverage, and accessing all medications to treat mental illness should be for all Canadians. Many of our clients with severe MDD are unable to work, leaving them without private insurance, and leaving them to obtain their medication in the public system. With this public system not having the extensive range of choice of drugs that address emotional, cognitive, and physical health facets, the probabilities of effective treatment are considerably poorer. The non-equitable situation impacts individuals, families, workplaces, and communities.

CMHA supports mental health parity, wherein mental health care is viewed and valued proportionately and equitably within our health care system, such that mental health has equal status with physical health. CMHA hopes to ensure the drug review process, specifically for mental health drugs, involves explicit communication and transparency with organizations that advocate for those who interact with the mental health care system. This is important 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.

CMHA Alberta also recognizes the importance of an efficient and robust drug review process that enhances access where appropriate, given that 930,000 Albertans consult physicians for addiction and mental health-related concerns each year and more than 500,000 Albertans fill antidepressant prescriptions during their treatment. Focus group participants' experiences enhance our understanding of the challenges Albertans experiencing depression face when existing treatment options have not provided relief. Although a small group, their remarkably unified responses concerning the impacts related to 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.

CMHA Alberta also believes that greater information sharing can support continuity of care can help decrease the stress associated with repeating traumatic experiences to each new provider. Support systems that consider the needs of the whole person are essential examples of ways that integration and enhanced information-sharing would benefit individuals living with MDD. 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.

Some of these identified approaches may exist elsewhere in Canada or the world and require dedicated implementation support to bring them to Canadians. Others need multi-sectoral collaborative efforts to overcome bias and stigma, entrenched clinical practice and other systems-level challenges.

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.

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.

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.

Janssen is also one of Hope + Me - Mood Disorders Association of Ontario's funders. Janssen assisted by providing patient contacts, upon their consent. They also provided reference material to the drug that was helpful in our process.

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 Pharmaceutical Companies of Johnson & Johnson provided CMHA National financial payment				Yes
Janssen Pharmaceutical Companies of Johnson & Johnson provided CMHA Alberta financial payment			Yes	
Lundbeck Canada Inc provided MDAO financial payment	Yes			
Janssen Inc. provided MDAO financial payment			Yes	

Canadian Biomarker Integration Network in Depression (CAN-BIND) provided MDAO 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: July 17, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**TBC esketamine hydrochloride**
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) is one of Canada's best-connected mental health consumer-led organizations. It has forged and maintained long term, high quality partnerships with the public, medical, private and non-profit sectors across Canada.

MDSC was incorporated in 2001 with the overall objective of providing a strong, cohesive national voice for people with mood disorders, their families and caregivers.
On behalf of its members, MDSC has sought to:

- Improve access to treatment and community programs
- Shape program development and treatment innovations
- Inform research
- Influence government policy
- Raise awareness that mood disorders are treatable medical issues
- Reduce stigma and discrimination
- Ensure that the voices of consumers, family members and caregivers are accurately communicated and heard on issues of national importance.

Its activities include:

- Building a national clearing house of patient and family-relevant information and resources about mood disorders
- Advocating for the creation of adequate and accessible stigma-free community and psychiatric programs for people living with mental illness and their families.

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.

MDSC has a large number of dedicated members with 50,000 social media followers and extensive daily visits to our main MDSC website.

Our depressionhurts.ca website alone has 500 visitors per day.

Our national mental health campaign, Defeat Depression, holds fundraising walks from coast to coast. Twenty thousand people take part yearly.

We have an online discussion and support chat line that has 2,500 discussion threads and over 32,000 posts.

These ongoing contacts ensures that MDSC is in close touch with the issues that concern our members.

MDSC also builds on the shared experiences of its many members and followers by asking for descriptions of their struggles with their illness.

For example, in a national online survey on treatment resistant depression conducted between March 3rd and March 22nd (2018), respondents offered a detailed understanding of living with depression (results included in this submission).

In addition, we report descriptions of lived experiences, along with consumers', family and caregivers' reflections that have been provided to us over the many years of MDSC's existence.

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?

People who've been diagnosed with depression describe it as the worst pain they've ever experienced. The mental, emotional and physical effects are serious and, for many, long term. Relationships, work and family networks are destabilized, sometimes permanently.
Depression comes in many forms:

- Mild
- Major depressive disorder

- Depression with anxiety
- Port-partum depression
- Seasonal affective disorder
- Treatment resistant depression (recurring bouts of depression for years). TRD is reported to affect 21.7% of people with depression but some research places this figure as high as 50 – 60%. Clinicians now refer to TRD as a chronic illness.

The World Health Organization reports that depression is the 3rd leading cause of disease burden, worldwide.

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

People with long-term medical conditions are more likely to experience depression and people with depression are more likely to experience physical illnesses.

> *The source for these figures and comments is a MDSC publication called Quick Facts on Mental Illness and Additions in Canada; available from the MDSC's website.*

Everyone who is touched by depression has their day-to-day life disrupted and their quality of life seriously compromised.

MDSC survey respondents describe their experiences:
69% or respondents had been dealing with their depression for more than 11 years.
49% reported that they were not doing well with their symptoms.

One-half of respondents reported that, in the last two weeks, they had felt:

- Tired, low energy, trouble sleeping, poor appetite, little pleasure in life, trouble concentrating and a general sense of hopelessness
- Slowing of movement and speech
- Thoughts of suicide or self-harm.

In addition to struggling with the illness itself, consumers (and family members) experience stigma – from employers, friends and even from medical professionals.
Treatment resistant depression has an especially serious and life-overwhelming effect. It involves:

- Loss of educational opportunities and, for those who are older, loss of employment
- Possible onset of co-morbid physical illness
- Loss of relationships with spouses, friends, and family
- Serial psychiatric hospital admissions
- The stigma of mental illness exacerbated by low employment and possibly poverty
- Much increased risk of suicide.

