



Canada's Drug and
Health Technology Agency

CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

cannabidiol (Epidiolex TSC)

(Jazz Pharmaceuticals Canada, Inc.)

Indication: Seizures associated with Tuberous Sclerosis Complex (TSC).

October 17, 2023

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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Patient Group Input

Name of Drug: Epidiolex

Indication: Seizures caused by TSC

Name of Patient Group: Tuberous Sclerosis Canada Sclérose Tubéreuse

Author of Submission: Cathy Evanochko

About Your Patient Group

Tuberous Sclerosis Canada Sclérose Tubéreuse (TSCST) is a voluntary, non-profit, charitable organization that was established in 1990 to provide awareness and support for individuals living with tuberous sclerosis complex (TSC) and their families.

<https://www.tscanada.ca/>

Information Gathering

Information was gathered from Canadian individuals and caregivers through a member survey done in September 2023. 11 responses were received. The following questions were asked:

- Age of TSC individual. Age of onset of seizures. Age of diagnosis.
- How many seizures does the TSC individual have in a day/week/month or year?
- What treatments have been tried for seizures? How many medications have been tried?
- What are the impacts on quality of life that living with a seizure disorder has?
- If you could choose any positive treatment outcome for the TSC individual, what would it be?

Disease Experience

TSC is a multi-system disease that can affect every major organ - it is the “gift that keeps on giving”. For their entire lives, individuals living with TSC worry about what is going to happen next. Different things appear at different stages of life. Early on, it is seizures, specifically Infantile Spasms. The result of uncontrolled seizures is catastrophic to infants and children. The lack of seizure control and age of onset of seizures can be directly linked to the severity of cognitive delays and physical disabilities. Infantile Spasms are especially devastating to infants. One parent wrote “My daughter’s EEG showed she was having between 500 and 700 seizures a day when she was first diagnosed at 7 months old. There was very little time for her to learn and achieve developmental milestones when seizing so often.” Another caregiver wrote “He is globally delayed, has a learning disability and at 11 years of age, he has a lack of social skills, no independence and no friends. Everything we have tried has not worked to control his seizures, but in the past 2 years, they have reduced to 1 or 2 a week and his development has improved immensely.” A mom writes “He was diagnosed at birth and was having infantile seizures that we did recognize until full blown tonic/clonic seizures started at about 1 and ½ years old. Now he has 4-6 tonic/clonic seizures per day and more complex partials than we can count. He has to be watched all the time since his seizures come with little or no warning and wears a seizure helmet all the time. On bad days, he can’t walk, is very sleepy, difficult to feed and is generally unhappy. I would love to hear him talk again.”

Stopping seizures is extremely important for quality of life and wellness for individuals living with TSC. Seizures associated with TSC are typically hard to control and require constant monitoring and medication changes to try to get a combination that works to control, or at least reduce, the number of seizures. Learning cannot happen when someone is seizing all of the time. Sleep is also difficult for these individuals. “My daughter typically has a seizure when she is just falling asleep or just waking up. So she never has been able to sleep through the night as she is awoken every time by a seizure. The doctor said she instead has micro-sleeps, which are short sleeps of about 15 minutes until a seizure wakes her up. She doesn’t ever get quality sleep time, so is tired, unable to concentrate, and irritable all of the time.”



Experiences With Currently Available Treatments

Seizures caused by TSC are very difficult to manage. Of the 11 responses to the survey, 8 of them have tried more than 4 different seizure medications or treatments, and none have achieved full seizure control.

One mom says "He has had a corpus callosotomy, tried VNS, monthly IVIG treatments and has tried pretty much every anti-seizure medication in various combinations. Nothing works for long." Another mom writes "We have tried Sabril, Valproic Acid, Clobazam, Keppra and Brivlera. Each worked for a short time, but then stopped working. Plus, the side effects are brutal. Especially on Keppra, he was impossible to deal with, he was so irritable! We always have to weigh the benefits of no seizures vs the severity of the side effects. At times, we have had to make the decision to allow some seizures as the medication being tried caused impossible behaviours." It is difficult to afford medications if they are not covered by insurance, or if guardians/individuals don't have insurance coverage "I wanted to try a mTOR inhibitor that is now showing effectiveness for people with TSC, but it is not available in my province and I cannot afford to pay the high prices to use it off-label. It is pretty bad when you have to decide if you can either get the medication your child needs or pay the mortgage. The side-effects sound scary, but I am willing to take the risk if it would just stop the seizures for a while."

Parents/caregivers are required to miss a great deal of time at work to take their individual to appointments and tests. "My daughter has to see the neurologist every 3 months, plus go for an annual MRI and EEG. This is just for neurology, she also has to go to see the Nephrologist, Pulmonary specialist, Cardiologist, and Psychiatrist annually, plus a Dermatologist occasionally too. It is very difficult to manage this while trying to work full time also."

There is currently NO anti-seizure medication that is very effective on seizures associated with TSC. "Even a reduction of the number of seizures would be an improvement!" Some individuals qualify for a brain resection if seizures are localized to a particular area of the brain. This would not be applicable to many individuals with TSC, and even if surgery is considered an option, it may not work. Medication that is effective in stopping or reducing seizures may be the only treatment available.

Improved Outcomes

It is important to note that there are treatments available for seizures associated with TSC. However, the majority of treatments are ineffective, or only work for a short time. The majority of individuals do not qualify for resection surgery, and most other treatments fall short of what we would consider effective. Improved seizure control improves more than developmental milestones, but day-to-day things too - fewer seizures means fewer postictal effects as well. People will have less instances of being tired, confusion, anxiety, headaches, etc.

