



8737 Colesville Road, Suite 400 | Silver Spring, MD 20910
800-225-6872 | info@tscalliance.org | tscalliance.org

TSC Alliance COVID-19 Vaccine Position Statement - Update ***August 18, 2021***

The United States continues to face an unprecedented public health challenge during the COVID-19 pandemic with more than 617,787 lives lost in 18 months. Throughout this time frame, the global medical and scientific community has rallied together to address detection of the virus, learn and implement best practices in clinical care, and develop vaccines to prevent or lessen infection and serious symptoms. Three vaccines (Pfizer, Moderna, and Johnson & Johnson) have received emergency use authorization (EUAs) from the FDA to slow the spread of COVID-19 and improve the protection and outcomes of the public. ALL U.S. citizens 12 years of age and older are eligible for vaccination. At the time of drafting this document, over 167 million individuals (~50% U.S. population) have been fully vaccinated. Ongoing clinical trials will hopefully extend eligibility for those younger than 12 years of age in the coming months.

Take Home Messages

- **If you have not yet received a COVID-19 vaccine, get vaccinated as soon as possible, even if you have already had COVID-19 infection.**
- **You do not need a prescription by your physician to get the vaccine.**
- **If you are currently taking Everolimus or Sirolimus for TSC, stay on these medications unless otherwise directed by your TSC clinician(s).**
- **If you are currently taking Everolimus or Sirolimus for TSC, and you have already received two doses of COVID-19 mRNA vaccine (Pfizer or Moderna), you are eligible for an additional, third dose of the vaccine, a “booster” vaccine.**
- **The TSC Alliance recommends a third vaccine dose for TSC individuals currently treated with Everolimus or Sirolimus who have previously received either the Pfizer or the Moderna vaccines.**
- **The current recommendations are to receive the same kind of vaccine for the third dose that you received for the first two doses i.e., Pfizer for Pfizer, Moderna for Moderna). Mixing vaccines is permitted if same vaccine type is not available.**
- **There is no recommendation yet regarding an additional dose for those individuals who have received a single dose vaccine such as the Johnson and Johnson vaccine.**

Hope no matter how complex



Considerations for an informed choice on getting vaccinated

Vaccine Response and mTOR Inhibitors

Vaccines train the immune system to recognize and help clear infectious agents such as viruses from the body. In such a response, the cells of the immune system develop antibodies against pieces of the virus called antigens. These antibodies attach to the antigen on the virus, providing a signal to the immune system cells to attack and remove the virus from the body. In the case of COVID-19, approved vaccines train the immune system to recognize COVID-19 antigens called “spike protein.”

Everolimus and Sirolimus are members of a class of drugs called mTOR inhibitors and are commonly used to treat brain, kidney, and lung manifestations of TSC, including subependymal brain tumors, kidney angiomyolipomas, epilepsy and LAM. The concern with those who take mTOR inhibitors (e.g., Everolimus and Sirolimus) for TSC is that this class of medicine might suppress the immune system (immunosuppressant), lowering the body’s ability to mount an effective attack (e.g., antibodies) against pathogens causing infections. Studies in people taking mTOR inhibitors along with other immunosuppressive drugs to prevent rejection after organ transplantation concluded that those individuals were less likely to have an effective immune response even after receiving the appropriate vaccinations. These studies provided strong supporting evidence to encourage the FDA to approve a third dose of vaccination in individuals taking immunosuppressants including Everolimus and Sirolimus.

The extent to which mTOR inhibitors alone reduce the production of an effective immune response following vaccination is not well understood. It is likely that patients on mTOR inhibitors alone mount a significantly better response to vaccination compared with other immunosuppressed patients such as post-transplant individuals who generally tend to be on multiple immunosuppressive medications. Small independent studies (non-published) in the TSC and LAM communities have demonstrated this response but require large scale validation. Given this uncertainty combined with the potential for severe complications in patients with TSC after COVID-19 infection, our consensus recommendation is for TSC patients on mTOR inhibitors to receive the additional (third) dose of vaccination. The consensus group also recommends continuing to take mTOR inhibitors for disease management and not to stop unless directed by your healthcare specialist.

COVID-19 Vaccines in Individuals with TSC

As part of the mission of the TSC Alliance to keep you informed, we compiled recent information regarding the safety and effectiveness of COVID-19 vaccination, vaccine hesitancy, vaccination response on mTOR inhibitors, long-term COVID-19 challenges, and school barriers in those living with TSC. With the large amount of information and misinformation available, our job as leading expert providers, researchers and advocates is to provide accurate information for you to make a well-informed decision regarding the benefits and safety of vaccination.

Why should individuals with TSC be vaccinated?

