CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	**Oral edaravone for the treatment of patients with amyotrophic lateral sclerosis (ALS)**
Name of the Patient Group	**The ALS Society of Canada**
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1. ABOUT THE ALS SOCIETY OF CANADA

The **ALS Society of Canada** is working to change what it means to live with amyotrophic lateral sclerosis (ALS), an unrelenting and currently terminal disease. Grounded in and informed by the Canadian ALS community, we respond to the urgent unmet need for life-changing treatments by investing in high-quality research that will fuel scientific discovery and by engaging industry, supporting increased clinical capacity and advocating for equitable, affordable and timely access to proven therapies. Responding to the tremendous need for current and credible ALS knowledge, awareness and education, we empower Canadians affected by ALS to navigate the current realities of ALS, be informed consumers of ALS information, and advocate effectively for change. In Ontario, we provide direct community services to help people navigate ALS. Founded in 1977, we are a registered charity that receives no core government funding – our work is powered by generous donors who share our vision of a future without ALS. www.als.ca

2. INFORMATION GATHERING

The information contained in this submission was gathered by ALS Canada through a 20-minute online survey that was disseminated in English and French. Survey respondents were recruited by ALS Canada through promotion via email, social media, blog posts, e-newsletters and other online platforms, with the following populations invited to take part: people living with ALS ("patients") and their caregivers and family members ("caregivers"). The online survey was open between November 10 and 24, 2021.

A total of 629 patients and caregivers responded to the English (558) and French (71) online surveys. Almost all were from Canada (primarily Ontario and Quebec), with a small number from the U.S., the U.K., Israel, and the Netherlands. Approximately 70% of respondents are, or were, caregivers to someone diagnosed with ALS. The remainder are currently living with the disease. Among the respondents living with the disease, approximately 60% indicated they had been diagnosed with ALS between six months and two years ago, with some having received their diagnosis more than three years ago. More than half of respondents were 55 years of age or older.

In February and March 2022, ALS Canada supplemented the information gathered through the survey by conducting telephone interviews with seven patients, all of whom had experience with oral edaravone. All the data was contributed anonymously.

3. DISEASE EXPERIENCE

ALS is a terminal disease that moves with startling swiftness. The disease gradually paralyzes people because the brain is no longer able to communicate with the muscles of the body that we are typically able to move at will. As the connection with muscles of the body breaks down, someone living with ALS will lose the ability to walk, talk, eat, swallow, and eventually breathe. Of those who receive an ALS diagnosis, four out of five will die within two to five years of diagnosis. Every year, approximately 1,000 Canadians die of ALS and a similar number are diagnosed. There are currently about 3,000 people living with ALS in Canada.

A diagnosis of ALS and the realities of living with the disease have a profound and pervasive effect on the lives of not only those who are struck by this devastating disease, but also anyone who loves and cares for them. The following is a summary of how the respondents of this survey – people living with ALS, caregivers, and family of those who are living or have lived with the disease – describe its impact on their lives.

With respect to the wide range of symptoms **patients** experienced due to ALS, among the most severe are decreased muscle tone, and related difficulties with mobility (including walking and standing), gripping/holding things, muscle cramping/twitching and fatigue caused by muscle exhaustion. These symptoms were also among the most important to control for people living with ALS, in addition to difficulties breathing, speaking, and choking episodes.

When asked how living with ALS has negatively affected their quality of life, **patients** indicated that their social life, travel/hobbies, and family life suffered the most as seen in the table below.

What aspects of your quality of life has ALS negatively affected? Choose all that apply.				
Answer Choices	Responses			
Family life	68.09%			
Relationship with spouse/partner	46.81%			
Relationship with children/grandchildren	47.52%			
Emotional/psychological well being	65.96%			
Social life	82.98%			
Work or school life	47.52%			
Ability to travel	75.18%			
Ability to pursue hobbies	69.50%			
Financial situation	40.43%			
Intimate/sexual relationships	57.45%			

The impact of ALS was said to be inescapable, especially the loss of independence which touched all aspects of patients' lives. Among patients who need help performing daily tasks, such as feeding themselves, drinking, bathing, and toileting, approximately half said they require support for up to five hours per week.

People living with ALS also indicated that they rely on a range of assistive devices with a walker, specialized bathroom equipment, non-invasive ventilation support, a lift chair, and standard and power wheelchairs identified as the most commonly used.

