COVID-19

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

Forty-fourth report

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OPS Organización Panamericana de la Salud
Organización Mundial de la Salud OFICINA REGIONAL PARA LAS Américas
In partnership with Canada

CONTENTS

BRAZIL

As of 17 March, 268 reports of adverse events following immunization (AEFI) with COVID-19 vaccines, citing the terms myocarditis/pericarditis, had been identified. Following an evaluation, the diagnosis of myocarditis/pericarditis was ruled out in 114 (42.5%) of the reports. This left 154 (57.5%) reports of AEFI with suspected cases of myocarditis and/or pericarditis, of which the majority (n=117; 75.9%) involved the Pfizer/Wyeth vaccine. An AEFI reporting rate of 0.04 cases of myocarditis/pericarditis per 100 000 doses for all COVID-19 vaccines was estimated, and 0.07 cases per 100 000 doses for the Pfizer/Wyeth vaccine alone.

Most cases occurred in males (64.9%), with a median age of 32 years, ranging in age from 5 to 78 years, following the first dose (56.5%). These individuals developed serious AEFI (70.1%), with a median time of 15 days between vaccination and the event, ranging from one to 420 days, thus suggesting inconsistencies in the investigation.

Source: Ministry of Health. Secretariat of Health and Environmental Surveillance. Epidemiological Bulletin 10, volume 54. Monitoramento da segurança das vacinas COVID-19 no Brasil até a semana epidemiológica nº 11 de 2023. 19 June 2023. Available from: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/c/calendario-nacional-de-vacinacao/esavi/monitoramento-dos-eventos/2023.

CANADA

As of 15 September, a total of 99 034 764 doses of COVID-19 vaccines had been administered, including 9 611 886 doses of bivalent vaccines. A total of 57 436 reports of AEFI were received, of which 11 231 cases were considered serious. Of total reports, 947 were related to bivalent vaccines, with 255 cases considered serious (0.003% of bivalent COVID-19 vaccine doses administered).

The majority of reported cases were in females (72.5%). The reporting rate in females was 79.1 per 100 000 doses, while in males the rate was 32.4 per 100 000 doses. However, in younger age groups (<18 years), reporting rates were similar in both sexes, or slightly higher in males,

possibly due to differences in care-seeking behavior and to biological differences between the sexes.

Number of reports and reporting rate (per 100 000 doses administered) of main adverse events of special interest (AESI), by vaccine, in the general population, as of 15 September 2023						
AESI	***Vaccine***					
	Pfizer-BioNTech		***Moderna***		***Covishield and AstraZeneca***	
	N*	Rate**	***N****	Rate**	***N****	Rate**
Guillain-Barré syndrome	5	0.01	5	0.02	12	0.43
Thrombocytopenia	108	0.18	37	0.14	52	1.85
Myocarditis/pericarditis	713	1.17	458	1.79	17	0.60
Thrombosis with thrombocytopenia syndrome (TTS)	22	0.04	8	0.03	56	1.99
Bell's palsy/facial paralysis	138	0.23	47	0.18	14	0.50
Anaphylaxis	558	0.92	178	0.70	25	0.89

*N = number of reports
**Rate: per 100 000 doses administered

Note: Information on the Janssen and Novavax vaccines 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; 29 September 2023. Available from: https://health-infobase.canada.ca/covid-19/vaccine-safety/. Data reproduced by PAHO/WHO.

COVID-19 Vaccination as a Trigger of IgA Vasculitis: A Global Pharmacovigilance Study

This observational study, published in April 2023, attempted to evaluate a potential safety signal regarding the association between COVID-19 vaccines and immunoglobulin A-associated vasculitis (IgAV). In this disproportionality study, the authors collected all individual case safety reports (ICSRs) of new cases of IgAV (occurring within 30 days after COVID-19 vaccination) related to COVID-19 vaccines (elasomeran, tozinameran, ChAdOx1 nCoV-19, and JNJ-Ad26.COV2.S) reported up to 1 June 2022 on VigiBase, using the previously validated Lowest Level Terms (LLT) from the Medical Dictionary for Regulatory Activities (MedDRA). All patients with specific MedDRA LLTs related to IgA vasculitis were included. New cases of IgAV were identified excluding those with underlying worsening of IgAV.

