

# COVID-19

## CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

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## BRAZIL

As of 1 February 2022, 250,807,361 doses of COVID-19 vaccines had been administered – excluding doses administered in the state of São Paulo – consisting of 58,780,720 doses of the Sinovac/Butantan vaccine, 88,934,873 of the AstraZeneca/Fiocruz vaccine, 98,347,456 of the Pfizer/Wyeth vaccine, and 4,744,312 doses of the Janssen vaccine. Doses administered in São Paulo had to be excluded because the state's reports of adverse events following immunization (AEFI) are not entered in the e-SUS reporting system, using instead its own SUS/MS data system; the state of São Paulo continues efforts to establish interoperability with the system used by the Ministry of Health.

As of the date of the report, with the exception of the state of São Paulo, 155,844 events were recorded in the AEFI module of the e-SUS information reporting system. Of these, 20,978 (13.5%) were vaccination-related errors, 134,241 (86.1%) were AEFI temporally associated with COVID-19 vaccines used in Brazil, and 625 (0.4%) were AEFI involving vaccination errors.

Among the reported AEFI temporally associated with vaccination, 91.7% were non-serious adverse events (NSAE), of which 90% occurred in the first week after vaccination. Among the 11,145 reports of serious adverse events (SAE), approximately 90% occurred in the month after vaccination.

AEFI	AstraZeneca/Fiocruz		Sinovac/Butantan		Pfizer/Wyeth		Janssen-Cilag		Total	
	N	Rate*	N	Rate*	N	Rate*	N	Rate*	N	Rate*
Non-serious	73,737	82.9	30,253	51.5	17,993	18.3	1,738	36.6	123,721	49.3
Serious	5,190	5.8	4,211	7.2	1,616	1.6	128	2.7	11,145	4.4
Total	78,927	88.7	34,464	58.6	19,609	19.9	1,866	39.3	134,866	53.8

N = number of events

\* Rate per 100,000 doses administered

The main signs and symptoms observed among NSAE were similar for all of the vaccines, primarily consisting of headache, pyrexia, and myalgia. For reported SAE temporally associated with the Sinovac/Butantan vaccine, the most common were: dyspnea (1.83/100,000 doses administered), pyrexia (0.88/100,000 doses administered), and cough (0.65/100,000 doses administered), with rates of these three reported events for the AstraZeneca/Fiocruz vaccine being 0.98/100,000, 0.49/100,000, and 0.31/100,000 doses administered, respectively.

Reported events for the Pfizer/Wyeth vaccine included dyspnea (0.27/100,000 doses administered), pyrexia (0.14/100,000 doses administered), and chest pain and headache (0.10/100,000 doses administered). Reported events associated with the Janssen vaccine consisted mainly of dyspnea (0.41/100,000 doses administered), and headache, asthenia, and paresthesia (0.18/100,000 doses administered for each).

Source: Brazil Ministry of Health, Secretariat of Health Surveillance. Special Epidemiological Bulletin No. 99.

Epidemiological Week 5, 30/1/2022 to 5/2/2022. Available at: <https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/boletins-epidemiologicos/covid-19/2022/boletim-epidemiologico-no-99-boletim-coe-coronavirus.pdf/view>.

## CANADA

As of 11 February 2022, 53,269,706 doses of the Pfizer-BioNTech COVID-19 vaccine, 22,358,853 doses of the Moderna vaccine, 2,794,893 doses of the AstraZeneca and Covishield vaccine (AstraZeneca vaccine manufactured by the Serum Institute of India), and 16,859 doses of the Janssen vaccine had been administered.

For these three vaccines, there were 37,975 individual reports of one or more AEFI (0.048% of doses administered). Of these, 7,999 reports involved serious events (0.010% of doses administered).

The majority of individual case reports were of non-serious adverse events. The most frequently reported adverse events were: paresthesia, injection-site pain, headache, pruritus, dyspnea, fatigue, urticaria, chest pain, and fever.

Number of reports and reporting rate of AEFI (per 100,000 doses administered), by type of vaccine administered						
As of 11 February 2022						
Vaccine	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered
Pfizer-BioNTech	17,210	32.31	5,472	10.27	22,682	42.58
Moderna	10,004	44.74	1,513	6.77	11,517	51.51
Covishield and AstraZeneca	2,705	96.78	813	29.09	3,518	125.87
Janssen	13	77.11	11	65.25	24	142.36
Total	29,932	38.16	7,809	9.96	37,741	48.11

On 19 November 2021, the Pfizer-BioNTech Comirnaty vaccine was authorized for children between the ages of 5 and 11. Information regarding adverse events in this population and, more generally, in the under-18-year-old population (already included in the above total for Pfizer-BioNTech) is broken down in the following table:

Number of reports and reporting rate of AEFI (per 100,000 doses administered) for the Pfizer-BioNTech vaccine in the under-18-year-old population, as of 11 February 2022						
Age group (doses administered, ds)	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N*	Rate per 100,000 doses administered	N*	Rate per 100,000 doses administered	N*	Rate per 100,000 doses administered
Ages 12 to 17	999	22.26	301	6.71	1,300	28.97
4,486,864 ds						
Ages 5 to 11	219	9.36	43	1.84	262	11.20
2,339,876 ds						
Total	1,218	17.84	344	5.04	1,562	22.88
6,826,740						

\* N = number of events

Note: The 5–11 age group also included reports of those born in 2017 who were not yet five years old at the time of vaccination.

Number of reports and reporting rate (per 100,000 doses administered) of main Adverse Events of Special Interest (AESI), by type of vaccine, as of 11 February 2022, in the general population						
AESI	Vaccine					
	Pfizer-BioNTech		Moderna		Covishield and AstraZeneca	
	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered
Anaphylaxis	572	1.07	171	0.76	27	0.97
Thrombosis with thrombocytopenia syndrome (TTS)	27	0.05	12	0.05	71	2.54
Guillain-Barré syndrome	54	0.10	26	0.12	39	1.40
Myocarditis/pericarditis	1,134	2.13	604	2.70	31	1.11
Myocardial infarction	72	0.14	22	0.10	0	0
Bell's palsy/facial paralysis	565	1.06	190	0.85	54	1.93
Category: Autoimmune disease	201	0.38	90	0.40	162	5.80
Category: Circulatory system	632	1.19	232	1.04	383	13.70
Category: Central and peripheral nervous systems	696	1.31	241	1.08	90	3.22
Fatal events	290* post-vaccination deaths					
*Following a medical review of the 290 deaths, 97 were determined to most likely be unrelated to administration of the COVID-19 vaccine, while 44 are still under investigation; in 149 cases, the cause of death could not be classified, due to insufficient information.						

Note: Information on the Janssen vaccine was not included, due to the small number of reported cases.