When asked to describe in their own words how their day-to-day life and quality of life have been impacted by ALS, patients said:

- *"In one short year ALS has taken my speech, career, and ability to live totally independently."*
- *"I've had to stop working to focus on my health. Work distracted me from physio, dietary considerations, exercise, and the intravenous treatments that take 3 hours 10 days of each month. Work also took time away from the planning and preparation for the future such as accessibility upgrades to my home. I need to walk very deliberately to avoid falls."*
- *"I am unable to live with my wife, go walking, participate in family activities, enjoy my grandkids, or go driving. It has forced me to rely on caregivers to manage my day-to-day life."*
- *"My sense of self has taken a huge hit and continues to be chipped away at with each small decline in my physical abilities. I am finding it very difficult to maintain a positive outlook."*
- *"I have become very depressed and don't want to talk to my loved ones as I have difficulty talking, eating and breathing."*
- *"I miss going hiking in the countryside, being surrounded by nature, traveling with friends, and seeing the stars at night. I will now be living the rest of my life in a 10' x 20' room, with little exposure to the outside world."*
- *« Quatre visites par jour pour changer la couche, me laver et m'habiller. De plus mon mari fait un cinquième changement de couche. Bien sûr pour me mettre au lit, ils prennent la lève personne et pour me mettre dans la chaise roulante, ils prennent la lève personne aussi. »*
- *« Beaucoup de solitude, vie sociale pratiquement nulle, ne peux plus sortir seule, fini les restaurants, je ne peux plus venir en aide à mes enfants, m'occuper de mon petit-fils comme je le faisais avant, congédiement de mon employeur après 33 ans de bons services, projets de retraite irréalisables, extrêmement difficile émotionnellement, loisirs personnels plus rien ne va. Épuisement juste à essayer de communiquer. Fatigue continuelle. Savoir qu'un médicament pourrait aider à ralentir la maladie et ne pouvoir y avoir accès est inhumain. Je suis passé de totalement autonome, emploi professionnel à devoir demander de l'aide et confiner à la maison et ça n'a pas fini de s'aggraver. »*

The results in the following table clearly illustrate the degree to which ALS has negatively impacted the lives of the **caregivers** who responded. Family life, emotional/psychological well-being and travel options were the aspects of caregivers' lives most impacted; with 44% of respondents saying that their family life had "completely changed." They specifically mentioned pervasive feelings of overwhelming grief and struggles with mental health, including stress, anxiety, and helplessness/hopelessness as they watched their loved one's body wither away and die. One person said: *"This disease has eaten away at our family emotionally and financially and has stripped us of all that we have."*

As someone providing care for a person living with ALS, please rate how much ALS has negatively affected these different aspects of your life.					
	No impact	Some impact	Moderate impact	Major impact	Completely
Family life	0.93%	6.25%	12.81%	35.63%	44.38%
Relationship with spouse/partner	13.38%	13.69%	20.38%	27.71%	24.84%
Emotional/psychological well being	0.00%	4.36%	13.40%	45.48%	36.76%
Social life	3.72%	8.70%	16.15%	35.40%	36.02%
Work or school life	17.80%	10.36%	14.24%	26.86%	30.74%
Travel options	10.03%	6.58%	8.46%	27.59%	47.34%
Hobbies	12.15%	11.21%	17.76%	29.91%	28.97%
Financial situation	14.51%	17.35%	22.08%	25.55%	20.50%
Intimate/sexual relationships	26.89%	10.82%	10.16%	17.05%	35.08%

The day-to-day lives of caregivers aiding people living with ALS are dramatically impacted by the disease. Needing to assist the patient under their care with aspects of daily living such as exercising (including physical therapy), bathing, walking, and using the toilet, were found to have "completely changed" the lives of approximately half the respondents.

Assistive devices and medical interventions are critical to the care of people living with ALS. Of the caregivers surveyed, with approximately 70% noting the need for specialized bathroom equipment, followed by hospital bed/mattress, walker, non-invasion ventilation support and standard/power wheelchairs.

When asked to describe in their own words how their day-to-day life and quality of life have been affected by providing care for someone living with ALS, caregivers said:

- *"The emotional toll on our family's life is immeasurable. The fact that this disease holds out NO hope makes day-to-day demands almost impossible to carry out."*
- *"This horrible nature of disease is not easy to describe in words. It literally steals the life bit by bit – day-by-day with tremendous cruelty. The hardship to the patient and family is worse than any other affliction I have ever witnessed."*
- *"Knowing your loved one is not going to get better but will eventually expire is a daunting daily emotional struggle. Physically having to care for a loved one with every aspect of their care is draining, stressful, emotional, and physically exhausting.*
- *"As a caregiver there really isn't much quality of life. Your ALS person is your focus every moment of every day. Your eating habits change, your sleeping habits change. There really isn't much else you have the energy for."*
- *"As the disease becomes more physically disabling for the person with ALS, it becomes more physically demanding to care for them. As a healthy and fit person, I have still developed injuries due to the caretaking needs. Learning how to navigate/advocate for needs of ALS patient and family, needing to be savvy, computer literate and able to keep up with resources, and technology. The impact of the steep learning curve for caregivers is the time it takes to learn, research, contact resources, and then live daily with the new equipment/assistive devices. As care becomes more complex and time-consuming, so do the learning requirements for equipment, and arranging all aspects of care."*

