



## TUBEROUS SCLEROSIS COMPLEX FACT SHEET

### WHAT IS TUBEROUS SCLEROSIS COMPLEX?

- Tuberous Sclerosis Complex (TSC) is a rare genetic disorder that causes benign tumors in many different organ systems, including the brain, kidneys, heart, eyes, lungs and skin<sup>1</sup>.
- Although the majority of tumors resulting from TSC are benign, they may lead to severe complications or death<sup>1</sup>.
- A wide variety of symptoms occur in people with TSC, including seizures, developmental delay, behavioral problems, autism, skin abnormalities, and kidney disease<sup>1</sup>.
- TSC can lead to lifelong impairment and have an impact on quality of life for both those living with it and their caregivers<sup>1</sup>.

### INCIDENCE AND PREVALENCE<sup>1</sup>

- Approximately one to two million people worldwide are affected by Tuberous Sclerosis Complex<sup>1</sup>.
- TSC affects an estimated one in 6,000 newborns, though many cases are undiagnosed in infants due to mild forms of initial symptoms<sup>1</sup>.

### WHAT CAUSES TUBEROUS SCLEROSIS COMPLEX?

- Tuberous Sclerosis Complex is caused by defects in the *TSC1* and *TSC2* genes<sup>2</sup>. In a normal state, these genes inhibit the activity of the mTOR protein, which regulates many activities, including cell growth. When either of these genes is mutated, this leads to increased activity of the mTOR protein, resulting in uncontrolled cell growth, and the formation of benign tumors throughout the body<sup>3,4</sup>.
- Up to 70 per cent of cases are the result of a random mutation, but TSC can be inherited from either parent with the condition<sup>5</sup>.
- Individuals affected by TSC have a 50 per cent chance of passing the genetic disease to their children<sup>6</sup>.

## WHAT ARE THE SYMPTOMS?

- Signs and symptoms may vary, depending on which organs are involved.
- Some symptoms may include, but are not limited to:
  - Benign tumor growth
  - Skin abnormalities
  - Seizures
  - Mental disabilities
  - Autism
  - Behavioral problems<sup>1,8</sup>
- Epileptic seizures are the most common neurological symptom of Tuberous Sclerosis Complex, affecting up to 90 per cent of patients, and starting as early as in infancy<sup>1,6,7,10</sup>
- Approximately one-half to two-thirds of individuals with TSC have mental disabilities, which can range from mild learning disabilities to severe<sup>1</sup>

## HOW IS TUBEROUS SCLEROSIS COMPLEX DIAGNOSED?

- Since Tuberous Sclerosis Complex affects many different organs, no single feature of TSC is diagnostic - all clinical features must be included in order to make a diagnosis
- Modern and complete diagnosis includes:
  - Detailed skin examinations
  - Brain imaging
  - Neurological examination
  - Ultrasound
  - Ophthalmological tests
  - Genetic counseling<sup>6</sup>
- Because symptoms vary from patient to patient and can take years to develop, many children are not diagnosed until later in life, often with the onset of seizures, skin lesions or other significant symptoms, such as developmental delays<sup>1</sup>.

## COMMON MANIFESTATIONS OF TUBEROUS SCLEROSIS COMPLEX

- Neurological Manifestations
  - Neurological manifestations is the most frequent cause of disease-related disability in patients with Tuberous Sclerosis Complex<sup>2</sup>
  - Seizures occur because of sudden, abnormal electrical activity in the brain and are present in up to 90 per cent of people with TSC<sup>8</sup>.
  - Mental disabilities experienced by people with TSC range from mild to severe learning disabilities and autism<sup>1,8</sup>.
  - One-half to two-thirds of people with TSC experience mental disabilities<sup>1</sup>.
- Common brain findings
  - Subependymal nodules (SENs) – detected in early childhood, and may start to grow and turn into a SEGA<sup>13</sup>
  - Cortical tubers – whose presence may be linked to the presence of epilepsy<sup>13</sup>
  - Subependymal giant cell astrocytoma (SEGA)
    - A type of benign brain tumor that primarily affects children and adolescents<sup>1,8,9</sup>
    - Occurs in up to 10 per cent of individuals with TSC<sup>10,11</sup>
    - SEGAs arise in the ventricles of the brain and may pose a significant medical risk, including potential for swelling in the brain, or hydrocephalus<sup>1,8,12</sup>

- Other common manifestations:
  - Facial angiofibroma
    - Reddish raised lesions usually seen on the face, which can be disfiguring, prompting laser treatment<sup>1</sup>.
    - One of the most common types of skin lesions, which affect virtually all Tuberous Sclerosis Complex patients<sup>1,7,13</sup>
  - Renal angiomyolipoma
    - Benign renal tumors composed of abnormal blood vessels, smooth muscle and fat<sup>6</sup>.
    - Present in 55 to 75 per cent of patients with TSC; it is the most common kidney lesion seen in individuals with TSC<sup>1,8</sup>
    - Prevalence of these tumors increase as patients age<sup>14</sup>.
    - May cause pain, kidney failure or severe bleeding, which may result in anemia or a life-threatening drop in blood pressure<sup>1</sup>.
  - Cardiac Rhabdomyoma
    - Lesions that form in the heart<sup>1</sup>.
    - Occurs in two thirds of newborns with TSC<sup>15</sup>.
    - May cause heart valve dysfunction or arrhythmias<sup>7</sup>.
  - Lymphangioleio-myomatosis (LAM)
    - A rare lung disease characterized by abnormal, muscle-like cell build-up in the lungs, lymph nodes and kidneys<sup>15</sup>.
    - Can cause “collapsed lung” with symptoms of pain and persistent shortness of breath<sup>17</sup>.

## HOW IS TUBEROUS SCLEROSIS COMPLEX TREATED?

- Although the prognosis for many people living with Tuberous Sclerosis Complex is generally good, careful monitoring of all organ systems and development is critical. Ultrasound in utero can detect heart tumours, assisting with early diagnosis and prompt monitoring in order to prevent complications related to TSC<sup>16</sup>.
- Treatment for people with TSC includes the management of seizures, special education for those who need it, and surgery, including plastic surgery.
- The first medication for the treatment of SEGAs has recently been approved in Canada: Afinitor\* (everolimus) tablets are indicated for the treatment of patients three years of age and older with SEGAs associated with TSC for whom surgery is not a suitable option<sup>17</sup>.
- Tuberous Sclerosis Complex research is progressing rapidly, giving hope to affected families for more effective treatments. Clinical trials of tumour-suppressing drugs continue to produce very encouraging results, with potential implications for treatment of multiple organ systems, and hopefully even of some of the seizures and developmental delays caused by the disorder<sup>16</sup>.



## REFERENCE

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