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# Vaccination Against Covid-19: Recommendations for Candidates and Transplant Recipients

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# Conflict of interest

Nothing to declare.

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Abstract: Covid-19 has strongly impacted solid organ transplants (SOT). Patients on the SOT list and those already transplanted belong to the priority population for covid-19 vaccination, which aims to reduce covid-19 morbidity and mortality. All vaccines used today against covid-19 can be administered in the SOT setting. The vaccination schedule (manufacturing platform, age, number of doses, indication of booster doses) varies from country to country.

Descriptors: Solid Organ Transplants; Immunosuppression; Covid-19, Vaccination.

#### INTRODUCTION

Covid-19 vaccines were developed in record time based on decades of studies conducted before the onset of the disease. Accordingly, the first Covid-19 vaccines were approved in late 2020, following the review and approval of clinical safety and efficacy studies involving thousands of volunteers.

By the end of the second year of the pandemic, December 31, 2021, almost nine billion doses of the vaccine had been applied worldwide, and more than 350 million doses in Brazil. By this date, 77% of the Brazilian population had already received at least one dose of the vaccine, and 67% had completed the vaccination schedule.<sup>1-3</sup>

The current recommendation is full Covid-19 vaccination for all children over 3 years of age and for adults, including transplant candidates and transplant recipients. The minimum age for starting vaccination, vaccination schedules, and available vaccines follow the recommendations adopted in each country. In Brazil, vaccination for Covid-19 is approved starting at the age of 5 years. The vaccines currently available for use in Brazil are from Instituto Butantan (CoronaVac), mRNA vaccines from Pfizer/Wyeth, and nonreplicating viral vector vaccines from Oswaldo Cruz Foundation (Fiocruz)/AstraZeneca and Janssen–Cilag. 4-6

None of the currently available Covid-19 vaccines contain live attenuated virus. Therefore, they are approved for use in immunocompromised patients; however, there are specifications for each vaccine according to age and if pregnant.

Table 1 lists the vaccines currently available in Brazil and Table 2 lists the main milestones of the Covid-19 vaccination campaign in Brazil, then guidelines for Covid-19 vaccination in adults and children in Brazil is showed, including transplant patients, according to current national guidelines.<sup>1,3-6</sup>

This document will be updated as needed.

Table 1. Covid-19 vaccines available in Brazil.

Vaccine	Plataform	Recommended age	Approval date in Brazil	
CoronaVac (Sinovac/Instituto Butantan)	Adsorbed covid-19 vaccine (inactivated)	People 6 years of age and older. Contraindicated for immunosuppressed children (5-17 years).	Jan. 17th 2021 (adults > 18 years old) Jan. 20th 2022 (age group between 6 and 17 years)	
ChAdOx1 (AstraZeneca/Fiocruz)	Recombinant covid-19 vaccine (nonreplicating)	People 18 years of age and older. Contraindicated for pregnant and postpartum women.	Jan. 17th 2021	
Comirnaty (Pfizer/Wyeth)	mRNA covid-19 vaccine	People 5 years of age and older.	Feb. 23th 2021 (adults > 18 years old) Dec. 16th 2021 (age group between 5 and 11 years and 11 months)	
Janssen-Cilag	Recombinant covid-19 vaccine (nonreplicating)	People 18 years of age and older. Contraindicated for pregnant and postpartum women.	Mar. 31st. 2021	

Table 2. Primary vaccination schedule and booster dose.