- *« L'imprévisibilité de l'évolution de la maladie, la peur de ne pas avoir les moyens financiers nécessaires pour accompagner jusqu'au bout, la conciliation travail/être présent pour aider, pouvoir continuer mes propres projets de vie est un facteur de stress élevé au quotidien. La peine engendrée par la dégénération constante de la personne et la peur qu'elle ne trouve plus de bonheur à vivre ainsi est un poids au quotidien. »*
- *« Ma santé mentale a été la première chose atteinte. L'effet de choc reste constant avec chaque petit changement chez la personne atteinte (ma mère). Vu la rapidité de la maladie, j'ai dû faire un choix sur ma carrière en diminuent mes heures pour les redonner comme proche aidant. Ce qui diminue mon revenu mensuel. De plus, mon moral au travail diminue de beaucoup, mon efficacité et mon rendement. Après avoir passé une journée avec ma mère malade, j'ai perdu tout désir, plaisir, et joie de vive. Ma tête reste sans arrêt dans l'inquiétude de n'être pas présente pour elle. »*

4. EXPERIENCES WITH CURRENTLY AVAILABLE TREATMENTS

Rilutek (riluzole)

When it comes to approved treatments for ALS, 101 **patients** said they are taking/have taken Rilutek (riluzole). As seen in the table below, among the benefits some patients believe they have seen from this therapy, all were identified as being the most important. That said, several patients commented that they are unsure if the drug is having an impact on their ALS, and others said it's too early to tell.

The benefits you believe you have seen from this treatment and how important those benefits are to you:					
	1 (least important)	2	3	4	5 (most important)
Maintained ability	24.42%	10.47%	12.79%	9.30%	43.02%
Slowed progression	18.60%	15.12%	12.79%	10.47%	43.02%
Increased survival	20.73%	15.85%	12.20%	10.98%	40.24%

Most patients said they didn't experience any side effects while taking Rilutek, but among those who did, the most difficult to manage were tiredness, weakness, muscle stiffness and gastrointestinal problems.

And while many patients haven't had any problems accessing Rilutek, some mentioned difficulty due to partial or no private coverage, strict funding criteria, out-of-pocket costs, and a shortage of supply due to COVID-19. As an oral treatment, taking Rilutek wasn't a problem for most patients. While some mentioned having difficulty swallowing it, many commented that they dissolve it in water to make it easier to swallow or take through their feeding tube.

Among the **caregiver** respondents, 156 supported a person living with ALS who used/had used Rilutek (riluzole). Similar to the patient responses, the benefits observed by some of these caregivers – slowing disease progression, maintained ability and increased survival – were all identified as important, as seen in the table below. However, there were several caregivers who stated that they could not tell or didn't know if Rilutek had helped the person living with ALS.

The benefits you have observed from this treatment and how important they are to the person you are caring for:					
	1 (least important)	2	3	4	5 (most important)
Maintained ability	14.16%	11.50%	29.20%	10.62%	34.51%
Slowed progression	14.04%	14.04%	21.05%	10.53%	40.35%
Increased survival	17.54%	8.77%	27.19%	7.02%	39.47%

Varied side effects of Rilutek were observed by caregivers, with most seemingly quite manageable including vomiting, runny nose, spinning sensation and nausea. Other caregivers noted that it can be difficult to tell the difference between the symptoms of ALS and the potential side effects of Rilutek.

Almost two-thirds of respondents reported no difficulty with patients accessing Rilutek, although just under 15% encountered "cost implications" as a challenge. Approximately 55% of respondents reported patients having difficulty swallowing Rilutek, with some saying that they crushed the pills to make them easier to swallow or take though a feeding tube. Several caregivers added that the person living with ALS had no difficulties receiving Rilutek.

When asked about any benefits caregivers had experienced as a result of taking Rilutek, approximately 45% reported having more time with the person under their care because of delayed progression of ALS. A smaller number reported "independence for the person I am providing care for" and being "able to maintain my daily schedule with less interruptions due to care requirements" as benefits, while several others reported that there were no benefits at all.