Unless otherwise contraindicated, everyone should receive a COVID-19 vaccination since all commercial COVID-19 vaccinations lower your risk of contracting COVID-19 and developing severe COVID-19 complications including hospitalization and need for the intensive care unit. They also reduce your chances of spreading the infection to others. TSC is a multi-system disease that

may put individuals at risk for severe COVID-19 illness. It is known that COVID-19 virus can cause inflammation of bodily organs. Multiple studies have shown the neurological impact of COVID-19 including persistent headaches, dizziness, mental fog, and difficulty articulating words. Those with epilepsy may be at risk for loss of seizure control or worsening seizures. Individuals with LAM and other associated pulmonary conditions may experience pneumonia or other severe illness due to the virus. COVID-19 may stress the kidneys, and those with high blood pressure or existing kidney disease are at an increased risk of developing more severe kidney disease, including kidney failure. It is especially important to prevent additional kidney damage in individuals with TSC and polycystic kidney disease (PKD). For those who need to receive the COVID-19 vaccination and their other childhood vaccinations, these vaccines can be administered at the same time – or within 14 days – as other vaccines. If your child is on an altered childhood vaccination schedule or there are additional concerns, we strongly recommend discussing this with your local pediatrician and or pediatric neurologist.

Why should family members get vaccinated?

It is important to understand those who are not eligible for a vaccination or choose not to be vaccinated are vulnerable to COVID-19 infection, and therefore their protection from the virus is dependent on all individuals in close living conditions or proximity take measures such as vaccination and wearing masks to prevent the spread. Family members, friends, teachers, aids, and others getting vaccinated significantly reduce the transmission of the virus to those who cannot receive a vaccination or achieve an adequate immune response.

Previous History of COVID-19 Infection – Should I still get vaccinated?

The simple answer is “yes”. Antibodies can be detected for about 4 weeks after having COVID-19, although it can take several months in some people. Data show antibodies are less consistently detectable after COVID-19 infection compared to after vaccination. We are starting to understand that natural antibodies mainly attach to one protein region while vaccination can produce antibodies attaching to several protein regions, creating better chance of protection against new virus variants that may emerge. We also know that re-infection rates are 2x higher among unvaccinated individuals with past COVID-19 infections compared to those who did get vaccinated after a COVID-19 infection. A study by the CDC demonstrated that the natural immune response did not protect against reinfection as well as vaccinations. In addition, the CDC also found that individuals who had not been vaccinated and developed a second COVID-19 infection, had more severe clinical COVID-19 illness.

Vaccine Hesitancy

As with any new treatments or recommendations it is natural to be skeptical. With the overwhelming amount of misinformation on social and other media outlets, and inconsistency of recommendations over the last year and half, we understand many remain cautious, and it is important we clarify common misconceptions. mRNA vaccines (Pfizer and Moderna) have been studied and researched by scientists since the 1990's.

All approved COVID-19 vaccines have been through rigorous and controlled clinical trials to establish both the safety and effectiveness. Clinical trials with Pfizer, Moderna and Johnson & Johnson vaccines evaluated the safety and effectiveness in over 150,000 participants. To put this

in perspective, key clinical trials for the approval of mTOR therapy for SEGAs and renal angiomyolipomas (EXIST-1 and EXIST-2) included approximately 235 clinical trial participants.

These vaccines have mild side effects that are considered a normal response (e.g., injection site pain, headache) and typically resolve within a few days. Severe vaccine side effects occur in less than 0.5% of those vaccinated. Generally, vaccines are safe with no evidence to support long term complications. Further, there is nothing in mRNA vaccines that would carry potential long term side effects. For short term effects, as with any vaccination that can lower seizure threshold, it is possible to have a breakthrough febrile (fever) associated seizure. However, there is currently no evidence that any of the COVID-19 vaccinations worsen preexisting seizure baseline. The consensus group continues to defer to your seizure action plan defined by your current provider. Finally, you cannot contract COVID-19 from any of the commercially available vaccines.

Third Dose of COVID-19 Vaccination (“Booster”)

On August 12 and 13, 2021, the FDA approved emergency use authorization (EUAs) for, and CDC recommended, additional doses of mRNA COVID-19 vaccines following a primary series in immunocompromised individuals. This amendment applies to the Pfizer COVID-19 vaccine for those 12 years old or older and Moderna COVID-19 vaccine for those 18 years old or older. Those who received the Johnson & Johnson COVID-19 vaccine are not eligible for an additional dose at this time due to insufficient data. Ongoing research is being conducted to ensure optimal vaccine protection for those who received the Johnson & Johnson vaccine, and recommendations will be updated once sufficient data is available.

The Centers for Disease Control (CDC) has prioritized an additional (third) dose of COVID-19 vaccine for the following immunocompromised people:

- Active or recent treatment for solid tumor and hematologic malignancies
- Recent of solid-organ or recent hematopoietic stem cell transplants
- Severe primary immunodeficiency
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids, alkylating agents, antimetabolites, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory
- Chronic medical conditions such as asplenia and chronic renal disease may be associated with varying degrees of immune deficit

Who is eligible for additional dose of the vaccine?

