CADTH

CADTH Reimbursement Review Patient Input

Name of Drug: Alsitek (masitinib)

Indication: For the treatment of patients with amyotrophic lateral sclerosis (ALS)

Name of Patient Group: The ALS Society of Canada

1. About the ALS Society of Canada

The ALS Society of Canada (ALS 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.

2. Information Gathering

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

A total of 629 (English 558 and French 71) patients and caregivers responded to the survey online surveys. Majority of respondents 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. At the time of the survey, approximately 60% of respondents living with the disease 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.

3. Disease Experience

Amyotrophic lateral sclerosis (also known as ALS, Lou Gehrig's disease or motor neuron disease) is a disease that progressively 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. Over time, as the muscles of the body break down, someone living with ALS may lose the ability to walk, talk, eat, swallow, and eventually breathe.

There are more than 3,000 Canadians living with ALS at any one time. Each year, approximately 1,000 Canadians are diagnosed with ALS and a similar number die. Any person has a 1 in 300 chance of receiving an ALS diagnosis in their lifetime and there is no cure. A diagnosis of ALS and the realities of living with the disease have a profound and pervasive impact on the lives of not only those who are struck by this devastating disease, but also anyone who loves and cares for them.

Patients:

The following is a summary of how the respondents of the survey – people living with ALS, caregivers, and family of those who are living or have lived with the disease – describe its affect on their lives:

- **Symptoms:** 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.

- **Quality of Life:** 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%

- **Disease Impact:** 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.

- **Equipment Needs:** 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:

- *"From a very independent, care providing person, I have quickly transformed into one who cannot take care of my own needs, leave my house alone, or provide even a modicum of assistance to others. 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."*
- *'My physical exhaustion from muscle loss and increased laboured breathing has prevented me from living a normal life. I'm dependent on my wife for preparing and serving food and I'll soon need assistance showering. I'm unable to interact with my grandkids and can't travel to see them. It's like a slow-moving checkout line'*
- *"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 feel more isolated since my speech has been impacted. I worry about what people are thinking when they hear me speak and if I am really being listened to or understood. I am not as outgoing or willing to try new things as I used to be."*
- *« 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. »*

Caregivers:

The results in the following table clearly illustrate the degree to which ALS has negatively impacted the lives of the **caregivers** who responded.

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%

- **Quality of Life:** 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.

- **Disease Impact**: 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.

- **Equipment Needs:** 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:

- *"Day to day life I once knew no longer existed. Physically and emotionally stressed. I felt isolated even with the help of my family, home support staff, and the occasional friend who would visit."*
- *"I had to stop working in order to manage the demands of the care routine and cannot leave the house any period of time without extensive planning and backup."*
- *"Every day I live on the edge worrying about the next possible loss that will occur."*
- *« 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 in Canada, 101 **patients** said they are taking/have taken Rilutek (riluzole).

- **Therapeutic Benefit:** 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%

- **Side Effects**: 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.
- **Access:** 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.
- **Administration**: 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).

- **Therapeutic Benefit:** 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%

- **Side Effects:** Caregivers observed varied side effects for Rilutek, 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.
- **Access:** Almost two-thirds of respondents reported no difficulty with patients accessing Rilutek, although just under 15% encountered "cost implications" as a challenge.
- **Administration:** 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), 43 **patients** said they have/had experience with the medication.

- **Therapeutic Benefit:** 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%

- **Side Effects**: 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.
- **Access:** While many patients haven't had 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.
- **Administration:** 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. 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).

- **Therapeutic Benefit** 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%

- **Side Effects:** 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.
- **Access:** 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. Thirty percent also reported challenges related to costs, including a lack of private/public coverage and restrictive coverage criteria.
- **Administration** 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. 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.

ALBRIOZA (AMX0035)

At the time of the survey, 10 patients had the opportunity to try AMX0035 and 10 caregivers reported a loved one had the opportunity to try AMX0035. Most said they received it through a clinical trial, with a few having accessed it through compassionate use from the manufacturer or Health Canada's Special Access Program.

Compared to other treatments they had taken, some **patients** on AMX0035 said they believed it was delaying their disease progression and most likely preserving speaking and breathing functions. While some patients and caregivers said it was too soon to see any impact from AMX0035.

One **caregiver** said AMX0035 slowed the progression of the disease, with the least amount of side effects. Other caregivers commented that AMX0035 has made them "feel at ease" that their loved one's disease progression is slowing down, and that *"it's given hope to our family, and some hope is better than no hope."*

Other Treatments

When **patients and caregivers** were asked what other treatments 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. 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.

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.

6. Experience With Drug Under Review

We were unable to connect with any patients in Canada who have experience with the drug under review.

7. Companion Diagnostic Test

N/A

8. Anything Else?

N/A

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

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.**

   A public affairs agency, who was hired by ALS Canada on a fee-for-service basis, 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.**

Company	Check Appropriate Dollar Range			
	$0 to $5,000	$5,001 to $10,000	$10,000 to $50,000	In Excess of $50,001
AB Science Pharmaceutical	X			
Alexion Pharma Canada Corp			X	
Amylyx Pharmaceuticals				X
Apellis Pharmaceuticals		X		
Apotex Inc	X			
AstraZeneca Canada Inc	X			
BASF Canada Inc	X			
Bayer Inc	X			
Biogen Canada			X	
Cytokinetics, Inc.			X	
DuPont Canada Inc.	X			
Glaxo Smith Kline Consumer Healthcare Inc.	X			
GlaxoSmithKline	X			
Hoffmann-La Roche Ltd	X			
Impres Inc.	X			
Impres Pharma Inc.	X			
Ingredion Canada Corporation	X			
Innovative Medicines Canada	X			
Ionis Pharmaceuticals Inc			X	

Johnson & Johnson Family of Companies	X			
Johnson & Johnson-Janssen Ortho Inc.	X			
Katz Group Canada Ltd.	X			
Mitsubishi Tanabe Pharma				X
Novartis Nutrition Corporation	X			
Novartis Pharma Canada Inc.		X		
Nuvo Pharmaceuticals Inc.	X			
Pharma Consultants Inc	X			
Procter & Gamble Inc.	X			
S C Johnson & Son Limited	X			
S.C. Johnson And Son Limited	X			
Sanofi-aventis Canada Inc.	X			
Taro Pharmaceuticals	X			
Zygo Rehabtek	X			