Radicava (IV edaravone)

With respect to Radicava (IV edaravone), the other approved treatment for ALS, 43 **patients** said they have/had experience with the medication. Among the benefits some patients believe they have seen from this therapy, slowing disease progression, maintained ability and increased survival were all identified as important, as in the table below.

The benefits you believe you have seen from this treatment and how important those benefits are to you:					
	1 (least important)	2	3	4	5 (most important)
Maintained ability	10.81%	10.81%	16.22%	8.11%	54.05%
Slowed progression	10.53%	10.53%	21.95%	7.89%	50.00%
Increased survival	15.79%	7.89%	23.68%	0.00%	52.63%

Most **patients** said they didn't experience any side effects while taking Radicava, but some had difficulty managing changes to their normal walking gait, skin irritation, pressure or pain at the injection site and headaches. And while many patients haven't had any problems accessing Radicava, some mentioned difficulty with out-of-pocket costs, travel to infusion clinics, and a lack of home care nurses available for infusions. Any difficulties with taking Radicava were related to the IV administration, including patients having to schedule activities of daily living around their infusion schedule and needing to have a port catheter implanted. One patient noted that they have had a port catheter inserted three times, as the first two procedures failed.

Another patient remarked: *"I am constantly fatigued and every two weeks I take Radicava infusion treatment for my ALS. While the results have been excellent in delaying muscle weakness, it is mentally difficult to come to terms with the fact that my life revolves around treating my ALS."*

Some patients commented that they had no difficulties receiving this treatment because they were taking the oral formulation of edaravone through clinical trial.

Of the **caregiver** respondents who supported a person living with ALS, 57 use/had used Radicava (IV edaravone). Interestingly, as seen in the following table, maintained ability, slowed progression, and increased survival ranked equally as important as benefits observed by these caregivers. However, there were also several caregivers who stated that they could not tell or didn't know if Radicava had helped the person living with ALS.

The benefits you have observed from this treatment and how manageable they are to the person you provide care for:

	1 (least important)	2	3	4	5 (most important)
Maintained ability	15.15%	15.15%	27.27%	9.09%	33.33%
Slowed progression	17.65%	14.71%	17.65%	14.71%	35.29%
Increased survival	10.00%	13.33%	23.33%	13.33%	36.67%

Varied side effects of Radicava were observed by caregivers, with most seemingly quite manageable including eczema, fungal infection, hypoxia, glycosuria and skin inflammation or rash. However, almost 18% noted changes from normal walking gait as a "most severe" side effect.

Caregiver respondents reported a number of difficulties with patients accessing Radicava, including travel to clinic/hospital/outpatient clinic for infusions, a lack of home care nurses available to do daily infusions, and out-of-pocket costs.

The difficulties caregivers noted with patients receiving Radicava are significant. **They include having to schedule activities of daily living around infusion schedules, being unable to self-administer Radicava, and the inability to get their IV started**. Similarly, most challenges encountered by caregivers (78%) were related to administering and scheduling around infusions, with 30% reporting challenges related to costs, including a lack of private/public coverage and restrictive coverage criteria. Some caregivers reported damage to patients' veins due to frequent injections and having to make repeated trips to the hospital due to blocked port catheters.

And finally, approximately 55% of respondents reported "more time with the person I am providing care for because of delayed progression" as a benefit to taking Radicava; however, many said they had experienced no benefits at all.

Other Treatments

When **patients and caregivers** were asked what treatments other than Rilutek and Radicava they were using to treat ALS or its symptoms, they mentioned a variety of natural supplements

including antioxidants, as well as cannabis/cannabis products and Chinese medicine. They also listed several prescription and OTC products intended for symptomatic relief including Fentanyl patch, Hydromorphone, Lorazepam, Gabapentin, Keppra, Amantadine, Baclofen, Domperidone, Prucalopride, Prevacid, Restoralax, Lactulose, Nuedexta, Quinidex, Botox injections, Atropine, Abreva, Tylenol/Aleve, etc., stem cell therapy, human growth hormone, anti-depressants, and diuretics. And some patients and caregivers mentioned participating in clinical trials for other investigational therapies.

5. IMPROVED OUTCOMES

When asked what improvements they would like to see in a new treatment for ALS that are not achieved in currently available treatments, most **patients** mentioned maintaining current function and independence, delayed progression, symptom reversal and increased survival. Some patients wanted to see specific improvements to their speech, mobility and energy levels, and others hoped for a cure for ALS and increased survival only if their symptoms improved. Related to the complexity of IV treatment delivery, some patients and caregivers indicated a preference for medications that can be taken orally (or through a feeding tube), which they say will allow them to spend less time and effort each day dealing with ALS, and more time enjoying life.