Aspects of the illness consumers and families want controlled:

People want symptom relief and the ability to return to full functioning. In other words, they want their medication (and other treatments) to work.

They also want to be viewed as individuals because depression and the journey to recovery can be different for each person.

For those with treatment resistant depression, some report sometimes feeling blamed for not getting well. In short, they want compassion - not frustration and impatience.

Overall, people with depression want to be treated with respect. They want their illness taken seriously. And they want timely access to effective individualized treatment and medication. They want to get well.

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).

The most ubiquitous treatment for depression is the prescription of anti-depressants. There are now a wide variety available which, as second generation medication, have been able to reduce – but not eliminate - side effects. There is no questions that many, many Canadians diagnosed with depression are well and functioning because of anti-depressants. There remain, however, some problems:

- Side effects such as blurred vision, weight gain and loss of sexual appetite.
- Also, it is not uncommon for patients to have to go through a lengthy cycle of “try this medication – wait – experience little improvement - so try this next medication.” If, eventually, an effective medication is found, patients are relieved to say the least.
- Some patients experience years of wellness on a particular medication only to have its efficacy fade. Then the try-and-try-again cycle begins once more.
- However, from 21.7% to as high as 50 – 60% do not find a medication that works for them for any length of time and experience long-term recurring bouts of depression called treatment resistant depression.

Respondents to MDSC 2018 survey reported the most common anti-depressants used were Wellbutrin and Effexor/Effexor XR followed by Celexa, Prozac, Cipralex and Paxil.
They also reported that it was not uncommon for them to be prescribed supplemental medications with the goal of potentiating the effect of their original anti-depressant. These

include atypical anti-psychotics (examples are Abilify, Resperdal and Zyprexa) and anti-convulsants (Lyric, Neurontin and Topamax). Benzodiazepines are prescribed sparingly.

Anti-depressants are generally available through provincial and territorial formularies and most employers with drug benefit plans cover them. However, new medication, while welcomed by our community, will not be covered publicly for a long time and private plans may be slow to respond.

> Note that psychotherapy is recommended in combination with medication for maximized outcomes but it is very rare to have it covered through public funding.

Additional treatments especially targeted at TRD are Electro-Convulsive Therapy (ECT) and repetitive transcranial stimulation (rTMS). Psychiatrists (and evaluative research) report positive outcomes but some patients remain skeptical and refuse to try these sorts of treatments.

> The source for the above information is MDSC's publication, Medications and You; available from the MDSC website.

Access to diagnostic programs, treatment and community programs is a serious problem for people with depression.

The Mental Health Commission of Canada reports that mental health services receive 7.2% of Canada's overall health budget as opposed to 10 – 14% in Australia, New Zealand and the U.K. One million six hundred thousand Canada report unmet mental health needs.

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 MDSC constituency lives in constant hope that a new and effective type of medication for depression will be discovered and marketed. We support all pharmaceutical research and development with this goal in mind. While it may be too much to expect to solve all the problems experienced with currently available medications, the above descriptions of people's lived experience demonstrate what is and it not presently working for patients. MDSC notes that pharmaceutical solutions for depression have come a long way over the decades but more progress can be made.

When patients consider a therapy their first wish is that there be no trade-offs. What they want is a relief of symptoms and a return to the fullest functioning possible so they can participate in their family, community, education and working lives.

Right now, patients have to take what's on offer and adjust their lives accordingly.

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?

MDSC has no knowledge of Canadian clinical trials on esketamine hydrochloride. Therefore, it reasonable to report that Canadians diagnosed with depression have no direct experience of the medication under review.

That said, it doesn't mean that they don't know about its development, its approval by the FDA and the few clinics in the US that make it available. Information on esketamine hydrochloride is readily available in the press and online for those interested in looking for it and MDSC members are nothing if not keenly interested.

Its potential approval in Canada is a very welcome prospect.

However, there are challenges:

***Prescribing protocol**:* Esketamine hydrochloride must be administered in the practitioner's office and patients will be required to remain there for two hours while they are monitored for any possible side effects such as drowsiness or dissociative symptoms. This may be viewed by some patients as a significant time in which to spend in a Dr's office, and could mean that people who work or have caregiving duties (children or aging parents) simply may have challenges in scheduling that time in their day.

Access: Given the US experience; esketamine hydrochloride has a limited availability. Patients will need to be informed on how to find it.

***Affordability**:* In line with other new medications, those who are willing to go forward despite the onerous prescribing protocol would very likely have to pay out of pocket. Esketamine

hydrochloride would not be covered on formularies and private plans could be slow to recognize it.

> Note: MDSC is familiar with private health care coverage for mental illness medications. It is our position that coverage leads to quicker recovery and extends to wellness maintenance for employees. This leads to significant benefits for the employer; quicker return to work and lower negative long-term impact on performance – not to mention the employees' life outside work and his or her family.

So far, available information would indicate that esketamine hydrochloride can be seen by some as challenging to use than available anti-depressants, and more difficult to access – even for those who can pay.

That said, people with TRD are desperate for relief and despite trepidations, would welcome any advance that promises to relieve their symptoms. Esketamine hydrochloride is a new offering for those who have struggled with finding the right medication that works for them.

7. Anything Else?

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

CADTH should not underestimate the level of hope that TRD patients retain that something – anything – can be discovered to return them to health. It is with great confidence that MDSC endorses forward movement with the approval of esketamine hydrochloride in Canada.

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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.

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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 Inc				X
Pfizer Canada				X
Janssen 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: June 3rd, 2019