- Individuals with TSC who are on immunosuppressive biologic agents (Everolimus or Sirolimus)
- 18 years of age or older who received two doses of the Moderna vaccine or 12 years of age or older who received two doses of the Pfizer vaccine
- Those who received the second dose of the Pfizer or Moderna COVID-19 vaccine series at least 28 days prior to receiving a third dose
- All attempts should be made to receive the same mRNA dose as the primary series, however if that is not feasible, an additional dose of the other mRNA vaccine is permitted.

- Contact your local pharmacies to schedule your additional dose. You do not need a physician prescription to receive the additional dose.

I have TSC but am not on Everolimus or Sirolimus. Do I qualify for an additional vaccine dose?

No, the current recommendations are only applicable to patients with TSC who are on Everolimus or Sirolimus or qualify under one of the other above-mentioned CDC criteria. It is likely that in the near future, all of us will require an additional dose of the COVID-19 vaccination to boost our protection.

Public Health Measures to Protect Individuals with TSC

Regardless of vaccination status, proper and basic public health measures should continue to be followed. It is strongly encouraged that all individuals wear a mask indoors when not at home and when in large crowds outdoors. Continue to stay 6 feet apart from others that do not live within the same dwelling. Avoid crowds and poorly ventilated spaces. Close contacts of those living with TSC should be strongly encouraged to be fully vaccinated against COVID-19.

In addition to masking and social distancing, we understand that many individuals are faced with profound barriers and concerns as schools and work are returning to in person environments. Nationally individual states and school districts have conflicting recommendations that make decisions even more difficult. Each individual situation is unique and requires carefully thought-out interventions to ensure safe return to school for social development and education, and fair and equal access to day and vocational programs for TSC individuals and the challenges with masking and unvaccinated individuals.

Here are some helpful tips that can easily be requested and added to individualized education plans (IEPs) and other individualized plans:

- Request arrival and dismissal times where there is reduced population
- Limit exposure during high-risk activities such as eating in the classroom and sharing of common items and avoiding communal items such as water fountains.
- Request all staff to always wear masks around high-risk individuals
- Request for HEPA Filter for classroom
- Request for Clorox 360 and other room cleaning devices to be used daily
- Request education to custodial staff to pay special attention to classroom
- Limit multiple room exposures and request additional services to come to classroom
- Highlight importance of seizure action plan as viruses that lower seizure threshold might be first sign of impending infection
- Proper notification to parent / guardian when there has been direct infectious exposure to at risk individual

Additional Resources and Recommendations

As the COVID-19 pandemic persists and new variants are emerging such as the Delta variant, we will continue to update and provide accurate information to the community. Variants such as Delta are proving that reinfection and breakthrough cases are possible, even in the vaccinated population. This stresses the importance that we keep our community safe. Despite showing breakthrough COVID-19 cases, those who are vaccinated are having less severe and fatal

consequences with quicker recovery times. Many geographical areas are facing unprecedented hospitalization records across pediatric and adult hospitals. More than ever, the TSC community must remain diligent with prevention measures.

Antibody testing after vaccination is not clinically necessary unless advised by a specialist. For those who wish to know their antibody response, we urge them to discuss with their local healthcare team to determine whether and how to be tested. Those who are already enrolled in the TSC Alliance Natural History Database and have had antibody testing and wish to have your antibody testing including in the study, please contact Dr. Gabrielle Rushing, PhD, at grushing@tscalliance.org.

Medical Review Note

This information was reviewed and approved by:

- Peter B. Crino, MD, PhD, Chair, TSC Alliance Board of Directors
- Darcy A. Krueger, MD, PhD, Chair, TSC Alliance Professional Advisory Board
- Mustafa Sahin, MD, PhD, Chair, TSC Alliance International Scientific Advisory Board and Co-Chair, TSC Alliance Science and Medical Committee
- John J. Bissler, MD, TSC Alliance Professional Advisory Board
- Nishant Gupta, MD, Director of LAM Clinic Network
- Elizabeth Thiele MD, PhD, Massachusetts General Hospital
- Joel Moss, MD, PhD, TSC Alliance Professional Advisory Board
- Elizabeth Petri Henske, MD, TSC Alliance Professional Advisory Board

For additional questions or concerns please reach out to Ashley Pounders MSN, FNP-C, TSC Alliance Director, Medical Affairs at apounders@tscalliance.org or 240-472-4302.

Disclaimer

This content was created for general informational purposes only. The content is not intended to be a substitute for professional medical advice. The risk profile for each individual is unique, and immunity from COVID-19 may be affected by factors such as age, chronic health conditions, and other medications. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding these recommendations.