If the desired improvements they hoped for in a new treatment were achieved, patients said the result would be:

- *"Not to be continually afraid of tomorrow, at least to stop the progression of the disease, to be able to live a little and not only to survive."*
- *"I could be independent again, enjoy life, and spend time with my grandchildren and children. I could speak again and eat again and talk again. I used to sing with my grandsons – we had so much fun together, now I can't even talk with them."*
- *"Not having to worry about running out of time and having to make judgements as to priorities. I would have more time with family and be able to dance at my daughters' weddings."*
- *"Hope is one of the biggest things I would like but don't have with ALS. Right from diagnosis it feels like a death sentence with just a declining sequence before that death. Having something that would provide hope is a positive thing."*
- *« Garder mon autonomie le plus longtemps possible est très important pour moi pour ne pas trop surcharger ma conjointe car nous avons 2 jeunes enfants à s'occuper. Prolonger ma vie est également très important pour moi pour pouvoir voir mes enfants grandir je souhaite au moins jusqu' à l'âge adulte. »*
- *« Conserver une certaine autonomie le plus longtemps possible serait rassurant en attendant un meilleur traitement. Mais plus on attend pour profiter d'une nouvelle médication, plus nos chances d'autonomie et de survie sont faible. »*

When asked about the improvements that **caregivers** would like to see in a new treatment for ALS, it is not surprising that they ranked all of the choices high – maintain current function and independence, delayed progression, symptom reversal and increased survival. Some caregivers expressed their hopes for a cure for ALS, as well as earlier diagnosis.

If the desired improvements they hoped for in a new treatment were achieved, caregivers said the result would be:

- *"Increased possibility of having a "normal" relationship, rather than one focused on dealing with constant losses, and no hope. All we do as caregivers is prepare for the inevitable. That is very difficult."*
- *"There was no time to adjust and adapt, just jump in and sink or swim. Improved treatment would have allowed more time for mom to function independently with a lower level of support, allowing caregivers like myself to maintain our own lives simultaneously. You basically give up your own life to care for ALS patients."*
- *« Nous aurions plus de temps d'imparti pour effectuer des activités, des voyages et passé du temps précieux en famille. Maintenir l'autonomie de mon mari le plus longtemps possible et surtout de lui permettre de s'exprimer de façon normale. »*
- *« Perte de l'autonomie de la personne et perte de jouissance de la vie car tout est concentré à aider et donner des soins, ça chambarde la vie du couple. Malgré que la progression de la maladie a été plus ou moins lente nous aurions certainement améliorer notre qualité de vie psychologique face à cette menace de perdre son conjoint. »*
- *« Permettre à mon frère de voir ses enfants grandir plus longtemps, augmenter le nombre d'opportunités pour passer du bon temps tous ensemble et construire des souvenirs, permettre aux autres membres de la famille d'avoir des projets de vie mis à part veiller aux soins de mon frère, permettre à mon frère d'avoir du temps pour réaliser certains rêves/projets de vie malgré le diagnostique. »*

6. EXPERIENCE WITH DRUG UNDER REVIEW – ORAL EDARAVONE

For this submission, seven patients were interviewed regarding their experiences with oral edaravone and its impact on their lives. All of those interviewed are from Canada and all have been able to access oral edaravone through clinical trials. As reflected in the stories below, for these patients oral edaravone was a welcome alternative to Radicava (IV edaravone), and for them, the choice – which they were grateful to have – was clear.

Patient A

Almost two years after being diagnosed with ALS, Patient A began taking oral edaravone through a clinical trial. He had begun treatment with Rilutek prior to starting the clinical trial with oral edaravone and continues to take both treatments today. This patient had considered taking Radicava but was concerned about the burden of the medication's IV delivery. Living a 90-minute drive to the nearest hospital, he would have had to travel 10 days out of each month to receive the IV therapy, which is why he welcomed the opportunity to try oral edaravone. This patient noted that in addition to avoiding long hours in the car and the hospital each month, he doesn't have to worry about the potential side effects and complications that go along with IV medications. The only side effect Patient A has experienced with oral edaravone was temporary headaches which occurred when he was off treatment for a brief period of time between two

clinical trials. As for benefits experienced and their impact on his quality of life, this patient remarked that he is still able to dress himself and walk – assisted by a cane, rather than a wheelchair – and he has been able to continue to travel to visit with family. He feels that oral edaravone has played a key role in delaying the progression of his disease and has given him "a definite sense of hope that it's helping to extend things." This patient, whose sister also had ALS and passed away due the disease, stressed that "any [treatment] delay reduces the quality of life and lifespan period" for people living with ALS. He thinks that publicly funded access to oral edaravone is very important because there's "almost nothing" when it comes to treatments for ALS. He added that, "anything that can give people like me a shot until something more effective comes down the pipeline is important" and that, "it comes down to whether the government wants to treat people and keep them alive or let them die because of dollars."

