



## Common Drug Review *Patient Group Input Submissions*

**everolimus (Afinitor)** for subependymal giant cell astrocytoma associated with tuberous sclerosis complex.

**Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.**

Tuberous Sclerosis Canada Sclérose Tubéreuse (TSCST) — permission granted to post.

**CADTH received patient group input for this review on or before September 19, 2014.**

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

## Tuberous Sclerosis Canada Sclérose Tubéreuse (TSCST)

### Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Everolimus (Afinitor), Subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC)
Name of the patient group	Tuberous Sclerosis Canada Sclérose Tubéreuse (TSCST)
Name of the primary contact for this submission:	██████████
Position or title with patient group	██████
Email	████████████████████
Telephone number(s)	██████████
Name of author (if different)	
Patient group's contact information: Email	<a href="mailto:TSCanadaST@gmail.com">TSCanadaST@gmail.com</a>
Telephone	1-888-223-2410
Address	92 Caplan Ave. Suite 125 Barrie, ONT, L9N-0Z7
Website	<a href="http://tscanada.ca">tscanada.ca</a>
Permission is granted to post this submission	Yes

#### 1.1 Submitting Organization

Tuberous Sclerosis Canada Sclérose Tubéreuse (TSCST) is a voluntary non-profit charitable organization dedicated to the principles of raising public awareness of tuberous sclerosis complex, encouraging mutual support between families with affected members and promoting research and education.

#### 1.2 Conflict of Interest Declarations

a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*

For the 2013/14 financial year, TS Canada ST received financial contributions from Novartis Pharmaceuticals Canada Inc. These contributions accounted for less than 20 percent of the organization's gross revenue in 2013/14. Contributions were used independently without any direction from Novartis and used mainly for patient and family support activities.

b) *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

n/a

## Section 2 — Condition and Current Therapy Information

### 2.1 Information Gathering

Several approaches were used to collect information on the experiences of patients with SEGA associated with TSC and their families. They included an on-line survey, telephone interviews, one-on-one conversations, analyses of messages posted on Facebook and Twitter, and unsolicited letters sent to TSCST. In total, they represented the views of 51 individuals, one third who are patients and two thirds who are caregivers.

### 2.2 Impact of Condition on Patients

Patients with TSC experience abnormal tissue growths in multiple organ systems including the brain, heart, skin, eyes, kidneys, and lungs. Each individual is affected differently; they could have one or all possible manifestations of the disease.

*“TSC affects my brain, skin, teeth, eyes, kidneys, spine and other internal organs - I have tumours everywhere.”*

These growths may develop quickly or slowly, and cause severe anxiety for patients and families. Also, as the growths become larger, symptoms worsen. They are often painful.

*“Our son suffers from bouts of depression, extreme anxieties and he also has frustration and anger issues at times.”*

Tumours in the brain (SEGA) are associated with severe headaches, epilepsy, hydrocephalous, intellectual disabilities, and behavioral issues. Some patients experience multiple seizures per day, affecting their ability to go to school or work or participate in recreational activities. In general, unexpected emergencies and the uncertainty of when a critical incident may occur are key stressors for both patients and families.

*“Our daughter has had seizures all her life (she is 7 now) and brain surgery at age 2 to try and get rid of the seizures. She has been on multiple drugs throughout her 7 years...it has been very hard on our family – it affects us all.”*

*“I had a large brain tumour removed as a child and since have been on high dosages of anti-seizure drugs to control and prevent seizures from occurring.”*

*“Her seizures have never been controlled in spite of multiple antiepileptic drugs, epilepsy surgery (right temporal lobe resection) and having the Vagus Nerve Stimulator. Her seizure injuries include a broken nose, broken elbow, broken fingers, ripped pinky toe, broken leg, broken tibia/fibula with surgical repair, broken front teeth, plus many, many, many sutures.”*

Growths in the kidneys often become so large that they cause extreme pain, shut down renal function and are subject to spontaneous bleeds, so that a kidney transplant is required.

*“I had multiple bleeding because of an enormous angioliopoma on my left kidney which almost killed me.”*

When growths are removed surgically from the brain or an organ, such as the lungs, they often reappear in the remaining tissue, leading to further surgeries. Multiple surgeries are often required for each of the affected organs. Each individual affected by TSC may have surgeries on many of their organs, many times over.

*"I had lung surgery in 2004 and 2006 and a double lung transplant in November 2011."*

The burden this disease places on patients and families becomes even greater as it progresses and symptoms worsen.