Administrative information, patient demographics, exposure characteristics, and IgAV characteristics were extracted from each ICSR. Of the 31 738 658 ICSRs in VigiBase retrieved as of 1 June 2022, 3 712 164 were related to COVID-19 vaccines, including 330 new cases of IgAV from 24 countries. The top three contributors were the United States (193/330; 58%), United Kingdom (31/330; 9%), and France (29/330; 9%). Among these patients, 50% were female (163/328), with a median age of 32 years (IQR 15–59), of which 17% (42/254) were children (ages 1–12), 17% (42/254) were adolescents (ages 12–17), 48% (122/254) were adults (ages 18–65), and 19% (48/254) were older adults (age > 65). The median time from vaccination to onset of IgAV was seven days (IQR 2–16), with 85% (280/330) of patients having received mRNA vaccines.

Based on WHO criteria, seriousness was reported in 188/324 cases (58%). Of the 147 cases in which information concerning the outcome of the disease was available at the time of reporting, 95 recovered (65%); of these, one had sequelae and two (1%) died. Positive re-exposure was reported in three out of four patients (75%) who received a new dose of COVID-19 vaccine.

A total of 2093 cases of IgAV associated with medications other than COVID-19 vaccines were identified, including 996 involving other vaccines. There was a small, significant increase in IgAV reporting with COVID-19 vaccines compared with all other medications (CI 0.22; 95% CI 0.04 to 0.35). No disproportionality signal was found between COVID-19 vaccines and other vaccines (CI -1.42; 95% CI -1.60 to -1.28). The results were consistent across all sensitivity analyses, with no significant over-reporting of IgAV found compared with other vaccines.

The results indicated that COVID-19 vaccines are associated with a slight but significant excess of IgAV reports, although no greater than that observed with other vaccines.

Despite the small number of cases considered, the existence of positive re-exposures with IgAV relapses in this study supports the hypothesis of a triggering effect of COVID-19 vaccines. One of the hypotheses proposed by the authors to explain this possible effect is a vasculitis-driven hypoglycosylated IgA-mediated response following vaccination. IgA responses have been observed following BnT162B2 and ChAdOx1 vaccination.

The authors conclude that COVID-19 vaccines, like other vaccines, could act as a trigger for a first episode of IgAV. However, this study provides results that support the safety of COVID-19 vaccines in relation to the occurrence of IgAV compared to other vaccines.

Source: Yanis Ramdani, Bérenger Largeau, Annie-Pierre Jonville-Bera, François Maillot and Alexandra Audemard-Verger. COVID-19 Vaccination as a Trigger of IgA Vasculitis: A Global Pharmacovigilance Study. The Journal of Rheumatology, Apr 2023, 50(4):564–567; DOI: https://doi.org/10.3899/jrheum.220629.

POTENTIAL SPECIFIC SIGNALS BASED ON SEX IDENTIFIED WITH THE USE OF COVID-19 VACCINES

Vulvar aphthous ulcers in perimenarchal adolescents after COVID-19 vaccination: a multicenter case series

On 25 June 2023, a study was published describing a series of eight cases of perimenarchal adolescents who developed vulvar aphthous ulcers following COVID-19 vaccination, with no evidence of prior SARS-CoV-2 infection, between April and September 2021.

The study was conducted in three pediatric and adolescent gynecology facilities at the following academic hospitals: Yale University Department of Obstetrics, Gynecology, and Reproductive Sciences, USA; University of Missouri–Kansas City, Children's Mercy Hospital, USA; and the Pediatric and Adolescent Gynecology Clinic, Faculty of Medicine, Monterrey, Mexico.

Each patient's clinical presentation, differential diagnosis, diagnostic workup, complications, treatment modalities, and overall course of illness were described. The aim was, through all the cases, to illustrate the clinical experiences of patients and healthcare personnel interfacing with vulvar aphthous ulcers, and to contribute to the emerging literature exploring the new association between vulvar aphthous ulcers and COVID-19 vaccination. To date, this is the largest described case series of this association in the literature.