Patient B

Patient B, a retired teacher, had been leading a full life with his wife, children and five grandchildren when he received his ALS diagnosis in November 2019. One month later, he began taking Rilutek and, less than a year after being diagnosed, he added oral edaravone to his treatment regimen which he accesses through a clinical trial. While he hasn't experienced side effects with either treatment, Patient B did note that oral edaravone has a better dosing schedule – he gets up in the middle of the night to take a dose of Rilutek. He says he is benefiting from oral edaravone both mentally and physically because he believes the treatment is preventing his disease from progressing and he no longer feels like he has been "thrown onto the scrap heap." And while he isn't under the illusion that he can beat ALS, Patient B says he is encouraged that he "isn't getting much worse and that's all that's important." He feels that oral edaravone has helped delayed his need for a wheelchair and for breathing support, and that it has allowed him to remain independent and physically active. He walks every day, makes his own meals, exercises with light weights, and hopes to soon be able to travel again and visit with his grandchildren in Australia. Patient B is convinced that oral edaravone is helping him by giving him hope and an improved quality of life for the past 19 months and based on his experience, he feels that no one with ALS should have to wait for access this medication with so few treatments available. While Patient B thanks governments for all they have done so far regarding ALS treatments, he wants them to know that they need to "move as fast as they can" when it comes to providing access to therapies because "1,000 people a year die [of ALS]."

Patient C

Patient C was diagnosed with Bulbar Onset ALS (when individuals first notice speech or swallowing problems) in April 2020 and has been taking oral edaravone through clinical trials for the past 17 months. The only other treatment for ALS that she tried was Rilutek which she had to discontinue due to dizziness, and she didn't feel that Radicava was a viable option. The IV delivery of Radicava was a deterrent for this patient due to concerns about port catheter infections and travel time to hospital (40 kilometers away), so she opted to wait for the oral format of edaravone. Having read studies showing that edaravone can help slow down the progression of ALS, Patient C and her husband were excited to be accepted into the initial and extension studies for oral edaravone, especially as the number of patients were limited. They both feel that publicly funded access to oral edaravone is very important. "There are so few options for ALS patients to defer the decline in quality of life remaining. Now that we're on it, we don't want to stop and we don't want [a lack of] funding to stop us," they said. For Patient

C, having access to oral edaravone would allow for "a continuation of the medication and thereby slowing the progression of this horrible disease." Her husband says that having access to oral edaravone has given them hope that his wife's quality of life will not deteriorate as quickly as it might have without it. He recalls that "when she was first diagnosed it was a real shock," and that starting oral edaravone "has given us hope that we have more time to allow for further advances in possible treatments." They also have more time to spend with each other, their son and granddaughter. As Patient C added, when you are living with ALS, "time is detrimental – time is really important."

Patient D

In March 2020, around the start of the COVID-19 pandemic, Patient D had just arrived in Florida (where he spends the winters) and was feeling great until he started experiencing shortness of breath, sudden and unexplained weight loss, as well as issues with his coordination when, for example, he would reach for a glass of water, misjudge the distance, and knock over the glass. After seeing a neurologist and a respirologist and undergoing several tests, Patient D was diagnosed with ALS in July 2020. He said it was a "bit of a shock" and that he never expected his symptoms were due to ALS. The first and only treatment he has been taking for ALS is oral edaravone which he began receiving in September 2020 through a clinical trial. He has not experienced any side effects from oral edaravone, finds it easy to take, and has noticed a difference in how he feels especially during the 10-day treatment cycle. For example, he has observed that his muscle twitches lessen considerably within the first couple of days of taking the medication and he continues to feel this physical benefit three to four days after completing his treatment cycle. Patient D has also noticed that he feels better mentally when he's taking oral edaravone – he's more optimistic and his wife has also observed that he has a more positive temperament during the treatment cycle. A year and half later, Patient D says that "oral edaravone is working and it's the reason I have been able to maintain my lifestyle." Last summer, he was still able to play golf and he is still able to take long walks with his wife (with the help of a walker for added security), can dress himself (apart from buttoning his shirt and tying his shoelaces) and eat on his own (using modified utensils). His neurologist feels he is doing well given his stage of ALS and encourages him to continue being physically active. Overall, Patient D says that being on oral edaravone has "meant everything" to him. He feels that it's the reason his disease hasn't progressed as quickly as it could have, and why he's been able to lead a fairly normal life until now. If oral edaravone wasn't made accessible quickly, he would be very disappointed because "it's giving a lot of people hope." He notes that, "not many people have this disease, so from a government spending perspective, it's not a big expense to take on. And it would reduce the overall cost to the healthcare system because patients wouldn't need to receive treatment in hospitals or clinics."