*"I had to find a new career and educational path."*

*"I could not get a job because my seizures could not be controlled."*

*"I had to change careers."*

*"I had to quit martial arts and weight lifting immediately."*

*"My son was born with a large SEGA that was blocking one of the ventricles. Any surgery on a fragile newborn baby is terrifying, especially in their brain where the surgery could cause huge problems."*

Some patients feel they can never have children because they "would not want to pass this condition onto their children". Therefore, this disease makes it very difficult for patients and families to lead normal lives.

### **2.3 Patients' Experiences With Current Therapy**

Currently, patients with SEGAs have limited options. There are no alternative disease-modifying medicines. When patients become acutely symptomatic, surgical resection of the tumours may be possible if they are in operable locations. However, the tumours often grow back again. Many of the tumours in the brain are inoperable. Multiple brain surgeries are often required, each of which can result in permanent cognitive disabilities, damage to motor skills, changes in personality, and other behavioral issues.

*"Surgery is not always possible for SEGAs, and even when it is, the resulting consequences, such as pneumothorax, increased seizures and associated trauma, are extremely invasive, injurious, and potentially life-threatening."*

*"A shunt was inserted to relieve the pressure in his brain because the SEGA that was blocking the flow of cerebral fluid was in an inoperable position."*

*"The brain surgeries were only effective until the tumours grew back."*

*"He was facing a third brain surgery."*

*"Surgical treatments for epilepsy and SEGAs have limited success because the tumours return."*

*"[Surgeries] are very invasive and not necessarily effective."*

No all medical centres perform these surgeries, so travel is often needed.

*“My son had to have surgery at the age of 3 in New York City as they were not offering the surgery in Canada.”*

*“Travelling with my adult child who was TSC is extremely difficult when she needed brain surgery. Because of the changes in her normal routines, her anxiety and behaviour issues escalated and she became impossible to manage.”*

Recovery is also difficult.

*“[They] can cause a great deal of recovery time that most people cannot afford.”*

Most patients are on anti-epileptic drugs to control their seizures, one of the main symptoms of the disease. For a very few, these drugs have been very effective.

*“Without them, my daughter would be dead from the seizures.”*

However, most have experienced limited effectiveness.

*“Actually, they increased seizure activity and behavioural problems.”*

*“Anti-epileptic drugs have been helpful, however difficult to find what drugs work well, plenty of trial and error and repetitious trips to far away neurologists.”*

*“My daughter has tried every kind of seizure medication there is – nothing works.”*

Almost all patients experience side-effects to the anti-epileptic drugs. Over one third, feel those side-effects are severe or very severe. Surgery is also used to treat tumours in other organs, but with limited benefit.

*“Laser surgery for the angiofibromas was helpful and stopped the bleeding for a time [about two years] but the angiofibromas grew back.”*

*“My daughter had multiple surgeries on her kidneys, but the tumours just keep growing back.”*

### **2.4 Impact on Caregivers**

The diagnosis of TSC affects the entire family.

*“My wife gave up her profession...”*

*“We keep missing work to take our child to appointments.”*

*“TSC changed the course of life for every member of our family. All of the attention is given to the child with TSC.”*

*“Siblings have had to give up so much because of our special needs child.”*

*“Constant visits to the emergency room...”*

*“Constant stress and strain on relationships and family life dealing with TSC and the many medical, behavioural and developmental challenges it brings.”*

Because of the susceptibility to seizures and uncertain tumour growth, the disease is also unpredictable. This unpredictability is a significant source of stress for families.

*“It is like a roller coaster or walking the desert not knowing when landmines could go off.”*

*“There is always something to be on the watch for, you never know what is coming next.”*

*“As parents, we are on guard and on call 24 hours a day, seven days a week.”*

*“We were informed that G’s SEGA had grown since his last MRI the year before and should he show signs of headache or unexplainable vomiting to rush him to the hospital. We are always on high alert.”*

## **Section 3 — Information about the Drug Being Reviewed**

### **3.1 Information Gathering**

The following information was collected through an on-line survey, telephone interviews, one-on-one conversations, analyses of messages posted on Facebook and Twitter, and unsolicited letters sent to TSCST. In total, they represented the views of 51 individuals, one third of whom were patients. The remaining two thirds were caregivers.

### **3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?**

#### *a) Expectations for Afinitor*

Expectations of patients and families centre on stabilization or reduction in the size and number of growths, reducing the number of surgeries required, increasing quality of life, and sparing organ function.

