



Tuberous Sclerosis Alliance

COVID-19 Considerations for TSC Medical Professionals

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Disclaimer: *This content was created for medical professionals and for the purposes of sharing current state of the knowledge about COVID-19 and the complications of tuberous sclerosis complex (TSC). The content is not intended to be a substitute for clinical decision making on an individual basis. Direct knowledge of the patient and his or her specific medical and social history takes precedence over the general considerations listed below.*

Tuberous sclerosis complex (TSC) is a multisystem disease with most significant disease morbidity and mortality resulting from lung, brain, and kidney involvement. mTOR inhibitors (e.g., sirolimus or everolimus) are now offered for treatment of lymphangioleiomyomatosis (LAM), subependymal giant cell astrocytoma (SEGA), renal angiomyolipoma (sometimes referred to as AML), and medically intractable epilepsy. mTOR inhibitors as a class of drugs have immunosuppressant properties and thus, may alter ability to fight infections.

There is widespread media coverage about coronavirus infection (COVID-19). Many TSC individuals are anxious, frightened, and concerned about the impact of COVID-19 on their health, especially in view of the many challenges presented by TSC. Frequent questions the Tuberous Sclerosis Alliance (TS Alliance) and a number of practitioners have heard thus far include: what to do to prevent COVID-19 infection, am I at particular risk for infection, should I continue current medications such as sirolimus or everolimus when they are known to weaken my immune system, and what happens if I become ill or am diagnosed with COVID-19?

This [COVID-19 FAQ Guide](#) on TS Alliance website contains useful information for TSC patients, including recommendations to check with TSC physicians for additional guidance. Because current data do not provide clear answers for many TSC patients' questions, drawing on opinions from key leaders in TSC clinical care, the TS Alliance's Science and Medical Committee offers some general considerations for how to answer questions from TSC patients about COVID-19 and how to provide individualized care for TSC patients during the COVID-19 pandemic based on the information available to date.

1) Are TSC patients at particular risk?

Having TSC does not make anyone more likely than anyone else to catch COVID-19, and TSC or TSC-LAM patients are not necessarily at greater risk of developing severe respiratory symptoms.

However, TSC patients who fall into one of the following “at risk” groups (sometimes called “higher risk” or “vulnerable” groups) should try to avoid COVID-19 infection if possible because symptoms might be more severe if you do get sick:

- If the patient is taking everolimus or sirolimus tablets or liquid.
- If the patient has lymphangioleiomyomatosis (LAM) or reduced lung function.
- If the patient has ongoing seizures or refractory epilepsy.

2) Are LAM patients at particular risk for infection with COVID-19?

If the patient has TSC-LAM or reduced lung capacity, then the patient may be at greater risk of developing severe symptoms if the patient becomes ill with COVID-19. While having LAM doesn't put the patient at a higher risk for catching COVID-19, it is likely that COVID-19 poses greater risk to patients with significant underlying lung disease (like LAM) and/or those who are taking immunosuppressive medications, such as mTOR inhibitors. Although there are currently no disease-specific data, members of The LAM Foundation Scientific Board, including Frank McCormack MD, an expert in LAM and TSC, have developed tiered guidance recommendations that are stratified based on LAM disease severity (see below).

Please keep in mind that the risk profile for individual patients may vary depending upon a number of other factors such as underlying health conditions, overall health status, and significant impairment in lung diffusion capacity. Dialog between you and your patients should take these recommendations into consideration, but you should exercise judgment rather than rely solely on these categories. All LAM patients should pay close attention to the prevalence of COVID-19 in their local communities. In case of local spread, LAM patients in the moderate risk category are advised to adopt the same precautions as the high-risk category. We will closely monitor the outbreak and update this document as needed.

Disease Category	Definition (any one of the listed criteria under the category)	Risk category	Recommendation
Mild	Lung function (FEV1) >70% and not on sirolimus	Low	Same as CDC general population recommendations
Moderate	1. Lung function (FEV1) >70% on sirolimus 2. Lung function (FEV1) between 50-70%, on sirolimus or not	Moderate	Follow CDC general population recommendations unless widespread COVID-19 is in your community, in which case you should follow CDC recommendations for underlying conditions
Severe	1. Lung function (FEV1) <50%	High	Same as CDC recommendations for elderly and those with underlying conditions

	2. Patients requiring supplemental oxygen regardless of lung function 3. Patients undergoing transplant evaluation 4. Post-transplant patients		
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You may find the following information published for people with lung conditions helpful:

- www.thoracic.org/patients/patient-resources/resources/coronavirus-patient.pdf
- www.cdc.gov/coronavirus/2019-ncov/index.html

3) Should patients travel to their doctor's offices for visits if they have TSC or LAM?

TSC and TSC-LAM patients who are doing well may want to postpone or remotely conduct routine clinic and clinical trial visits until the COVID-19 outbreak passes. Preparation of a Skype or Zoom infrastructure for TSC and/or LAM patients may be prudent.

4) Should mTOR inhibitors be stopped in TSC-LAM patients as a plan to prevent or diminish likelihood or severity of COVID-19 infection?