Improved seizure control is one of the most important factors in determining the quality of life a person with TSC will have over their lifetime. Infantile spasms and uncontrolled seizures in infancy lead to developmental delay and other medical issues. People are affected by seizures before and after the actual seizure occurs, and this can have a huge impact on many of the quality of life indicators - more than health is affected. A person's emotional well-being, ability to access education and employment, and ability to build and maintain social interactions are all impacted by seizures

"My child's entire life is affected by the number of seizures she has. She can't learn if she is having seizures all day long. We will try anything to try reducing her seizures to give her a better chance at developing normally. This is it, the bottom line... we have to stop the seizures."

Experience With Drug Under Review

No one who responded to the survey has experience with Epidiolex. There have not been any clinical trials in Canada so far; however, several families are ready to register once trials come to Canada. One parent stated "I keep reading about how effective this medication has been in the USA. Why can't we get it in Canada? If it works well, we shouldn't have to wait, we need it NOW!" A commonality of TSC is that the seizures are very hard to control. We need to keep identifying possible treatments until we find some that work better than what is available now.



Companion Diagnostic Test

We have no individuals or caregivers who have any experience with this drug, and therefore no experience with this testing..

Anything Else?

It is horrendous to watch your child have seizure after seizure each day. To be a young adult who cannot hold a job as their seizures cannot be controlled. To be a parent who has to make a decision between getting access to medication or paying their mortgage. TSC seizures are very hard to control. That is a fact. When we learn of a treatment that has very good results in another country, why do we, as Canadians, have to do without, or wait until all the studies are repeated? Canada is a first world country, and our patients here deserve to have first world treatments for things like epilepsy associated with TSC. Please don't make the mistake in thinking that there are already treatments and anti-epilepsy drugs available. We keep trying and trying and trying them all, but the majority of time they don't work. Give Canadians the chance to try a treatment that has very good efficacy in stopping or improving seizures.

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.
No
2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.
No
3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
None				

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: Cathy Evanochko

Position: Chair

Patient Group: Tuberous Sclerosis Canada Sclérose Tubéreuse

Date: October 16, 2023



About Your Patient Group

The Canadian Epilepsy Alliance (CEA) is a Canada-wide network of grassroots organizations dedicated to the promotion of independence and quality of life for people with epilepsy and their families, through support services, information, advocacy, and public awareness. www.canadianepilepsyalliance.org

Information Gathering

Information for this submission has been gathered by the President of the Canadian Epilepsy Alliance, drawing on the knowledge and experiences of its 24 member associations, and the lived experiences and firsthand knowledge of: patients, caregivers, clinicians, volunteers, and supporters (donors/funders) through the decades of experience and the work that each of the member associations performs in communities across Canada.

Disease Experience

Current therapies work for nearly 70% of persons with Epilepsy. The remaining 30% try to remain hopeful that someday a medication will be found that will help them. New drugs like Epidiolex bring hope to many who are close to giving up. When epilepsy is not controlled by medications, the impact of the disease on individuals and their families is significant. Individuals with uncontrolled epilepsy can be socially isolated due to stigma due to fear of rejection in social, work, and educational situations. There is a high correlation of mental illness such as depression and anxiety that accompany and initial diagnosis and these can linger when anti-seizure medications do not provide relief.

When someone has epilepsy, the whole family is affected. Everyone's life revolves around the seizures. There is anxiety around when and where the next seizure will occur, and what impact it will have. A husband is afraid his wife might have a seizure and drop the baby; parents are nervous if their child is invited to a birthday party; a teenager is anxious as he watches his father leave for work. Is today the day that something terrible will happen?

Some caregivers are afraid to leave the person with frequent seizures alone, contributing to a loss of independence and the lack of self-esteem we see so often with this patient population. Compassion fatigue in the care giver is always of concern. Many caregivers are sleep deprived as they either try to stay awake all night in case a seizure happens or go to bed and find they are too anxious to sleep.

As well, caregivers often have to live with the sometimes highly unpleasant side effects of various medications that their loved ones are taking. Mood swings, sexual dysfunction, suicidal thoughts, memory loss, problems with concentration, fatigue, exhaustion, depression – all can prove devastating to the person involved, and also to those around them.

Experiences With Currently Available Treatments

No drug works for everyone, and each new drug brought to market offers hope to the 30% of epilepsy sufferers whose seizures are uncontrolled by one or a combination of existing therapies. Even a reduction in the absolute number of seizures that these individuals experience can potentially improve overall quality of life. Seizure freedom may become a reality. Patients without seizure control are always hopeful that a new therapy lies around the corner and without access to safe, approved therapies, some begin to experiment with alternative medicines or practices (cannabis and other unregulated substances). This experimentation can ultimately prove not only detrimental, but also hazardous to the health of those affected.

Improved Outcomes

People with intractable epilepsy are very often unemployed or under-employed because of the frequency of their seizures. They usually live on very restricted incomes, and because they are not working, or are only working parttime, the majority is without access to employer-funded insurance plans. If new medications are not placed on the Provincial formulary, the majority of those with intractable epilepsy, the ones who need them the most, will never be given the opportunity to find out if this new drug will work for them.

Experience With Drug Under Review

These are questions we cannot answer at this time. We support the concept of a new drug that, through the results of trials, offers hope - that in itself offers improvement in an individual's overall outlook, health and well-being.

Companion Diagnostic Test

The Canadian Epilepsy Alliance does not have sufficient data to comment on this at this time.



Anything Else?

No.

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Name: Laura Dickson

Position: President

Patient Group: Canadian Epilepsy Alliance

September 29, 2023

Clinician Group Input

No clinician group input was received by CADTH for this review.