Source: Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada. February 18, 2022. <https://health-infobase.canada.ca/covid-19/vaccine-safety/>. Data reproduced by PAHO/WHO.

## ENGLISH-SPEAKING CARIBBEAN

As of 15 February 2022, VigiBase, the Global Individual Case Safety Report (ICSR) database, had received 1,300 reports of AEFI associated with COVID-19 vaccines in the English-speaking Caribbean.

Reports from Barbados, Jamaica, and Saint Vincent and the Grenadines, were mainly in people under 65 years of age (85.4%), and were primarily in females (980 reports, 75.4%). There were 80 additional reports as of 15 February 2022, for which the most frequently reported reactions were headache (31.8%), fever (21.1%), dizziness (19%), fatigue (18.6%), chills (18.3%), and myalgia (15.8%). Of individual case safety reports (ICSRs), 196 (15.1%) were classified as serious, including 42 deaths.



The reported ICSRs were associated with the following COVID-19 vaccines: AstraZeneca, Sputnik V, Pfizer-BioNTech, J&J/Janssen, Sinopharm, Moderna, and unspecified COVID-19 vaccines.

Note: Individual case safety reports describe events that occurred following vaccination, and may include coincident events not attributable to the vaccine(s).

Source: The Caribbean Public Health Agency (CARPHA). Caribbean Regulatory System. Vigicarib News, 18 February 2022. For additional information, see: <https://carpha.org/What-We-Do/CRS/VigiCarib>.

## COLOMBIA

As of 15 February 2022, a total of 75,320,803 doses of COVID-19 vaccines had been administered. As of the cut-off date, 40,114 individual reports of AEFI had been received through VigiFlow,<sup>®</sup> including serious cases reported to the National Institute of Health (INS). An individual case report may include one or more adverse events. The reporting rate was 53 per 100,000 doses administered, with AEFI reported by 0.05% of people vaccinated. Colombia uses the phrase (in Spanish) “Adverse Event Following Vaccination” (with the acronym EAPV).

Of total individual case reports, 3.4% (1,360 reports) involved serious AEFI; 68% of reported events (27,077) were in women. Analyzing the distribution of reports by age, the highest percentage of reports, 12.5% (5,003), was in the 25-to-29-year-old age group, followed by those between the ages of 30 and 34, representing 11.6% of reports (4,645).

The most frequently reported signs and symptoms, without a breakdown by type of vaccine administered, were: headache (17.1%), fever (7.9%), injection-site pain (6.4%), muscle pain (7%), malaise (7.4%), and weakness (5.1%).

Source: Colombia Ministry of Health, National Food and Drug Surveillance Institute (INVIMA), National Institute of Health (INS). Bulletin No. 10: February 2022, Surveillance of Adverse Events Following Vaccination (EAPV) with COVID-19 vaccines in Colombia. Reporting period: 17 February 2021 to 15 February 2022. Available at: <https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/boletin10-farmacovigilancia-vacunas-feb2021.pdf>.

## UNITED STATES

The following is updated information from the U.S. Centers for Disease Control and Prevention (CDC) regarding serious adverse events of special interest.

Anaphylaxis, a severe type of allergic reaction, can occur after any kind of vaccination. Anaphylaxis after COVID-19 vaccination is rare and has occurred in approximately five people per million vaccinated in the United States.

Thrombosis with thrombocytopenia syndrome (TTS) after Johnson & Johnson’s Janssen (J&J/Janssen) COVID-19 vaccination is rare. TTS is a rare but serious adverse event that causes blood clots in large blood vessels and low platelets (blood cells that help form clots). As of 10 February 2022, more than 18.2 million doses of the J&J/Janssen



COVID-19 vaccine had been administered in the United States. The CDC and FDA identified 57 confirmed reports of people who got the J&J/Janssen COVID-19 vaccine and later developed TTS. The CDC has also identified nine deaths that have been caused by or were directly attributed to TTS following J&J/Janssen COVID-19 vaccination. Women ages 30-49 years, especially, should be aware of the increased risk of this rare adverse event. There are other COVID-19 vaccine options available for which this risk has not been seen.

To date, three confirmed cases of TTS following vaccination with the Moderna mRNA COVID-19 vaccine have been reported to VAERS, after administration of more than 526 million doses of mRNA COVID-19 vaccines (Moderna and Pfizer-BioNTech) in the United States. Based on available data, there is not an increased risk for TTS after mRNA COVID-19 vaccination.

Guillain-Barré syndrome (GBS) in people who have received the J&J/Janssen COVID-19 vaccine is rare. GBS is a rare disorder where the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis. Most people fully recover from GBS, but some have permanent nerve damage. After more than 18.5 million J&J/Janssen COVID-19 vaccine doses administered, there have been approximately 310 preliminary reports of GBS identified in VAERS as of 10 February 2022. These cases have largely been reported about two weeks after vaccination and mostly in men, many in those ages 50 years and older. Based on the data, the rate of GBS within the first 21 days following J&J/Janssen COVID-19 vaccination was found to be 21 times higher than after Pfizer-BioNTech or Moderna mRNA vaccines. After the first 42 days, the rate of GBS was 11 times higher following J&J/Janssen COVID-19 vaccination than for the mRNA vaccines.

Cases of myocarditis and pericarditis after COVID-19 vaccination are rare. Myocarditis is inflammation of the heart muscle, and pericarditis is inflammation of the outer lining of the heart. Most patients with myocarditis or pericarditis after COVID-19 vaccination responded well to medicine and rest and felt better quickly. As of 10 February 2022, VAERS has received 2,239 preliminary reports of myocarditis or pericarditis among people ages 30 years and younger who received COVID-19 vaccines. Most cases have been reported after receiving Pfizer-BioNTech or Moderna vaccines, particularly in male adolescents and young adults.

Reports of deaths after COVID-19 vaccination are rare. The FDA requires healthcare providers to report any death after COVID-19 vaccination to VAERS, even if it is unclear whether the vaccine was the cause. Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem. More than 547 million doses of COVID-19 vaccines were administered in the United States from 14 December 2020 through 14 February 2022. During this time, VAERS received 12,304 reports of death (0.0022%) among people who received a COVID-19 vaccine. CDC and FDA clinicians review deaths reported to VAERS, including death certificates, autopsies, and medical records, and often rule out a causal association.

Source: Centers for Disease Control and Prevention (CDC). Selected Adverse Events Reported after COVID-19 Vaccination. Updated 25 February 2022. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html>.

## PARAGUAY

As of 11 February 2022, 7,706,155 doses of COVID-19 vaccines had been administered. A total of 2,668 AEFI reports have been reported since the start of the vaccination program (22 February 2021 to 11 February 2022), representing 0.03% of total doses administered. A total of 438 cases were considered serious, representing 0.006% of total doses administered.