Patient E

About four years ago, Patient E retired and at the time was in good health and she and her husband were looking forward to starting a new chapter in their lives once he retired, as well. Then, in the summer of 2020, Patient E started slurring her speech and drooling, so she went to the hospital thinking she'd had a minor stroke. After about five months and a battery of tests, she received a diagnosis of Bulbar Onset ALS which means that her speech, swallowing, and breathing are being affected first, rather than her mobility. "What a shock it was….it would have been easier to cope with a diagnosis of multiple sclerosis or even cancer because I know

there are [treatment] options, but with ALS options are severely limited with no cure in sight," she recalls. Soon after her diagnosis, Patient E started on Rilutek – one of two approved treatments for ALS in Canada – but declined to try the other one (Radicava) due to its IV delivery which she felt for her would be untenable. Then, "hope for a prolonged life" came to her in the form of a clinical trial with oral edaravone for which she felt lucky to be considered eligible. Early in the trial, she felt some light-headedness, as she had when she first started taking Rilutek, but it quickly subsided and so far, there have been no other side effects. Patient E is still able to feed and dress herself and has no issues walking. She had started experiencing muscle twitching in her legs, but not since starting oral edaravone. At her one-month clinic visit after starting oral edaravone, her tests showed no change in neurological or respiratory function which she sees as "good news." She recently went on a vacation and found it easy to travel with her medication, as long as she had access to a refrigerator. But more than a year after her diagnosis, Patient E is conscious of her "continuum of isolation" due to her ALS and says that "spontaneity is a thing of the past." She fears the inevitable loss of mobility and concedes that most of her and her husband's retirement plans will not be realized, although she is hoping to see her niece's first child walk. Patient E feels it is very important that ALS patients have access to oral edaravone. "If it prolongs your life or gives you hope, it's well worth the small amount of money the government would have to shell out. There are not many ALS patients and most of us may not be alive for another therapy that becomes available."

Patient F

Prior to Patient F's diagnosis with ALS, he had been experiencing numbness in his arm and neck for several months. He underwent some tests which were inconclusive, and one specialist thought he may have arthritis in his neck but wanted to investigate further. Finally, in February 2020 at age 66, he was diagnosed with a slow-progressing form of ALS. Almost immediately, Patient F started treatment with Rilutek, however, he discontinued it after only a few months because he experienced uncomfortable side effects. He had considered trying Radicava but decided against it because of concerns with the IV delivery, so he was very grateful to be accepted into a clinical trial for oral edaravone in July 2020. He has experienced no side effects with oral edaravone, finds it very easy to take and really likes the "app" that he was given to use with the treatment. Because he has a slower progressing form of ALS, Patient F says it's hard to notice changes in his symptoms, however, his physician had noticed some progression before beginning treatment with oral edaravone which has since lessened. Some of his ALS symptoms include a heavy feeling in his legs when he walks and feeling like a weight band has been wrapped around his waist and on his shoulders, as if he's wearing a heavy backpack. These symptoms generally appear towards the end of the day, but in the morning he feels fine. He no longer runs, but he goes for walks and plays golf, even though his grip on his clubs isn't as firm as it once was. He also finds it difficult to tie a shoelace and write, and while he can eat on his own, he has problems holding chopsticks. Even with these challenges, Patient F has enough use of his hands to take care of himself – it just takes him a bit longer to do things then it would for someone without ALS. He says that having access to oral edaravone has given him and his family hope that he could live longer with this disease, until other new drugs and even a cure are discovered. Even though he feels that "every treatment gives more time," he does worry about the future and what life will be like for him as his disease progresses. He wants his wife, his three children and six grandchildren to remember him as "still doing things, not the old guy in the wheelchair" without the ability to speak or feed himself. Patient F underscores that ALS

doesn't just affect the person diagnosed but also the mental health and wellness of the whole family. Treatments like oral edaravone are important, he says, "because they give families hope that somehow their loved one's life is being extended."

