

Stakeholder Input

Stakeholder Input - Patient Input

Name of Drug: Everolimus

Indication: Renal angiomyolipoma associated with tuberous sclerosis

Name of Patient Group: TSC Canada

Author of Submission: Dr. Jennifer Flinn

1. About Your Patient Group

TS Canada ST is a voluntary, non-profit, charitable organization dedicated to the principles of raising public awareness of tuberous sclerosis complex, encouraging mutual support between individuals with TSC and their families, and promoting research and education. Our organization is solely voluntary, and our Board of Directors has members who have Tuberous Sclerosis or are caregivers of people who have Tuberous Sclerosis. We are a cross Canada organization.

<https://www.tscanada.ca>

2. Information Gathering

The data informing this submission has been gathered from a variety of sources, over time. Individual patient experiences, survey results, families who have reached out to our organization to seek help in accessing Everolimus, and the experiences of the members of the board of Tuberous Sclerosis Canada. This information has been gathered over the last ten years, and represents a wide variety of opinions, input and the lived experience of individuals affected and their caregivers from across Canada.

3. Disease Experience

Living with Tuberous Sclerosis Complex affects every aspect of the patient and caregiver's life. It is a complex, multi organ genetic disease with a variety of challenging symptoms to manage. There are medical, behavioural and psycho-social implications of living with Tuberous Sclerosis. TSC causes the growth of tumours in many different organs, primarily in the brain, eyes, heart, kidney, skin and lungs. In the kidneys, most people with TSC develop some form of kidney disease over their lifetime. Most will develop angiomyolipoma (AMLs), usually in both kidneys. These must be monitored for growth, as large AMLs are at risk of hemorrhage, the leading cause of mortality among patients who have TSC. People with TSC can also develop renal cysts and sometimes kidney cancers. Women are at risk of

developing a lung disease called LAM. In the brain, multiple issues directly impact quality of life. Most patients with TSC have epilepsy, often refractory. Lesions in the brain can also grow, causing life threatening blockages of cerebral spinal fluid. Developmental disability, intellectual disability and autism are all common for people with TSC. 'TSC Associated Neuropsychiatric Disorders' or 'TAND' issues are well reported to have a direct and negative impact on the patient and caregiver's quality of life (see International consensus recommendations for the identification and treatment of tuberous sclerosis complex-associated neuropsychiatric disorders (TAND) <https://jneurodevdisorders.biomedcentral.com/articles/10.1186/s11689-023-09500-1>).

The incidence and severity of the various aspects of TSC can vary widely between individuals.

It is essential for patients and caregivers to be able to access proper medical treatment and management of medical issues in TSC. Many families report challenges with accessing appropriate monitoring and treatment for the various manifestations. This takes an enormous toll on the quality of life of both patients and caregivers, as a lot of time and effort must be put into advocating, researching and searching for appropriate treatments. This is a well recognized issue around the world, including locally in all areas of Canada (see [https://www.pedneur.com/article/S0887-8994\(21\)00152-1/fulltext](https://www.pedneur.com/article/S0887-8994(21)00152-1/fulltext)).

Beyond the medical aspects, patients and families struggle continually with the TAND aspects of the disease. Most families report they cannot access appropriate support and treatment for the behavioural, developmental and psycho-social impacts of TSC for themselves or their family member. Dealing with the day to day management of the manifestations of the disease is extremely taxing on individuals and family members.

The medical aspects are very important to have under control with proper surveillance and treatment. Everolimus treats the genetic pathway of the disease. So it treats the whole individual with proven results. Renal manifestations, particularly angioliipomas, cause very serious, sometimes life threatening complications for individuals, so it is essential to have access to appropriate treatment. The International Treatment Guidelines recommend Everolimus as the first line of treatment for these lesions, and families need access to this medication (See **Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations** ([https://www.pedneur.com/article/S0887-8994\(21\)00151-X/fulltext](https://www.pedneur.com/article/S0887-8994(21)00151-X/fulltext))).

4. Experiences With Currently Available Treatments

The alternative therapies to Everolimus are very invasive and do not address the underlying cause and continued development of AMLs throughout the lifetime. One treatment is surgical removal of an AML. In this treatment, the AML is surgically removed, but normal, functional kidney issue also ends up being lost. There is risk of the kidney being damaged in the surgical process. The procedure is extremely invasive, painful, and difficult to undergo for patients, especially those with developmental and intellectual disabilities who struggle with changes in routine such as hospital stays. The procedure

itself removes the AML, but patients with TSC are likely to continually develop AMLs in their kidneys overtime, bilaterally, and so the removal of one or multiple AMLs does not prevent future AMLs from developing. With the high likelihood of developing kidney disease in this population, any procedure that negatively impacts kidney function and volume should be avoided. Another treatment sometimes employed for AML treatment is embolization. This procedure is very painful, and again only targets one AML at a time. It does nothing to prevent future AMLs from developing. The procedure is very invasive, and can also result in healthy kidney tissue being damaged. It is very challenging for patients who have intellectual disabilities to undergo invasive painful medical procedures. Both surgery for removal of an AML and embolization to treat an AML cause lost time at work for the patient if they are capable of working, and for the caregiver. There is an extra burden of travel to a center that is capable of performing a procedure such as this for families that do not live in proximity to a major hospital in Canada. These treatment options are not well tolerated and are not effective in managing the natural progression of Tuberous Sclerosis Complex. Surgeries and embolization are not in any way effective. Kidney embolization or removal of AMLs do not stop the continuation of the overgrowth of AMLs. In other words, surgery does not work.