The highest reported rate of AEFI is associated with the CoronaVac vaccine (418.58/100,000 doses administered), followed by Covaxin (80.37/100,000 doses administered) and AstraZeneca (67.04/100,000 doses administered). Of the reports associated with the CoronaVac vaccine, 94% were non-serious AEFI; 71% (1,893) of AEFI reports involved females. Reports of AEFI were mostly seen (1,797 out of 2,668) in the 25-49-year-old age group.

Source: Paraguay Ministry of Public Health and Social Welfare. AEFI Surveillance Information Bulletin No. 48 Regarding COVID-19 Vaccination. National Program on Immunopreventable Diseases and Expanded Program on Immunizations, 11 February 2022. Available at: <https://pai.mspbs.gov.py/wp-content/uploads/2022/02/48-Boletin-Epidemiologico-ESAVI.pdf>.

## Publications on potential safety signals identified with the use of COVID-19 vaccines

Final efficacy analysis, interim safety analysis, and immunogenicity of a single dose of recombinant novel coronavirus vaccine (adenovirus type 5 vector) in adults 18 years and older: an international, multicenter, randomized, double-blinded, placebo-controlled phase 3 trial

On 13 January 2022, a study was published with the final efficacy analysis, and interim safety analysis, of the phase 3, double-blinded, randomized, international, placebo-controlled, endpoint-case-driven clinical trial in adults ages 18 years and older, at study centers in Argentina, Chile, Mexico, Pakistan, and Russia. Participants were eligible for the study if they had no unstable or severe underlying medical or psychiatric conditions; had no history of a laboratory-confirmed SARS-CoV-2 infection; were not pregnant or breastfeeding; and had not previously received an adenovirus-vector, coronavirus, or SARS-CoV-2 vaccine. After informed consent was obtained, 25 mL of whole blood was withdrawn from all eligible participants who were randomized in a 1:1 ratio to receive a single intramuscular dose of 0.5 mL placebo or a 0.5 mL dose of  $5 \times 10^{10}$  viral particle (vp)/mL Ad5-nCoV vaccine; study staff and participants were blinded to treatment allocation. All participants were contacted weekly by email, telephone, or text message to self-report any symptoms of COVID-19 illness, and laboratory testing for SARS-CoV-2 was done for all participants with any symptoms. The primary efficacy objective evaluated Ad5-nCoV in preventing symptomatic, PCR-confirmed COVID-19 infection occurring at least 28 days after vaccination in all participants.

The primary safety objective evaluated the incidence of any serious adverse events or medically attended adverse events postvaccination in all participants who received a study injection. One dose of Ad5-nCoV showed a 57.5% (95% CI 39.7-70.0,  $p=0.0026$ ) efficacy against symptomatic, PCR-confirmed, COVID-19 infection at 28 days or more postvaccination (21,250 participants; 45 days median duration of follow-up [IQR 36-58]). In the primary safety analysis, there was no significant difference in the incidence of serious adverse events (14 [0.1%] of 18,363 Ad5-nCoV recipients and 10 [0.1%] of 18,354 placebo recipients,  $p=0.54$ ) or medically attended adverse events (442 [2.4%] of Ad5-nCoV recipients and 411 [2.2%] of placebo recipients,  $p=0.30$ ). In the extended safety cohort, 1,004 (63.5%) of 1,582 Ad5-nCoV recipients and 729 (46.4%) of 1,572 placebo recipients reported expected systemic adverse events ( $p<0.0001$ ), of which headache was the most common (699 [44%] of Ad5-nCoV recipients and 481 [30.6%] of placebo recipients;  $p<0.0001$ ); 971 (61.3%) of 1,584 Ad5-nCoV recipients and 314 (20.0%) of 1,573 placebo recipients reported an injection-site adverse event ( $p<0.0001$ ), of which pain at the injection site was the most frequent. The authors conclude, based on these data, that one dose of Ad5-nCoV is efficacious and safe in unvaccinated healthy adults aged 18 years and older.

Source: Scott A Halperin, Lingyun Ye, Donna MacKinnon-Cameron, et al. Final efficacy analysis, interim safety analysis, and immunogenicity of a single dose of recombinant novel coronavirus vaccine (adenovirus type 5 vector) in adults 18 years and older: an international, multicenter, randomized, double-blinded, placebo-controlled phase 3 trial. Lancet 2022; 399: 237–48 doi: 10.1016/S0140-6736(21)02753-7. <https://pubmed.ncbi.nlm.nih.gov/34953526/>.

### SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study

On 30 November, a population based cohort study was published in Denmark investigating the association between SARS-CoV-2 vaccination and myocarditis or myopericarditis. A total of 4,931,775 individuals aged 12 years or older residing in Denmark participated. The primary outcome, myocarditis or myopericarditis, was defined as a combination of a hospital diagnosis of myocarditis or pericarditis, increased troponin levels, and a hospital stay lasting more than 24 hours. Follow-up time before vaccination was compared with follow-up time 0-28 days from the day of vaccination for both first and second doses. During follow-up, 269 participants developed myocarditis or myopericarditis, of whom 108 (40%) were 12-39 years old and 196 (73%) were male.

Of the total events involving myocarditis or myopericarditis, 200 occurred before vaccination, in unvaccinated individuals, or in those vaccinated with other vaccines (Vaxzevria and Janssen, before being discontinued), and 69 in the 28 days after vaccination with Comirnaty or Spikevax (almost 4 million people).

Of 3,482,295 individuals vaccinated with BNT162b2 (Pfizer-BioNTech), 48 developed myocarditis or myopericarditis within 28 days following the vaccination date compared with unvaccinated individuals (adjusted hazard ratio 1.34 (95% CI 0.90 to 2.00); absolute rate 1.4 per 100,000 vaccinated individuals within 28 days following vaccination (95% CI 1.0 to 1.8). The adjusted risk ratios between female and male participants were 3.73 (95% CI 1.82 to 7.65) and 0.82 (0.50 to 1.34), respectively, with the corresponding absolute rates of 1.3 (95% CI 0.8 to 1.9) and 1.5 (1.0 to 2.2) per 100,000 individuals vaccinated within 28 days following vaccination, respectively. The adjusted hazard ratio among 12-39-year-olds was 1.48 (95% CI 0.74 to 2.98) and the absolute rate was 1.6 (95% CI 1.0 to 2.6) per 100,000 vaccinated individuals within 28 days following vaccination.