Eight cases of adolescents were identified with vulvar aphthous ulcers who had received the Pfizer-BioNTech COVID-19 vaccine one to two days before the onset of the ulcers. Ages ranged from 12 to 17 years, with an average age of 14.6 years. Seven of the eight adolescents developed the ulcers after receiving a second dose of vaccine. One adolescent girl, with a history of ulcers, developed symptoms after the first dose. None had a known history of COVID-19 or recent exposure to SARS-CoV-2. Systemic symptoms included fever, headaches, and myalgia prior to the appearance of vulvar symptoms. The average onset of vulvar pain and dysuria occurred two days after the second dose, with peak symptoms between day two and day five after vaccination.

Resolution of symptoms ranged from 10 to 24 days. One patient was hospitalized for urinary retention due to swollen labia and had positive genital cultures for *Corynebacterium* and *Bacteroides fragilis*. Various tests were performed, all with negative results for Epstein-Barr, cytomegalovirus, and herpes. The culture-positive patient was treated with cephalexin. Another patient with a positive culture for *Staphylococcus aureus* was treated on an outpatient basis with amoxicillin.

Two patients with previous episodes of ulcers underwent rheumatological studies. One was hospitalized and the other had a vulvar biopsy that showed chronic inflammation. Both tested negative for various autoimmune diseases.

Five patients required only symptomatic support, three received oral steroids, and two received antibiotics due to positive vulvar cultures. Complete resolution ranged from 10 to 25 days, depending on treatment. Symptomatic treatment included anti-inflammatory drugs, paracetamol, creams, sitz baths, and topical lidocaine.

One patient had a recurrence of ulceration after her Omicron booster vaccination, 12 months after initial vaccination. Her symptoms began two days after the booster, and she was given oral

prednisone. Her overall course was milder, with complete resolution of ulceration seven days later.

These eight cases illustrate the temporal association of vulvar ulcers with the Pfizer-BioNTech COVID-19 vaccine in adolescent females and support the growing number of reports with similar findings. Thus, COVID-19 vaccination could represent a new etiology for vulvar aphthous ulcers. Although the pathogenesis of these ulcers remains uncertain, it is posited that an immune response to an infection produces a type 3 hypersensitivity reaction. Since COVID-19 vaccination elicits a strong immune response, this inflammatory response could also contribute to the development of vulvar aphthous ulcers. Such findings support the hypothesis that these ulcers are an immune response and not a sign of a genital infection.

Treatment for vulvar aphthous ulcers includes steroids, specific antibiotics, and analgesics. Although there is no evidence of faster recovery with steroids, the study has limitations, such as its retrospective nature and lack of long-term follow-up. Moreover, not all ulcers were documented with photos. There are concerns that steroids may decrease the desired immune response to the COVID-19 vaccine. Further research is required regarding optimal treatments. Given the possible higher incidence of vulvar ulceration after vaccination, this study seeks to better prepare physicians to avoid misdiagnoses and delays in treatment.

The authors conclude that this case series could contribute to the emerging literature describing vulvar ulceration following COVID-19 vaccination and may further clarify typical clinical features and optimal treatment modalities.

Source: Sartor RA, Lawson A, Moncada-Madrazo M, Altchek C, Vash-Margita A, Cron J. Vulvar aphthous ulcers in peri-menarcheal adolescents following COVID-19 vaccination: a multicenter case series. J Pediatr Adolesc Gynecol. 2023; S1083–3188(23)00003–7. doi:10.1016/jpag2023.01.003.

COVID-19, Coronavirus Vaccines, and Possible Association with Lipschütz Vulvar Ulcer: A Systematic Review

On 26 June, the following systematic review of the literature was published, attempting to identify acute Lipschütz ulcer events associated with COVID-19 or SARS-CoV-2 vaccination, using recognized databases, and following established guidelines. Specific selection criteria were established to identify relevant cases, excluding those with other diseases or conditions. The severity of (microbiologically confirmed) COVID-19 was classified into five stages, as suggested by the National Institutes of Health: (1) asymptomatic (no symptoms or signs); (2) mild (any symptoms or signs such as malaise, headache, fever, cough, sore throat, or myalgia without shortness of breath, dyspnea, or abnormal thoracic imaging); (3) moderate (evidence of lower respiratory tract disease through clinical evaluation or imaging, and oxygen saturation on room air ≥94%); (4) severe (respiratory rate >30/min, oxygen saturation on room air <94%, or pulmonary infiltrates >50%); and (5) critical (hypercapnia, septic shock, or multiple organ dysfunction).