Vaccine	Primary vaccination schedule		Booster	
	Immunocompetent patient	Immunosuppressed patient*	Interval	Vaccine
CoronaVac (Sinovac/Instituto Butantan)	Two doses of 0.5 mL, 3 to 4 weeks interval between doses	Two doses + additional dose of 0.5 mL, interval between first and second dose three to four weeks, interval between second and third dose eight weeks. Only individuals aged 18 years or older	Four months after the last dose of the primary schedule	AstraZeneca, Janssen-Cilag or Pfizer/Wyeth
ChAdOx1 (AstraZeneca/Fiocruz)	Two doses of 0.5 mL, interval between doses four to 12 weeks. (Adopted eight-week interval since October 5th, 2021). Contraindicated for pregnant and postpartum women	Two doses + additional dose of 0.5 mL, interval between doses 8 weeks.  Contraindicated for pregnant and postpartum women	Four months after the last dose of the primary schedule	AstraZeneca, Janssen-Cilag or Pfizer/Wyeth
Comirnaty (Pfizer/Wyeth)	Two doses of 0.5 mL, interval between doses three to 12 weeks. (Adopted eight-week interval since October 5th, 2021).	Two doses of 0.5 mL, interval between doses three to eight weeks. Children 5 years and older and adults, minimum interval between doses is 4 weeks Additional dose (third dose) from 12 years of age and older	Four months after the last dose of the primary schedule	AstraZeneca, Janssen-Cilag or Pfizer/Wyeth
Janssen-Cilag	One dose of 0.5 mL. Contraindicated for pregnant and postpartum women	One dose + additional dose of 0.5 mL (additional dose eight weeks after the first dose). Contraindicated for pregnant and postpartum women	Four months after the last dose of the primary schedule	AstraZeneca, Janssen-Cilag or Pfizer/Wyeth

<sup>\*</sup>Individuals with a high degree of immunosuppression: severe primary immunodeficiency (inborn errors of immunity); cancer chemotherapy; solid organ or hematopoietic stem cell transplant recipients on immunosuppressive drugs; persons living with human immunodeficiency virus (HIV)/human immunodeficiency syndrome (AIDS); use of corticosteroids at doses  $\geq$  20 mg/day of prednisone, or equivalent,  $\geq$  14 days; use of immune response modifying drugs; autoinflammatory diseases, inflammatory bowel diseases; patients on hemodialysis; patients with chronic inflammatory immune-mediated diseases.

# VACCINATION SCHEME AGAINST COVID-19 IN BRAZIL

The Covid-19 vaccination program in Brazil began in January 2021.¹ Covid-19 vaccination is recommended for all individuals aged 5 years or older, including transplant candidates, recipients, living donor transplantation, as well as home contacts and caregivers of patients with immunodepression, to reduce the risk of SARS-CoV-2 infection in immunosuppressed individuals.¹-3,6

# Primary vaccination schedule

The primary vaccination schedule for immunocompetent patients is *two doses of vaccine*, preferably from the same platform. For Janssen-Cilag's vaccine, the primary vaccination schedule for immunocompetent patients is *one dose*.

Numerous studies demonstrate reduced immune response to Covid-19 vaccine in immunosuppressed individuals, including transplant patients. Thus, since September 15th, 2021, the primary vaccination schedule for patients with a high degree of immunosuppression, including patients with organ dysfunction on the transplant list and solid organ transplant patients, is *three doses of vaccine*, preferably from the same platform. In the case of the Janssen-Cilag vaccine, the vaccination schedule in immunosuppressed patients is *two doses*.<sup>5,6</sup>

The recommendation is detailed in the Technical Note No. 43/2021-SECovid/GAB/SECovid/MS<sup>7</sup> and in the Technical Note No. 11/2022-SECovid/GAB/SECovid/MS.<sup>6</sup>

From December 16th, 2021 it is recommended to vaccinate *children aged 5 to 11 years with immunosuppression exclusively with the Pfizer/Wyeth* vaccine, in the three-dose vaccine schedule (Technical Note No. 8/2022-SECovid/GAB/SECovid/MS)<sup>3</sup>.

# Administration of the booster dose

It is recommended, since November 17th, 2021, *a booster dose of the* Covid-19 vaccine for all individuals over 18 years of age, regardless of the immunizer applied (updated Technical Note No. 65/2021-SECovid/GAB/SECovid/MS<sup>2</sup> and Technical Note No. 11/2022-SECovid/GAB/SECovid/MS<sup>6</sup>).