Among 498,814 individuals vaccinated with mRNA-1273 (Moderna), 21 developed myocarditis or myopericarditis within 28 days following the vaccination date (adjusted hazard ratio 3.92 [CI 95% 2.30 to 6.68]; absolute rate 4.2 per 100,000 vaccinated individuals within 28 days of vaccination [CI 95% 2.6 to 6.4]). Adjusted hazard ratios among women only and men only were 6.33 (CI 95% 2.11 to 18.96) and 3.22 (95% CI 1.75 to 5.93), respectively, with corresponding absolute rates of 2.0 (CI 95% 0.7 to 4.8) and 6.3 (3.6 to 10.2) per 100,000 vaccinated individuals within 28 days following vaccination, respectively. The adjusted hazard ratio among 12-39-year-olds was 5.24 (CI 95% 2.47 to 11.12), and the absolute rate was 5.7 (CI 95% 3.3 to 9.3) per 100,000 vaccinated individuals within 28 days following vaccination.

The authors conclude that vaccination with mRNA-1273 was associated with a significantly increased risk of myocarditis or myopericarditis in the Danish population, primarily driven by an increased risk among individuals aged 12-39, while BNT162b2 vaccination was only associated with a significantly increased risk among women. However, the absolute rate of myocarditis or myopericarditis after SARS-CoV-2 mRNA vaccination was low, even in younger age groups. The benefits of SARS-CoV-2 mRNA vaccination should be taken into account when interpreting these findings. Larger multinational studies are needed to further investigate the risks of myocarditis or myopericarditis after vaccination within smaller subgroups.

Source: Husby A, Hansen JV, Fosbøl E, Thieson EM, Madsen M, Thomsen RW et al. SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study. *BMJ* 2021;375:e068665.

### [Myocardial infarction, stroke, and pulmonary embolism after BNT162b2 mRNA COVID-19 vaccine in people aged 75 years or older, in France](#)

On 22 November 2021, a population-based study was published in which the short-term risk of serious cardiovascular events was evaluated among individuals in France aged 75 years or older after administration of the BNT162b2 mRNA vaccine. This study used the French National Health Data System linked to the national COVID-19 vaccination

database. Eligible participants were all unvaccinated or vaccinated with the BNT162b2 vaccine, aged 75 years or older, admitted to the hospital between 15 December 2020 and 30 April 2021, for acute myocardial infarction, hemorrhagic stroke, ischemic stroke, or pulmonary embolism. The authors used within-person comparisons using a self-controlled case-series method adapted to cardiovascular event-dependent exposures and high event-related mortality that can cancel or defer subsequent vaccination or increase short-term mortality. Exposure risk intervals were days one through 14 following each of the two vaccine doses. The exposure risk interval was further subdivided into days one through seven and days eight through 14. Except for the vaccination day, the remaining periods were regarded as nonrisk periods. Unvaccinated persons were included to account for temporal effects. Unbiased estimating equations were used to calculate the relative incidence (RI) adjusted for temporality (in 7-day increments) to consider any changes in background rates of both events and vaccination. Over the observation period, 11,113 persons aged 75 years or older were hospitalized for an acute myocardial infarction, 17,014 for an ischemic stroke, 4,804 for a hemorrhagic stroke, and 7,221 for pulmonary embolism, of whom 58.6%, 54.0%, 42.7%, and 55.3%, respectively, received at least one dose of the vaccine. In the 14 days following either dose, no significant increased risk was found for any outcome: the RI for myocardial infarction for the first dose was 0.97 (95% CI, 0.88-1.06), and for the second dose, 1.04 (95% CI, 0.93-1.16); for ischemic stroke for the first dose, 0.90 (95% CI, 0.84-0.98) and for the second dose, 0.92 (95% CI, 0.84-1.02); for hemorrhagic stroke for the first dose, 0.90 (95% CI, 0.78-1.04) and for the second dose, 0.97 (95% CI 0.81-1.15); and for pulmonary embolism for the first dose, 0.85 (95% CI, 0.75-0.96) and for the second dose, 1.10 (95% CI, 0.95-1.26). No significant increase for any of the cardiovascular events was observed in the two subdivided exposure intervals (days 1-7 and days 8-14).

The authors conclude that in this nationwide study with people aged 75 years or older in France, no increase in the incidence of acute myocardial infarction, stroke, and pulmonary embolism was detected 14 days following each BNT162b2 mRNA vaccine dose.

Source: Marie-Joëlle Jabagi, Jérémie Botton, Marion Bertrand, et al. Myocardial Infarction, Stroke, and Pulmonary Embolism After BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older. JAMA. 2022;327(1):80–82. doi: 10.1001/jama.2021.21699.

### Cases of myocarditis reported after mRNA-based COVID-19 vaccination in the U.S. from December 2020 to August 2021

On 25 January 2022, a descriptive study of reports of myocarditis to the Vaccine Adverse Event Reporting System (VAERS) that occurred after administration of mRNA-based COVID-19 vaccines (vaccination with BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna]) between December 2020 and August 2021, in 192,405,448 individuals older than 12 years of age in the U.S., was published. Data were processed by VAERS as of 30 September 2021. Reports



of myocarditis to VAERS were for all age groups. Crude reporting rates were calculated across age and sex strata. Expected rates of myocarditis by age and sex were calculated using 2017-2019 claims data. For persons younger than 30 years of age, medical record reviews and clinician interviews were conducted to describe clinical presentation, diagnostic test results, treatment, and early outcomes. The results showed that among 192,405,448 persons receiving a total of 354,100,845 mRNA-based COVID-19 vaccine doses during the study period, there were 1,991 reports of myocarditis to VAERS, and 1,626 of these reports met the case definition of myocarditis. Of those with myocarditis, the median age was 21 years (IQR, 16-31 years) and the median time to symptom onset was two days (IQR, 1-3 days). Males comprised 82% of the myocarditis cases for whom sex was reported. The crude reporting rates for cases of myocarditis within seven days after COVID-19 vaccination exceeded the expected rates of myocarditis across multiple age and sex strata. The rates of myocarditis were highest after the second vaccination dose in adolescent males aged 12 to 15 years (70.7 per million doses of the BNT162b2 vaccine), in adolescent males aged 16 to 17 years (105.9 per million doses of the BNT162b2 vaccine), and in young men aged 18 to 24 years (52.4 and 56.3 per million doses of the BNT162b2 vaccine and the mRNA-1273 vaccine, respectively). There were 826 cases of myocarditis among those younger than 30 years of age for whom detailed clinical information was available; of these cases, 792 of 809 (98%) had elevated troponin levels, 569 of 794 (72%) had abnormal electrocardiogram results, and 223 of 312 (72%) had abnormal cardiac magnetic resonance imaging results. Approximately 96% of persons (784/813) were hospitalized and 87% (577/661) of these had resolution of presenting symptoms by hospital discharge. The most common treatment was nonsteroidal anti-inflammatory drugs (589/676; 87%).

The authors conclude that based on passive surveillance reporting in the US, the risk of myocarditis after receiving mRNA-based COVID-19 vaccines was increased across multiple age and sex strata and was highest after the second vaccination dose in adolescent males and young men. This risk should be considered in the context of the benefits of COVID-19 vaccination.