Patient G

When Patient G retired in 2013, she was in good health and was leading an active and full life, with her five grandchildren and a thriving chocolate business keeping her busy. About five years later while on vacation in late 2018, she began to experience intense back pain and difficulty walking. In the year and a half that followed, her symptoms persisted and over time she saw a chiropractor, physiotherapist, and kinesiologist for treatment, but to no avail. By the start of the pandemic, Patient G's doctor informed her that her symptoms might be due to a neurological condition, and she was eventually referred to another physiotherapist who worked with a neurosurgeon. In May 2020, she finally received a diagnosis from the neurosurgeon – the cause of her symptoms was ALS. Patient G immediately started taking Rilutek and, by August 2020, she began taking oral edaravone, as well, through a clinical trial. She finds both medications easy to take and hasn't experienced any side effects with either one. So far, the impact of her ALS has been limited to Patient G's back and legs; even before her diagnosis, she began using a cane and eventually transitioned to a walker. By November 2020, she got a wheelchair to allow her to travel to the hospital more easily, which she now uses full-time. She is still able to stand with assistance but relies on a lift to get in and out of her wheelchair (with her husband's assistance.) While Patient G finds that she gets very tired, she is thankful to still have full use of her arms and hands and to be able to talk and eat normally, which gives her pleasure. She says she can't imagine having to take the IV version of edaravone at this stage, saying that "it's very exhausting just to get dressed and [especially] in the wintertime, to get yourself out and then sit through an infusion and get yourself home, 10 days out of a month. I would probably find it very difficult." With oral edaravone, she gets up in the morning, takes her medication and then, she says, "life goes on. I'm able to still be happy, see my grandchildren and all my friends. I still do a lot, even though I'm in a wheelchair." While she says it's difficult to know for sure, she believes that oral edaravone is saving her life and giving it meaning, considering that the disease hasn't really worsened since she started on the clinical trial. "If it's working, I want it to keep working. I want to be here if I can 10 years or more from now. I just keep my fingers crossed."

7. COMPANION DIAGNOSTIC TEST

N/A

8. ANYTHING ELSE?

When asked if there was anything else they wanted to share about living with ALS or about their experience with oral edaravone, this is what **patients** and **caregivers** said:

- *"Since ALS is currently without treatment to do anything except possibly slow progression by a number of months, any new therapies should be given an expedited review given the high unmet medical need."*

- *"I have given up many things and am losing more abilities each month. Anything that can slow down this progression is needed immediately! I am running out of time, and the future losses – paralysis, eating, talking, and breathing – are terrifying."*
- *"Remember, people are dying while you are doing this review. People with ALS have literally nothing to lose. Any advancements are crucial."*
- *"Living with ALS, time is not on our side. Any new treatments give patients and caregivers hope. Right now, there is not much hope, and it is much needed."*
- *"This is a terminal disease. If a drug causes headaches, that's manageable. We have to use every tool and drug to stop the progression of the disease, to stop the deaths and suffering."*
- *"Most ALS patients are looking for any glimmer of hope that a potential drug can provide. We don't expect or need a drug to solve all our ALS woes but to 'buy more time' for us. We live in constant hope and anticipation that one or more drugs will be available in our lifetime. Many patients before us have died because time 'ran out' for them. You must understand that delaying the availability of potential drugs can be a death sentence for us."*
- *« Tout traitement qui peut ralentir la maladie est plus que la bienvenue dans un contexte où la maladie évoluée très rapidement. »*

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   ALS Canada completed the submission independently and with external support from a public affairs agency who was hired by ALS Canada on a fee-for-service basis.

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.

   As noted above, a public affairs agency supported data collection and analysis along with internal resources.

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.

   The companies listed below have sponsored ALS Canada signature events, the ALS Canada Research Forum scientific conference, and provided general donations.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AB Science Pharmaceutical	X			
Alexion Pharma Canada Corp.			X	
Amylyx Pharmaceuticals			X	
Apellis Pharmaceuticals			X	
Biogen Canada			X	
Cytokinetics Inc.		X		
DuPont Canada Inc.	X			
Hoffmann-La Roche Ltd.	X			
Impres Pharma Inc.	X			
Ingredion Canada Corporation	X			
Innomar Strategies	X			
Innovative Medicines Canada	X			
Ionis Pharmaceuticals Inc.	X			
Johnson & Johnson Family of Companies	X			
Mitsubishi Tanabe Pharma Canada				X
Novartis Pharma Canada Inc.		X		
Pharma Consultants Inc.	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: Lauren Poplak
Position: Manager, Stakeholder Relations
Patient Group: ALS Society of Canada
Date: April 1, 2022