A booster dose is recommended 4 months after the primary vaccination has been completed. People who have received Janssen-Cilag vaccine and are 18 years or older and not pregnant should receive a booster dose at least two months after the primary vaccination schedule with one dose.

The vaccine to be used for the booster dose should preferably be of the mRNA platform (Pfizer/Wyeth) or, alternatively, of viral vector (Janssen-Cilag or AstraZeneca) (Technical Note No. 59/2021-SECovid/GAB/SECovid/MS<sup>8</sup> and Technical Note No. 11/2022-SECovid/GAB/SECovid/MS<sup>6</sup>).

The booster dose is also recommended for highly immunosuppressed individuals from 12 years of age and older, with a minimum interval of 4 months from the third vaccine dose of the primary vaccination schedule. Thus, the booster dose corresponds to the fourth dose for immunosuppressed individuals.<sup>3</sup>

Children aged 5 to 11 years and 11 months with high-grade immunodepression should receive a mandatory booster dose 4 months after the second vaccine dose of the primary vaccination schedule with the Pfizer vaccine.<sup>3</sup>

#### Interval between Covid-19 vaccines and other vaccines

- Above 12 years of age: Covid-19 vaccines can be given at the same time as the other vaccines or at any interval;
- For children 5 to 11 years and 11 months of age: A period of 15 days must be allowed between the Covid-19 vaccine and the other vaccines in the National Immunization Program. This guidance is temporary and based on pharmacovigilance measures, since the use of Covid-19 vaccines in children in Brazil is recent.

# Interval between Covid-19 vaccines and Covid-19 diagnosis

It is recommended to postpone vaccination in people with a suggestive or confirmed Covid-19 condition, to avoid confusion with other differential diagnoses. Ideally, vaccination should be delayed for at least four weeks from the onset of symptoms or the date of the diagnostic test (reverse transcriptase followed by polymerase chain reaction – RT-PCR –, or antigen test), in the case of individuals with asymptomatic infection.

However, there is no cause for concern if vaccination occurs within 4 weeks of Covid-19 diagnosis, because it is unlikely that vaccinating infected individuals will result in decreased vaccine efficacy or increased risk of disease complications.

# Vaccination of transplant patients and other immunosuppressed patients

The use of Covid-19 vaccines from the platforms currently available in Brazil (inactive virus, mRNA, and nonreplicating viral vector) is safe for immunosuppressed individuals, including transplant patients.

It is unlikely that there is an increased risk of adverse events in this population compared to the population without immunosuppression. Covid-19 vaccines should preferably be administered in the pretransplant period, with a minimum interval of two days for inactivated virus vaccines (CoronaVac) and seven days for the others between vaccination and transplant.

In the post-transplant period, vaccination can be done with a minimum interval of 30 days after transplant, according to the epidemiological situation, even for individuals submitted to transplant with thymoglobulin induction.

Discontinuation, even temporarily, of immunosuppressants is not recommended for the administration of the vaccine. There is no evidence to date that temporary suspension of immunosuppressants is beneficial for the immune response to the immunizer, with likely additional risk of rejection associated with this practice.

# FINAL CONSIDERATIONS

Vaccinated individuals should maintain adherence to all protective measures to avoid SARS-CoV-2 infection, including the use of high-filtration masks and social distancing.

Routine checking of the humoral (presence of antibodies) or cellular immune response postvaccination is not recommended.

# **AUTHORS' CONTRIBUTION**

Substantive scientific and intellectual contributions to the study: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC; Conception and project: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC; Technical procedures: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC; Data analysis and interpretation: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC; Manuscript writing: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC; Critical review: Stucchi RWB, Santoro-Lopes G, Santos DW, Abdala E, Clemente WT, Pierrotti LC.

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