Data were collected and extracted on Lipschütz ulcer episodes temporally related to COVID-19 or SARS-CoV-2 vaccination, and included demographic information, medical history, and clinical characteristics. For episodes associated with the vaccine, the vaccine type and dose were considered. Standardized methods were used for data presentation and analysis. Discrepant views among the researchers were discussed, and specific statistical techniques were used to analyze the variables.

In the final analysis, 18 studies published between 2020 and 2023 in three different languages were analyzed. These studies were mainly from the United States and Europe and described 33 individuals who presented with a total of 39 episodes of vulvar Lipschütz ulcer. The quality of the reports was generally high, with most rated as excellent or good.

A total of 33 patients with 39 episodes of Lipschütz ulcer were analyzed, 18 of which were associated with COVID-19 infection and 21 with SARS-CoV-2 vaccination. Most cases associated with vaccination occurred after receiving the Comirnaty vaccine (BNT162b2). Some patients experienced multiple episodes of ulcers. Four subjects with two or more episodes had ulcers both after vaccination and after COVID-19 infection.

The patient with four episodes had an initial event associated with a mild form of COVID-19 and three events following immunization against SARS-CoV-2. The first two episodes occurred after receiving the Spikevax vaccine (mRNA-1273), while the third occurred after receiving the Comirnaty vaccine (BNT162b2). Three patients developed the characteristics of Lipschütz ulcer, after both vaccination with Comirnaty (BNT162b2) and in the context of mild COVID-19. Interestingly, these three patients had a history of Lipschütz ulcer associated with a flu-like illness. Presentation, treatment, and duration of disease were similar in both types of events. In most episodes (77%), acute Epstein-Barr virus infection was ruled out.

The authors concluded that a temporal association between COVID-19 and SARS-CoV-2 vaccines and Lipschütz ulcer had been observed; and while there was no direct causation, there were factors that suggest a possible link. Lipschütz ulcer has similar clinical features, regardless of the associated cause, but recurrence appears to be more common with COVID-19 and vaccination. The study had certain limitations, including the small number of cases, and more research is needed to confirm any link.

Source: Vismara SA, Ridolfi A, Faré PB, Bianchetti MG, Lava SAG, Renzi S, Piccoli BTB, Milani GP, Kottanattu L. COVID-19, Coronavirus Vaccines, and Possible Association with Lipschütz Vulvar Ulcer: A Systematic Review. Clin Rev Allergy Immunol. 2023 June 26. doi: 10.1007/s12016-023-08961-5. Epub ahead of print. PMID: 37358748.

Effect of COVID-19 vaccination on menstrual cycle patterns of reproductive-age women: a multicenter observational study

On 8 June, a multicenter observational study was published attempting to investigate the effects of COVID-19 vaccination on the menstrual cycle, and on premenstrual and postmenstrual symptoms, and to correlate these with the type of vaccine received, in women between 18 and 45 years of age.

The study was conducted in six national institutes in different Indian states over a period of one year. A total of 5709 participants who met the inclusion criteria were enrolled. Data on the impact of the vaccines (COVISHIELD and COVAXIN) and of prior COVID-19 infection on the menstrual cycle and its associated symptoms were obtained through online and face-to-face interviews.

Of the 5709 participants, 78.2% received COVISHIELD and 21.8% received COVAXIN. Of these, 333 (5.8%) developed menstrual changes following vaccination, 32.7% with frequent cycles, 63.7% with prolonged cycles, and 3.6% with intermenstrual bleeding.

A total of 301 participants noticed changes in the amount of bleeding: 50.2% reported excessive bleeding, 48.8% scant bleeding, and 0.99% amenorrhea followed by heavy bleeding. In addition, menstrual cycle irregularities and their duration were significantly higher in the COVAXIN group (7.2%) compared with the COVISHIELD group (5.3%).