*“We are hoping it will decrease the size of the tumours so he doesn’t need any more brain surgery.”*

*“We are hoping it will help save her from losing the one kidney that she has left.”*

*“I don’t expect Afinitor to be a panacea for TSC, but it could have amazing treatment possibilities. For instance, it could prevent further brain surgeries, kidney transplants, reduce kidney embolization, reduce facial angiofibromas, perhaps increase cognitive function, improve mood, reduce seizures, and increase quality of life.”*

*“...making surgeries less necessary and perhaps less psychological and psychiatric involvement in TSC affected individuals.”*

*“It is a critical alternative to invasive and possibly life-threatening surgeries”*

*“...reduce the need for other medications”*

*“Shrinkage of tumours and improved quality of life.”*

*“My expectations are that Afinitor will shrink tumours hopefully to the point of atrophy. For very large tumours, it could be beneficial to shrink them enough to make surgery safer.”*

*“Surgery may be avoided and organ function can be preserved.”*

*“Reduce more invasive surgical options.”*

*“More available to people in remote areas - you can ship pills but not surgical sites. Reduce need for other medications. “*

Patients are hoping for treatment alternatives that prevent tumour progression, treat all aspects of this multi-organ disease, and are less invasive.

*“Surgery on the SEGA did not treat the tumours she has in her kidneys, liver, pancreas, lungs, face, and other parts of her brain...”*

*b) Patients’ Experience with Afinitor*

The impact of Afinitor was described as overwhelmingly positive by those with Afinitor experience. The following is based on the experiences of 16 patients who have been treated with Afinitor.

*“In my sister it has shrunk the AMLs, stopped the SEGA from getting any bigger, halted the progression of LAM, reduced seizures, reduced the presence of facial angiofibromas, and increased cognitive functioning. It is amazing!”*

*“Afinitor was prescribed to shrink the tumour so that my infant son could grow bigger, and the surgery wouldn’t be as risky. After four months, the tumour has shrunk so much, he doesn’t require surgery any longer!”*

*“He has only 3 seizures a day now, shrinking SEGA in his brain, plus only small cysts in his kidneys.”*

*“Afinitor has slowed the progression of the disease in my granddaughter and it is giving her a better quality of life.”*

*“For my son, it has eliminated his seizures and reduced all of his tumours, most notably the SEGAs.”*

*“Seen shrinkage in tumours, lessened the amount of seizures...”*

*“He has been taking everolimus [Afinitor] for the past 3 years with huge success. He has the potential for long term health now. He didn’t before, now the brain tumour is incidental, not life threatening. This drug has changed my son’s life.”*

*“Three years ago we were told he needed brain surgery for hydrocephalus and that it would leave him with deficits...his life would have meant memory problems, tumour regrowth, deficits, but the drug eliminated all of that. We were one month away from surgery for the SEGA but the tumour has shrunk! More than expected actually...it’s over 50% shrinkage...this was enough to avoid surgery.”*

**What difference does the drug make to patients long term health and wellbeing?**

There is no other drug therapy for TSC. Afinitor has the ability to significantly enhance and maintain long term health and well-being for individuals with TSC, and reduce the anxiety and stress on the whole family. The reduction in tumour size may subsequently reduce multiple symptoms associated with organ damage and numerous surgeries.

*“Without this medication, he’d be at hospital all the time. He’d be under constant doctor’s care. He’d miss school. He would worry. The family would worry. It would be devastating, horrible. On the drug, he has avoided all of that. He only misses school for check-ups that tell us he is doing great. These are not the check-ups we used to have where they only told us it was getting bigger. Now, for three years the tumour has done nothing but shrink.”*

**What are the side effects of the drug which ones are patients prepared to put up with and which ones do they find unacceptable?**

Few side effects were reported. Some patients experienced mouth sores that were manageable.

*“My sister prevented these by taking her Afinitor with cool whip.”*

**How does the drug compared with other available treatments in terms of efficacy, side effects and other practical implications (e.g. administration, time, costs)?**

There are no other treatments. All other medical interventions are invasive procedures, usually in response to critical incidents.

Three quarters of patients experienced “much” improved appearance of skin cysts. 60% experienced “much” improved cognitive functioning. Half experienced “much” improved kidney functioning, seizure episodes, and behavior. About one third experienced “much” improved lung functioning.

*“If it helps keep tumours from growing it will reduce the surgeries and help decrease the effect in tumours have on people.”*

*“So far it’s the best option for treating the whole disease, and improving the quality of life for a person with TSC.”*

*“If this medication can improve a patients’ everyday life, it is an important medication for them.”*

*“It will improve so many medical issues in TSC with the use of just one drug.”*

*“This is the first treatment that addresses the disease at the cellular level - where the disease originates.”*



*“It is the first treatment that may provide some stability to the patient's condition and allow them to manage the disease in the long term.”*

*“This drug has the ability to change lives for the better. There was nothing worse for us, then knowing there was a treatment for my son that I was unable to obtain for him. It broke my heart to know that he would need another brain surgery.”*