Source: Matthew E. Oster; David K. Shay, et al, Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the U.S. From December 2020 to August 2021. JAMA.2022;327(4):331–340. doi: 10.1001/jama.2021.2410.

### [Myocarditis after COVID-19 vaccination in a large health care organization in Israel](#)

A retrospective cohort study was published on 6 October 2021 that looked at the frequency and severity of myocarditis after vaccination with mRNA COVID-19 vaccines. The frequency of reports of myocarditis after receiving at least one dose of BNT162b2 mRNA vaccine was assessed at Clalit Health Services, the largest health care organization (HCO) in Israel, and the clinical course and severity of the disease were described based on a review of patients' medical histories. The diagnosis of myocarditis was made by cardiologists using the case definition used by the Centers for Disease Control and Prevention (CDC). The authors performed a Kaplan-Meier analysis of the incidence of myocarditis

up to 42 days after the first vaccine dose. Among more than 2.5 million vaccinated HCO members who were 16 years of age or older, 54 cases met the criteria for myocarditis. The estimated incidence per 100,000 persons who had received at least one dose of vaccine was 2.13 cases (95% confidence interval, 1.56 to 2.70). The highest incidence of myocarditis (10.69 cases per 100,000 persons) was reported in male patients between the ages of 16 and 29 years (95% CI, 6.93 to 14.46). A total of 76% of cases of myocarditis were described as mild and 22% as intermediate; one case was associated with cardiogenic shock. After a median follow-up of 83 days after the onset of myocarditis, one patient had been readmitted to the hospital, and one had died of an unknown cause after discharge. Of 14 patients who had left ventricular dysfunction on echocardiography during admission, 10 still had such dysfunction at the time of hospital discharge. Of these patients, five underwent subsequent testing that revealed normal heart function.

The authors conclude that among patients in a large Israeli health care system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons; the highest incidence was among male patients between the ages of 16 and 29. Most cases of myocarditis were mild or moderate in severity.

Source: Witberg G, Barda N, Hoss S, et al. Myocarditis after Covid-19 Vaccination in a Large Health Care Organization. *New England Journal of Medicine*, December 2, 2021, 385(23):2132.

### Evaluation of the safety, immunogenicity, and efficacy of SARS-CoV-2 mRNA-1273 vaccine in adolescents

On 11 August 2021, a study was published evaluating the safety, immunogenicity, and efficacy of the SARS-CoV-2 mRNA-1273 vaccine in adolescents in the U.S. In this ongoing phase 2–3, placebo-controlled trial, healthy adolescents (12 to 17 years of age) were randomly assigned in a 2:1 ratio to receive two injections of the mRNA-1273 vaccine (100 µg in each) or placebo, administered 28 days apart. The primary objectives were evaluation of the safety of mRNA-1273 in adolescents and the noninferiority of the immune response in adolescents as compared with that in young adults (18 to 25 years of age) in a phase 3 trial. Secondary objectives included the efficacy of mRNA-1273 in preventing Covid-19 or asymptomatic severe acute respiratory syndrome coronavirus 2 infection. A total of 3,732 participants were randomly assigned to receive mRNA-1273 (2,489 participants) or placebo (1,243 participants). In the mRNA-1273 group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 93.1% and 92.4%, respectively), headache (in 44.6% and 70.2%, respectively), and fatigue (in 47.9% and 67.8%, respectively); in the placebo group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 34.8% and 30.3%, respectively), headache (in 38.5% and 30.2%, respectively), and fatigue (in 36.6% and 28.9%, respectively). No serious adverse events related to mRNA-1273 or placebo were noted. The geometric mean titer ratio of pseudovirus neutralizing antibody titers in adolescents relative to young adults was 1.08 (95% confidence interval 0.94 to 1.24), and the absolute difference in serologic response was 0.2 percentage points



(95% CI, -1.8 to 2.4), which met the noninferiority criterion. No cases of Covid-19 with an onset of 14 days after the second injection were reported in the mRNA-1273 group, and four cases occurred in the placebo group.

The authors conclude that the mRNA-1273 vaccine had an acceptable safety profile in adolescents. The immune response was similar to that in young adults, and the vaccine was efficacious in preventing Covid-19.

Source: Ali K, Berman G, Zhou H, et al. Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents. *New England Journal of Medicine*, December 9, 2021, 385(24):2241.

### Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicenter, randomized, controlled, phase 2 trial

On 2 December 2021, a multicenter, randomized, controlled, phase 2 trial of a third dose booster vaccination against COVID-19 (COV-BOOST) was published. The trial was conducted at 18 sites in the UK to assess the safety and immunogenicity of seven COVID-19 vaccines as booster doses. Participants were aged older than 30 years, and were at least 70 days post two doses of ChAdOx1 nCov-19 (Oxford–AstraZeneca; hereafter referred to as ChAd) or at least 84 days post two doses of BNT162b2 (Pfizer–BioNtech; hereafter referred to as BNT) primary COVID-19 immunization course, with no history of laboratory-confirmed SARS-CoV-2 infection. Eighteen sites were divided into three groups (A, B, and C). Within each site group (A, B, or C), participants were randomly assigned to an experimental vaccine or control. Group A received NVX-CoV2373 (Novavax; hereafter referred to as NVX), a half dose of NVX, ChAd, or quadrivalent meningococcal conjugate vaccine (MenACWY) control (1:1:1:1). Group B received BNT, VLA2001 (Valneva; hereafter referred to as VLA), a half dose of VLA, Ad26.COV2.S (Janssen; hereafter referred to as Ad26) or MenACWY (1:1:1:1:1). Group C received mRNA1273 (Moderna; hereafter referred to as m1273), CvnCov (CureVac; hereinafter, CVn), half a dose of BNT or MenACWY (1:1:1:1). Participants and all investigatory staff were blinded to treatment allocation. Coprimary outcomes were safety, reactogenicity, and immunogenicity of anti-spike IgG measured by ELISA. The primary analysis for immunogenicity was on a modified intention-to-treat basis; safety and reactogenicity were assessed in the intention-to-treat population. Secondary outcomes included assessment of viral neutralization and cellular responses.