Of the participants, 721 (12.6%) reported recent or aggravated pre- and postmenstrual symptoms, including severe dysmenorrhea with or without diarrhea (55.3%), severe low back pain (9.4%), persistent lower abdominal pain (18.0%), general weakness and body aches (8.9%), vaginal pain (1.7%), and increased vaginal discharge (0.7%), in addition to various nonspecific symptoms in 5.96% of participants.

Of the total, 721 participants (12.6%) had previously experienced a COVID-19 infection either during or after completing vaccination. Of these, 584 (81.0%) had been vaccinated with COVISHIELD and 137 (19.0%) with COVAXIN. No significant differences in the incidence of COVID-19 infection were observed between the two vaccines. No significant associations were found when comparing menstrual abnormalities among those with a history of COVID-19 infection.

The authors concluded that, in a small percentage of participants, the COVISHIELD and COVAXIN vaccines may be associated with changes in the menstrual cycle and pre- and postmenstrual symptoms. However, 94.7% experienced no change in bleeding during menstruation following vaccination. The menstrual irregularities observed with COVAXIN were significantly higher, but further study is needed regarding the duration of these post-vaccination changes.

Source: Kumar N, Gangane N, Mohapatra I, Rukadikar C, Sharmila V, Pushpalatha K, Eerike M, Santhoshi G, Samantaray SR, Seth S, Trigunait P, Reddy NJ, Patel S, Rani S, Mishra R, Negi K. Effect of COVID-19 Vaccination on menstrual cycle patterns of reproductive-age women: a multi-

center observational study. Curr Drug Res Rev. 2023 Jun 8. doi: 10.2174/2589977515666230608140606. Epub ahead of print. PMID: 37291775.

Interim recommendations for the use of inactivated and protein subunit COVID-19 vaccines from the WHO Strategic Advisory Group of Experts on Immunization (SAGE)

On 31 August, WHO's SAGE published interim recommendations for the use of inactivated COVID-19 vaccines, along with interim recommendations for the use of protein subunit COVID-19 vaccines.

The interim recommendations for the use of inactivated COVID-19 vaccines summarize the recommendations for inactivated COVID-19 vaccines included in the Emergency Use Listing (EUL): Bharat Biotech's COVAXIN, Beijing Institute of Biological Products Co-Ltd's Sinopharm, Sinovac's CoronaVac, and Valneva Austria GmbH's Valneva.

For protein subunit vaccines, the interim recommendations summarize the recommendations for the use of the following EUL vaccines: Novavax's Nuvaxovid, Bological E Limited's Cobervax, SK bioscience's SKYCovione, HIPRA Human Health S.L.U.'s BIMERVAX, and Sanofi-GSK's VidPrevtyn Beta.

Additional information available from: https://iris.who.int/bitstream/handle/10665/372713/WHO-2019-nCoV-vaccines-SAGE_recommendation-inactivated-2023.1-eng.pdf?sequence=1.

https://iris.who.int/bitstream/handle/10665/372724/WHO-2019-nCoV-vaccines-SAGE_recommendation-protein_subunit-2023.1-eng.pdf?sequence=1.

The Committee for Medicinal Products for Human Use (CHMP), of the European Medicines Agency (EMA), recommends approval of the new adapted Comirnaty COVID-19 vaccine

On 30 August, the EMA's CHMP recommended authorizing Pfizer's adapted Comirnaty vaccine targeting the Omicron XBB.1.5 subvariant for adults and children ages 6 months and older. In line with previous recommendations from the EMA and the European Centre for Disease Prevention and Control (ECDC), adults and children 5 years and older who require vaccination should receive a single dose, regardless of their COVID-19 vaccination history. Children from 6 months to four years of age will be able to receive one or three doses, depending on whether they have completed a first vaccination course or have had COVID-19.

In deciding upon the recommended authorization, the CHMP considered all available data on the Comirnaty vaccine and its other adapted vaccines, including safety, efficacy, and immunogenicity data, along with new laboratory data showing a strong response to the adapted vaccine against Omicron XBB.1.5 and related strains of the COVID-19 virus.

As Omicron XBB.1.5 is closely related to other currently circulating variants, the vaccine is expected to help maintain optimal protection against COVID-19 caused by Omicron XBB.1.5 and other circulating variants.

Additional information available from: https://www.ema.europa.eu/en/news/comirnaty-ema-recommends-approval-adapted-covid-19-vaccine-targeting-omicron-xbb15.