At this time, there are no strict guidelines about whether to empirically discontinue mTOR inhibitors in TSC patients and especially in TSC-LAM patients to prevent or diminish the likelihood of infection. Current advice may change from week to week depending on the Government's assessment of the risk to the US population from the virus (this is assessed as low, moderate, or severe), how many people in the general population have already caught the virus, and how the virus is affecting people (which may change over time).

It is currently not known whether taking an mTOR inhibitor increases the risk of complications from COVID-19. TSC-LAM experts believe that the question about stopping mTOR inhibitor is very different for LAM versus almost all other TSC manifestations. With LAM, patients lose lung function when mTOR inhibitors are stopped, and that lost function might not be re-gained even if the mTOR inhibitor is re-started. Given the potential for lung function decline when mTOR inhibitors are discontinued, we recommend that LAM patients do not stop taking mTOR inhibitors as a precautionary measure during the outbreak. Certain circumstances, such as active infection with COVID-19 may necessitate a dose reduction or interruption in mTOR inhibitor use. In such circumstances, the decision to change dosing or holding mTOR inhibitor should be made on an individual basis closely considering the risk:benefit ratio and patient safety.

LAM patients with a significant burden of disease (pulmonary symptoms, any abnormal lung function tests, desaturation on six-minute walk test, or more than a minimal profusion of cysts on

CT) should continue mTOR inhibitors. You may wish to discuss these options with patients and assess the risk-benefit of continuing mTOR inhibitors if there are other underlying co-morbidities including diabetes, heart disease, hypertension, cancer, and rheumatological disorders.

5) Should mTOR inhibitors be stopped empirically in patients with renal angiomyolipomas (sometimes referred to as AMLs) as a plan to prevent or diminish likelihood or severity of COVID-19 infection?

At this time, there are no strict guidelines about whether to empirically discontinue mTOR inhibitors in TSC patients with renal angiomyolipomas. Based on current CDC statements and how recent influenza outbreaks like the H1N1 in 2009 were managed, it is recommended that patients remain on mTOR inhibitors unless they or an immediate family member or a close contact, e.g., schoolmate or work colleague, are diagnosed with COVID-19. You may wish to discuss these options with patients and assess the risk-benefits continuing mTOR inhibitors if there are other underlying co-morbidities including diabetes, heart disease, hypertension, cancer, and rheumatological disorders.

If patients are taking mTOR inhibitors for kidney angiomyolipoma, then there may be less risk of rapid disease progression associated with a break from mTOR inhibitor treatment if they become exposed to coronavirus or become ill with COVID-19. TSC practitioners may consider stopping mTOR inhibitors for a short period for such patients who are exposed to the virus or in patients with COVID-19 until they recover.

6) Should mTOR inhibitors be stopped empirically in patients with subependymal giant cell astrocytomas (SEGAs) as a plan to prevent or diminish likelihood or severity of COVID-19 infection?

At this time, there are no strict guidelines about whether to empirically discontinue mTOR inhibitors in TSC patients with SEGA. Again, based on current CDC statements and how recent influenza outbreaks like the H1N1 in 2009 were managed, it is recommended that patients remain on mTOR inhibitors unless they or an immediate family member or a close contact, e.g., schoolmate or work colleague, are diagnosed with COVID-19. You may wish to discuss these options with patients and assess the risk-benefit continuing mTOR inhibitors if there are other underlying co-morbidities including diabetes, heart disease, hypertension, cancer, and rheumatological disorders.

If patients are taking mTOR inhibitors for SEGA, there may be a risk of re-growth associated with cessation of mTOR inhibitor treatment if they are exposed to coronavirus or become ill with COVID-19. TSC practitioners may consider stopping mTOR inhibitors for a short period for patients who are exposed to the virus or in patients with COVID-19 until they recover with appropriate monitoring of neurological exam and possibly neuro-imaging, i.e., CT or MRI, to look for declining neurological function or re-growth of SEGA.

7) Should mTOR inhibitors be stopped empirically in patients with medically intractable epilepsy as a means to prevent or diminish likelihood or severity of COVID-19 infection?

At this time, there are no strict guidelines about whether to empirically discontinue mTOR inhibitors in TSC patients with medically intractable epilepsy. If a patient has refractory epilepsy, then the patient may wish to take extra care to avoid catching coronavirus as infectious illnesses and fever are often associated with a deterioration or loss of seizure control, despite seizure medication compliance (see [American Epilepsy Society webpage](#)). TSC practitioners may consider stopping mTOR inhibitors for a short period for patients who are exposed to the virus or in patients with COVID-19 until they recover with appropriate monitoring of neurological status, seizure frequency and severity, and EEG. If the decision is to stop mTOR inhibitors, alternative anti-epileptic drug treatments may be considered to “bridge” the patient until the mTOR inhibitor can be safely restarted.

8) What to do about sirolimus cream?

Using sirolimus cream (sometimes called topical sirolimus) should not increase patients’ risk of serious symptoms if they catch coronavirus. The patient should be able to keep using the cream as normal, but it may be advisable to stop if they are exposed to or contract COVID-19.

9) Older adults with TSC?

The odds of developing severe COVID-19 infection increase with age, starting at age 60. It is especially dangerous for people over 80. Elderly patients and those with underlying chronic conditions, such as diabetes, hypertension, heart or lung disease, are advised to take additional precautions including social distancing, handwashing, and avoiding face touching.

Medical Review Note

The material above was reviewed and approved by:

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