A total of 2,878 participants met eligibility criteria and received COVID-19 vaccine or control. The median ages of ChAd/ChAd-primed participants were 53 years (IQR 44–61) in the younger age group and 76 years (73–78) in the older age group. In the BNT/BNT-primed participants, the median ages were 51 years (41–59) in the younger age group and 78 years (75–82) in the older age group. Three vaccines showed overall increased reactogenicity: m1273 after ChAd/ChAd or BNT/BNT; and ChAd and Ad26 after BNT/BNT. For ChAd/ChAd-primed individuals, spike IgG geometric mean ratios (GMRs) between study vaccines and controls ranged from 1.8 (99% CI 1.5–2.3) in the half VLA group to 32.3 (24.8–42.0) in the m1273 group. GMRs for wild-type cellular responses compared with controls ranged

from 1.1 (95% CI 0.7–1.6) for ChAd to 3.6 (2.4–5.5) for m1273. For BNT/BNT-primed individuals, spike IgG GMRs ranged from 1.3 (99% CI 1.0–1.5) in the half VLA group to 11.5 (9.4–14.1) in the m1273 group. GMRs for wild-type cellular responses compared with controls ranged from 1.0 (95% CI 0.7–1.6) for half VLA to 4.7 (3.1–7.1) for m1273. The results were similar between those aged 30–69 years and those aged 70 years and older. Fatigue and pain were the most common solicited local and systemic adverse events, experienced more in people aged 30–69 years than those aged 70 years or older. Serious adverse events were uncommon, similar in active vaccine and control groups. In total, there were 24 serious adverse events: five in the control group (two in control group A, three in control group B, and zero in control group C), two in Ad26, five in VLA, one in VLA-half, one in BNT, two in BNT-half, two in ChAd, one in CVn, two in NVX, two in NVX-half, and one in m1273.

The authors conclude that findings from this trial demonstrate that the immunogenicity of homologous or heterologous third dose boost with all tested vaccines was superior to control regardless of which vaccine had been received in the initial course, apart from VLA, which did not achieve predefined criteria for minimum clinically important difference following BNT/BNT. No specific safety issues were noted. Substantial differences in humoral and cellular responses and vaccine availability will influence policy choices for booster vaccination.

Source: Munro APS, Janani L, Cornelius V, Aley PK, Babbage G, Baxter D et al. Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicenter, randomized, controlled, phase 2 trial. *Lancet* 2021; doi: 10.1016/S0140-6736(21)02718-5.

## COVID-19 vaccines safety update, for vaccines authorized by the European Medicines Agency

On 20 January and 17 February 2022, the European Medicines Agency (EMA) released safety updates for the following vaccines, which are summarized below:

- **The Janssen vaccine and AstraZeneca's Vaxzevria:** Product information will be updated to
  - add transverse myelitis as a side effect.
  - In regard to thrombosis with thrombocytopenia syndrome (TTS), this update will remove the current statement that reported TTS cases occurred mostly in women, since the sex imbalance seems smaller than previously observed. The update indicates: The observed cases occurred within the first three weeks following vaccination, mostly in individuals under 60 years of age.
- **Moderna's Spikevax Vaccine:** Product information has been updated to include paresthesia as a rare adverse effect.
- **Pfizer-BioNTech's Comirnaty Vaccine and Moderna's Spikevax:** Product information has been updated to include the use of these vaccines during pregnancy and lactation.

For additional information on these updates, see: [https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccines-safety-update-20-january-2022\\_en.pdf](https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccines-safety-update-20-january-2022_en.pdf).

[https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccines-safety-update-17-february-2022\\_en.pdf](https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccines-safety-update-17-february-2022_en.pdf).

## Report on the Global Regulatory Response to the Omicron Variant from the International Coalition of Medicines Regulatory Authorities (ICMRA)

On 21 January 2022, The International Coalition of Medicines Regulatory Authorities (ICMRA) published a report on the global regulatory response to the Omicron variant, which includes recommendations regarding the composition of the new vaccines and regulatory aspects related to their authorization. In this regard, they emphasize the need to explore the feasibility of developing bivalent or multivalent variant vaccines to determine if they offer advantages to monovalent vaccines.

In relation to the clinical studies necessary to support the use of the new vaccines, they indicated that these should be designed to demonstrate that the immune response, measured as neutralizing antibodies, generated by the updated vaccine is superior to that achieved with current vaccines, as well as their ability to cross-neutralize other variants of concern.

In addition, international regulators emphasized the need for regulatory alignment, in order to expedite and streamline global development and authorization of new or modified COVID-19 vaccines against emerging coronavirus variants.

For additional information on this report, see: <https://www.ema.europa.eu/en/news/international-regulators-recommendations-covid-19-vaccines-omicron-variant>.

## COVID-19 vaccines and their use in children, pregnant women, and immunocompromised individuals

Given the importance of differentiating the recommended conditions of use for the different COVID-19 vaccines authorized to date, and the importance of avoiding errors or confusion in their administration, the following summarizes the recommendations for the use of vaccines widely distributed in the Region, in children, pregnant women, and immunocompromised individuals, taking into consideration recommendations of WHO's Strategic Advisory Group of Experts (SAGE) on Immunization and the National Regulatory Authorities of Regional Reference.

It is recommended that this summary table be disseminated among health personnel involved in the use of COVID-19 vaccines.

## Summary of conditions of the use of COVID-19 vaccines in children, pregnant women, and immunocompromised individuals

COVID-19 vaccine	Indication, dose, and interval					
	Ages 5 to 11	Ages 12 to 17	Pregnant and breastfeeding women	Moderately or severely immunocompromised individuals		
				Ages 5 to 11	Ages 12 to 17	Ages 18 and older
COVISHIELD, manufactured by the Serum Institute of India SII	-	-	<u>SAGE:</u> Pregnancy: Only if the benefits outweigh the potential risk.	-	-	<u>SAGE:</u> Two doses (0.5 mL) at 4–12-week intervals.
AstraZeneca's VAXZEVRIA	-	-	Breastfeeding: Use is recommended.	-	-	
Pfizer BioNTech's COMIRNATY	<u>SAGE:</u> Two doses of 10 µg (0.2 mL) at 2–8-week intervals* ●	<u>SAGE:</u> Two doses of 30 µg (0.3 mL) at 2–8-week intervals* ●	<u>SAGE:</u> Two doses of 30 µg (0.3 mL) at 2–8-week intervals* ●	<u>SAGE:</u> Two doses of 10 µg (0.2 mL) at 2–8-week intervals* ●	<u>SAGE:</u> Two doses of 30 µg (0.3 mL) at 2–8-week intervals,* one dose of 30 µg (0.3 mL) at 1–3-months, and one booster dose at 4–6-months.	
CanSino's CONVIDECIA	–	-	ISP/Chile: Pregnancy and breastfeeding: When the benefits outweigh the potential risks.	-	-	ISP/Chile: When the benefits outweigh the potential risks.
Sinovac's CORONAVAC	ISP/Chile: Starting at three years of age, two doses (0.5 mL) at 2–4-week intervals, and one booster dose (0.5 mL) at four months.	ISP/Chile: Two doses (0.5 mL) at 2–4-week intervals, and one booster dose (0.5 mL).	<u>SAGE:</u> Pregnancy: Only if the benefits outweigh the potential risks. Breastfeeding: Use is recommended.			<u>SAGE:</u> Two doses (0.5 mL) at 3–4-week intervals, and one dose (0.5 mL) at 1–3-months.
Bharat Biotech's COVAXIN	-	-	<u>SAGE:</u> Pregnancy: Only if the benefits outweigh the potential risks. Breastfeeding: Use is recommended.	-	-	<u>SAGE:</u> Two doses (0.5 mL) at one-month intervals, and one dose (0.5 mL) at 1–3 months.
Sinopharm inactivated (vero cell)	Argentina: Starting at three years of age, two doses (0.5 mL) at a minimum of three-week intervals.	Argentina: Two doses (0.5 mL) at a minimum of three-week intervals.	<u>SAGE:</u> Pregnancy: Only if the benefits outweigh the potential risks. Breastfeeding: Use is recommended.			<u>SAGE:</u> Two doses (0.5 mL) at 3–4-week intervals, and one dose (0.5 mL) at 1–3 months.
Moderna's SPIKEVAX	-	<u>SAGE:</u> Two doses (100 µg, 0.5 mL) at 4–8-week intervals,* and one booster dose of 50 µg (0.25 mL) ● at 4–6 months.	<u>SAGE:</u> Pregnancy and breastfeeding: Use is recommended.	-	<u>SAGE:</u> 3 doses of 100 µg at 4–8-week intervals, and one booster dose of 50 µg at 3–6 months.	
Janssen Ad26.COV2-S (recombinant)	-	-	<u>SAGE:</u> Pregnancy: Only if the benefits	-	-	<u>SAGE:</u> Two doses (0.5 mL) at 1–3-month intervals.