Brazil's Health Surveillance Agency (ANVISA) authorizes extension of the expiration dates of monovalent and bivalent COVID-19 Comirnaty vaccines

On 4 September, ANVISA announced that it was authorizing extension of the shelf life of the monovalent and bivalent versions of Pfizer's Comirnaty COVID-19 vaccine, from 18 months to 24 months when stored at between -90°C and -60°C. The measure covers vaccines for all approved age groups.

ANVISA analyzed the available data and concluded that there is a positive benefit-risk ratio for changing the expiration date. This extension has also been approved by the European Medicines Agency (EMA).

On 6 September, ANVISA announced that it was authorizing applying the 24-month shelf life to batches of the monovalent and bivalent Comirnaty COVID-19 vaccine, in all of its presentations, that have already been imported and distributed by the Ministry of Health, regardless of the expiration date (12 or 18 months) printed on the vaccine packaging. In practice, the measure authorizes an additional six months of shelf life for vaccines initially labeled with a shelf life of 18 months, and an additional year for those with a labeled shelf life of 12 months.

The measure approved by ANVISA also authorizes importation of batches of the monovalent and bivalent Comirnaty vaccine with an expiration date of less than 24 months printed on the packaging, applying the 24-month expiration authorized by ANVISA. The company is responsible for maintaining information on the batches and their shelf life, and for updating the Ministry of Health, professionals involved in administering the vaccines, and the citizenry.

Additional information available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2023/anvisa-autoriza-ampliacao-dos-prazos-de-validade-das-vacinas-comirnaty-pfizer-monovalente-e-bivalente.

https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2023/autorizada-ampliacao-dos-prazos-de-validade-das-vacinas-comirnaty-pfizer-monovalente-e-bivalente.

The U.S. Food and Drug Administration (FDA) takes action to approve and authorize emergency use of updated COVID-19 vaccines

On 11 September, the U.S. Food and Drug Administration (FDA) announced that it was taking action to approve and authorize emergency use of updated COVID-19 vaccines for the 2023–2024 season, manufactured by Moderna TX Inc. and Pfizer Inc., to include a monovalent component corresponding to the Omicron XBB.1.5 variant.
The actions taken by the FDA are summarized below:

- Pfizer Inc.'s mRNA COVID-19 vaccine Comirnaty: Amended marketing authorization to include the 2023–2024 formula, and a change to a single dose for individuals 12 years of age and older. Comirnaty was previously approved as a two-dose series for individuals 12 years of age and older.

  The emergency use authorization for Pfizer's COVID-19 vaccine in people ages 6 months to 11 years was amended to include the 2023–2024 formula, and additional doses were authorized for certain immunocompromised people ages 6 months to 11 years.

- Spikevax mRNA COVID-19 vaccine from Moderna TX Inc.: Amended marketing authorization to include the 2023–2024 formula, a change to a single dose for individuals 18 years of age and older, and approval of a single dose for individuals 12 through 17 years of age. Spikevax was previously approved as a two-dose series for individuals 18 years of age and older.

  The emergency use authorization for Moderna's COVID-19 vaccine in people ages 6 months through 11 years has been amended to include the 2023–2024 formula, while lowering the age eligibility for receipt of a single dose from 6 months to 5 years of age. Additional doses are also authorized for certain immunocompromised individuals ages 6 months through 11 years.

The FDA reported that the updated mRNA vaccines are being manufactured using a process similar to previous formulations, and that the extent of neutralization against currently circulating viral variants, including EG.5 and BA.2.86, observed in nonclinical studies of the updated

vaccines, appears to be of a similar magnitude to the extent of neutralization observed with vaccines against previous variants.

The FDA states that unless a markedly more virulent variant emerges, the composition of COVID-19 vaccines may need to be updated annually, as is done with the seasonal flu vaccine.

Additional information available from: https://www.fda.gov/news-events/press-announcements/fda-takes-action-updated-mrna-covid-19-vaccines-better-protect-against-currently-circulating.