5. Improved Outcomes

The outcomes that are important for patients are treatment of AMLs that is noninvasive, easy to access and easy to take. Prevention of future development of AMLs in the kidneys, positive impacts on epilepsy and the TAND issues in TSC are important outcomes for patients and caregivers. Patients and caregivers want access to treatments that are easy to take, are non-invasive, preserve healthy kidney tissue and decrease the risks of AMLs hemorrhaging. Treatment with Everolimus for AMLs has a direct positive impact on the lives of patients and caregivers. It is non-invasive, simple to take, and it positively impacts many aspects of the disease. Importantly, taking Everolimus decreases the size of current AMLs and also prevents or slows the development of new AMLs. Patients consider their doctors and medical professional's opinions when deciding on therapies. Often patients and caregivers have a difficult time accessing medical professionals who have expertise in TSC specifically, and this can be a barrier to appropriate treatment. Patients and caregivers want access to medical treatment that is in line with the peer reviewed international treatment guidelines for TSC, which includes Everolimus as a first line treatment for AMLs of the kidneys (see [https://www.pedneur.com/article/S0887-8994\(21\)00151-X/fulltext](https://www.pedneur.com/article/S0887-8994(21)00151-X/fulltext)). They also consider whether a therapy is covered by insurance, both public and private. Provincial drug plans as well as private drug companies make decisions about drug coverage based on CADTH's recommendations. Many families have had difficulty accessing Everolimus because of CADTH not recommending this treatment.

6. Experience With Drug Under Review

Patients and caregivers have accessed Everolimus treatment through compassionate access programs, some provincial publicly funded plans and through some private insurance companies. Many families

have struggled to access this drug because of previous rulings from CADTH. Some private insurance companies deny access based on CADTH's ruling. Some provincial plans do not fund access to this drug because of CADTH's recommendation. Many families have struggled to gain access to this drug because of a lack of medical expertise in this area. It is difficult for patients and caregivers to find medical professionals who have enough knowledge and expertise in the treatment and management of TSC. This is particularly true for families in remote and rural areas who may only have access to generalist medical practitioners. A positive ruling supporting Everolimus as a first line treatment from CADTH will help improve access to this life saving treatment by improving access through provincial and private insurance as well as helping encourage medical experts to prescribe this medication as the recommended treatment for AMLs in this population.

Treatment with Everolimus has dramatically decreased the size of AMLs in patients. It has prevented the need for invasive surgeries, and procedures such as embolization. It improved quality of life by improving kidney outcome. There was no recovery time as there would be with surgical intervention. Patients' quality of life was improved by not having to endure a hospital stay. This is challenging for patients and caregivers, especially in cases where there are developmental and intellectual disabilities. Hospital stays can be frightening and take a toll on all involved. For families who do not live in close proximity to a medical facility that can perform surgical interventions, an additional burden is created by having to travel to access treatment. Patients who are able to live and work independently must take time off from work for treatment and difficult recovery from surgical interventions. Treatment with Everolimus can be done remotely, does not require hospital stays or painful procedures. There is no recovery time, no lost work time, no interruption to the activities of daily living for patients or caregivers. The treatment with Everolimus is very easy to take, is well tolerated and improves quality of life dramatically compared to traditional treatments involving surgical intervention. The challenge patients and families have is in accessing treatments such as Everolimus. CADTH's ruling on medication can act as a gatekeeper in accessing medication, both in terms of publicly funded drug plans as well as private health insurance plans who often make decisions based on CADTH's ruling on a particular medication.

Patients and caregivers want treatment that is easy to take, easy to tolerate, does not involve painful procedures, preserves healthy kidney tissue and prevents further complications to the kidney from development of future AMLs. They want this treatment to be readily available and funded under both public and private insurance companies. They want medical professionals who are familiar with this treatment as the first line of defense for treatment of AMLs as per the international guidelines.

7. Companion Diagnostic Test

8. Anything Else?

We would just like to reiterate the alternative treatment options of surgery or embolization are not cost effective or effective in treating the disease. Everolimus treats the genetic pathway of the disease, treating the whole individual with proven results. Surgeries and embolization are not in any way effective. Kidney embolization or removal of AMLs do not stop the continuation of the overgrowth of AMLs. Patients and caregivers want access to Everolimus as a well-tolerated, safe and effective treatment for renal Angiolipomas.

1 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.

2 Table 12: 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
<Enter Name Here>				

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: Jennifer Flinn

Position: Board of Directors

Patient Group: Tuberous Sclerosis Canada

Date: September 23, 2023