			outweigh the potential risks. Breastfeeding: Use is recommended.			
Novavax's NUVAXOVID	-	-	SAGE: Pregnancy: Only if the benefits outweigh the potential risks. Breastfeeding: Use is recommended.			SAGE: Two doses (0.5 mL) at 3–4-week intervals, and one dose (0.5 mL) at 1-3 months.
Gamaleya's SPUTNIK V/SPUTNIK LIGHT	-	-	ISP/Chile: Pregnancy and breastfeeding: When the benefits outweighs the potential risks.	-	-	-

Source: WHO Recommendations of the WHO Strategic Advisory Group of Experts (SAGE) on Immunization. Accessed 25 Feb. 2022. Available at: <https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>.

Argentina Ministry of Health. COVID-19 Pediatric Vaccine FAQ. Accessed 25 February 2022. Available at: <https://www.argentina.gob.ar/coronavirus/vacuna/preguntas-frecuentes-pediatricas>.

ISP, Chile. Convidencia suspension for injection (recombinant Ad5-nCoV COVID-19 vaccine). Accessed 25 February 2022. Available at: <https://www.ispch.cl/wp-content/uploads/2021/05/FIV-CanSinoV01-25052021B.pdf>.

ISP, Chile. Vaccine information sheet on CoronaVac vaccine suspension for injection (inactivated SARS-CoV-2, virion, adsorbed). Accessed 25 Feb. 2022. Available at: <https://www.ispch.cl/wp-content/uploads/2021/05/FIV-CanSinoV01-25052021B.pdf>.

ISP, Chile. Technical sheet on Gam-COVID-Vac injectable suspension (Ad.26COV2-S, Ad.5COV2-S, recombinant COVID-19 vaccine). Accessed 25 Feb. 2022. Available at: <https://www.ispch.cl/wp-content/uploads/2021/05/FIV-CanSinoV01-25052021B.pdf>.

● According to the WHO roadmap for prioritization criteria, available at <https://www.who.int/publications/i/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines>, preferably 8 weeks, since a longer interval is associated with greater vaccine efficacy and a potentially lower risk of myocarditis/pericarditis.

### Updated recommendations of the WHO Strategic Advisory Committee of Experts (SAGE) on Immunization for the Pfizer-BioNTech mRNA COVID-19 vaccine

On 21 January 2022, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization issued updated recommendations for the use of Pfizer-BioNTech's mRNA COVID-19 vaccine (BNT162b2); a summary of the key updates is provided below.

- **Indication:** For individuals ages 5 years or older, according to the prioritization criteria for the various population groups in the WHO prioritization roadmap.
- **Administration:** Individuals ages 12 years and older, two doses of 30 µg (0.3 ml); children ages 5 to 11, two doses of 10 µg (0.2 ml), 4 to 8 weeks after the first dose; preferably 8 weeks, since a longer interval is associated with increased vaccine efficacy and a potentially lower risk of myocarditis/pericarditis.
- **Booster:** One booster dose is recommended for the highest priority groups (adults and health workers, individuals with comorbidities) according to the WHO prioritization roadmap, 4 to 6 months after completing the primary series. Once high booster dose coverage has been achieved in the highest priority group, consider a booster for lower priority groups. The need for, and timing of, booster doses for children ages 5 to 11 have not yet been determined.
- **Interchangeability with other COVID-19 vaccines:** Use of the same vaccine (homologous schedule) is considered standard practice based on comprehensive safety data. However, WHO supports a flexible approach, using heterologous schemes with any EUL vaccine.
- **Pregnant and breastfeeding women:** Given current evidence on the safety and efficacy of this vaccine in pregnancy, WHO recommends use of the BNT162b2 vaccine in pregnant and breastfeeding women.
- **Individuals who are moderately or severely immunocompromised:** One-third dose of 30 µg starting at age 12 is recommended, and 10 µg in individuals ages 5 to 11, one to three months after the second dose of the standard primary series. Given the appearance of Omicron, one booster dose (fourth dose) may be considered 4 to 6 months after the additional dose for immunocompromised individuals.
- **Storage period:** Based on additional stability studies, the maximum permissible storage period for an unopened thawed vial, preserved at between 2°C to 8°C (after removal from deep-freeze conditions) was extended from five days to one month (31 days).

For additional information, see: [https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-BNT162b2-2021.1](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1).



## Updated recommendations of the WHO Strategic Advisory Committee of Experts (SAGE) on Immunization for the Moderna mRNA COVID-19 vaccine

On 23 February 2022, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization issued updated recommendations for use of the Moderna mRNA COVID-19 vaccine (mRNA-1273); a summary of the key updates is provided below.

- **Indication:** For individuals ages 12 or older, according to the prioritization criteria for the various population groups in the WHO prioritization roadmap.
- **Administration:** Two doses of 100 µg (0.5 ml), 4 to 8 weeks after the first dose; preferably 8 weeks, since a longer interval is associated with increased vaccine efficacy and a potentially lower risk of myocarditis/pericarditis.
- **Booster:** One booster dose of 50 µg (0.25 ml), half the primary series dose, is recommended for the highest priority groups (adults and health workers, individuals with comorbidities), according to the WHO prioritization roadmap, 4 to 6 months after completing the primary series.
- **Interchangeability with other COVID-19 vaccines:** WHO supports a flexible approach, using heterologous schedules with any EUL vaccine for the two doses of the primary series.
- **Heterologous booster:** A 50 µg (0.25 ml) dose of the Moderna vaccine can be used as a booster for any of the EUL COVID-19 vaccines.
- **Pregnant and breastfeeding women:** Given current evidence on the safety and efficacy of this vaccine in pregnancy, WHO recommends use of the Moderna vaccine in pregnant and breastfeeding women.
- **Individuals who are moderately or severely immunocompromised:** One-third of a full dose of 100 µg for immunocompromised individuals is recommended, and given the appearance of Omicron, one booster (fourth) dose of 50 µg 3 to 6 months after the third dose.

For additional information, see: <https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19>.

## The EMA Pharmacovigilance Risk Assessment Committee assessed reported cases of menstrual disorders with COVID-19 mRNA vaccines

At the meeting of 7-10 February 2022, the Pharmacovigilance Risk Assessment Committee (PRAC), of the European Medicines Agency (EMA), assessed reported cases of heavy menstrual bleeding (heavy periods) and absence of menstruation (amenorrhea) with the COVID-19 vaccines Comirnaty and Spikevax.

In October 2021, the Committee had analyzed reports of menstrual disorders and had concluded that there was insufficient evidence to suggest a causal relationship between COVID-19 mRNA vaccines and menstrual disorders; but at the meeting held in February 2022, it decided to further assess the occurrence of heavy

periods or amenorrhea after vaccination with Comirnaty and Spikevax, in view of the spontaneous reports of menstrual disorders received with both vaccines.

The Committee noted that, at present, it is not yet clear whether there is a causal link between COVID-19 vaccines and reports of heavy periods or amenorrhea. There is also no evidence to suggest that COVID-19 vaccines affect fertility. The EMA will provide further information when it becomes available.

For additional information on the PRAC meeting, see:

<https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-10-13-january-2022>.

### WHO authorizes shelf-life extension of Moderna's COVID-19 mRNA vaccine

The World Health Organization authorized extension of the shelf-life of Moderna Biotech's Spikevax mRNA COVID-19 vaccine from seven months (stored at between -15°C and -25°C) to nine months. Within the nine months of shelf life, the vaccine can be stored for 30 days at 2°C -8°C.

For additional information on this vaccine, see: <https://extranet.who.int/pqweb/vaccines/covid-19-mrna-vaccine-nucleoside-modified>.

### Self-study course on the WHO methodology for AEFI causality assessment

WHO, through the WHO iLearn platform, made available the course WHO - AEFI causality assessment. This e-learning course consists of two training components:

- AEFI causality assessment; and
- How to use the AEFI causality assessment software.

To take this course, the participant must register on the WHO iLearn platform at:

<https://who.csod.com/selfreg/register.aspx?c=aefi%20causality%20assessment>.

Users registered on this platform can access the course at:

<https://who.csod.com/phnx/driver.aspx?routename=Learning/Curriculum/CurriculumPlayer&TargetUser=46361&curriculumLoid=5c653f1e-79f5-4230-84c3-f8dff4f83515>.

### The European Medicines Agency updates the guidance for preparing risk management plans for COVID-19 vaccines

On 8 February 2022, the European Medicines Agency (EMA) updated its guidance for preparing risk management plans for COVID-19 vaccines authorized in the European Union (EU).

This guidance reflects the EMA recommendations, based on current knowledge and experience. As the pandemic situation evolves and further evidence becomes available for the authorized vaccines, EMA guidance should be taken into account when planning for post-marketing vaccine surveillance, in the context of marketing authorization in the EU.

For additional information on this update, see: [https://www.ema.europa.eu/en/documents/other/consideration-core-requirements-rmps-covid-19-vaccines\\_en.pdf](https://www.ema.europa.eu/en/documents/other/consideration-core-requirements-rmps-covid-19-vaccines_en.pdf).

## Decisions of the Region's Regulatory Authorities

### National Health Surveillance Agency (ANVISA), Brazil

On 7 January 2022, ANVISA authorized including the Oswaldo Cruz Foundation (Fiocruz) as a manufacturer of the active ingredient of the COVID-19 vaccine produced by Fiocruz/AstraZeneca. In reaching this decision, ANVISA evaluated the studies that compared the imported vaccine with the vaccine developed in the country, which demonstrated that the two vaccines were similar.

On 22 February 2021, Fiocruz reported on its website that it had delivered to Brazil's Ministry of Health the first batch of COVID-19 vaccine made entirely in the country.

Additional information can be found at: <https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2022/anvisa-aprova-o-registro-do-insumo-da-fiocruz-e-o-brasil-tera-vacina-100-nacional>.

<https://portal.fiocruz.br/en/node/172206>.

## Health Canada, Canada

On 24 February 2022, Health Canada reported authorization of Medicago's COVIFENZ COVID-19 vaccine for adults 18 to 64 years of age, with a two-dose immunization schedule of 3.75 micrograms per dose, 21 days apart. This is the first licensed COVID-19 vaccine developed by a Canadian-based company, and the first to use plant-based protein technology.

In clinical trials, the vaccine was found to be 71% effective against symptomatic infection and 100% effective against severe disease caused by COVID-19, and demonstrated efficacy against the Delta and Gamma variants, with data suggesting efficacy against the Alpha, Lambda, and Mu variants. With regard to the Omicron variant, it noted that preliminary and exploratory data show that COVIFENZ produces neutralizing antibodies against this variant of concern. The phase 3 clinical trial to evaluate the safety, efficacy, and immunogenicity of COVIFENZ compared to placebo was conducted in individuals 18 years of age and older in North America, South Africa, and the United Kingdom, with 24,076 participants.

Additional information can be found at:

<https://www.canada.ca/en/health-canada/news/2022/02/health-canada-authorizes-medicago-covid-19-vaccine-for-adults-18-to-64-years-of-age.html>.

<https://covid-vaccine.canada.ca/info/regulatory-decision-summary-detail.html?linkID=RDS00921>.

## Administration errors in Uruguay

On 1 February 2022, Uruguay's Ministry of Public Health reported that 158 children had been vaccinated with one-fifth of a dose of Sinovac's COVID-19 vaccine, rather than with Pfizer-BioNTech's pediatric vaccine, and that no AEFI had been reported immediately or post-vaccination.

Doctors from the epidemiology and immunizations section of the Ministry contacted each of the families to inform them of the error, answer any questions, and provide follow-up on each of the cases. In addition, they reported that, from the technical point of view, adverse effects are considered a low probability considering the dose concentration administered, and the fact that, in 14 days, these children will be given the intended Pfizer pediatric vaccine.

For more information, visit:

<https://www.gub.uy/ministerio-salud-publica/comunicacion/noticias/informacion-opinion-publica-0>.

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