Health Canada authorizes the use of Moderna's Spikevax COVID-19 vaccine targeting the Omicron XBB.1.5 subvariant

On 12 September, Health Canada announced that it was authorizing the use of Moderna's Spikevax COVID-19 vaccine targeting the Omicron XBB.1.5 subvariant for people 6 months of age and older.

People ages 5 and older should get one dose, regardless of their COVID-19 vaccination history. Children between 6 months and 4 years of age should receive two doses if they have not previously been vaccinated with a COVID-19 vaccine, or one dose if they were previously vaccinated with one or more doses of a COVID-19 vaccine.

Health Canada also said it is reviewing the authorization application of Pfizer-BioNTech's Omicron XBB.1.5 subvariant COVID-19 vaccine for people 6 months of age and older, and Novavax's application for its COVID-19 vaccine targeting the Omicron XBB.1.5 subvariant for people 12 years of age and older.

Because vaccine protection wanes over time, Health Canada recommends vaccination with the new formulation of the COVID-19 vaccine if six months have elapsed since the last dose, in order to provide better protection against variants of concern.

Additional information available from: https://www.canada.ca/en/health-canada/news/2023/09/health-canada-authorizes-moderna-covid-19-vaccine-targeting-the-omicron-xbb15-subvariant.html.

EMA recommends approval of adapted COVID-19 vaccine Spikevax targeting Omicron XBB.1.5

On 14 September, the EMA's CHMP recommended authorizing Moderna's adapted Spikevax COVID-19 vaccine, which targets the Omicron subvariant XBB.1.5., for adults and for children 6 months of age and older.

In line with previous recommendations from the EMA and the European Centre for Disease Prevention and Control (ECDC), adults and children ages 5 and older who require vaccination should receive a single dose, regardless of their COVID-19 vaccination history. Children ages 6 months to 4 years will be able to receive one or three doses, depending on whether they have completed a primary vaccination course or have had COVID-19.

In deciding to recommend authorization, the CHMP considered all available data on Spikevax and its other adapted vaccines, along with laboratory data showing that the adapted vaccine is capable of triggering an adequate immune response against XBB.1.5. They also looked at data from a study in which Spikevax XBB.1.5 was administered to adults as a booster. The study showed that the vaccine produced an immune response against the Omicron XBB.1.5 subvariant, as measured by an increase in the level of antibodies against that strain. The vaccine also produced an immune response against other strains of the virus that cause COVID-19, including the currently circulating Omicron XBB.1.16 subvariant.

Additional information available from: https://www.ema.europa.eu/en/news/spikevax-ema-recommends-approval-adapted-covid-19-vaccine-targeting-omicron-xbb15.

Annex to the SAGE/WHO interim recommendations for the use of Biological E. Limited's COVID-19 vaccine Corbevax (BECOV-2)

On 25 September, WHO's SAGE published an annex to the interim recommendations for the use of Biological E. Limited's COVID-19 vaccine Corbevax (BECOV-2). This document contains GRADE tables summarizing the efficacy and safety studies on this vaccine, and the evidence considered in recommending its use.

Additional information available from: https://iris.who.int/bitstream/handle/10665/373015/WHO-2019-nCoV-vaccines-SAGE_recommendation-BECOV-2-annexes-2023.1.pdf?sequence=1.

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

There are no clarifications/conclusions to report at present.

The Public Health Agency of Canada's (PHAC) National Advisory Committee on Immunization (NACI) publishes guidance on the use of COVID-19 vaccines in the fall of 2023.

On 11 July, NACI, of the Public Health Agency of Canada, published guidance on the use of COVID-19 vaccines in the fall of 2023. In January, the Committee had published its Guidance on COVID-19 vaccine booster doses: Initial considerations for 2023, and in March, published Guidance on an additional COVID-19 booster dose in the spring of 2023 for individuals at high risk of severe illness due to COVID-19.

Considering the recommendations of 18 May 2023, from the WHO Technical Advisory Group on COVID-19 Vaccine Composition on updating the composition of COVID-19 vaccine antigens, NACI is now providing guidance on the use of COVID-19 vaccines as of the fall of 2023.

Available from: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-use-covid-19-vaccines-fall-2023/statement.pdf.

Brazil's ANVISA authorizes a new clinical trial stage for the SpiN-Tec MCTI UFMG vaccine candidate

On 30 August, ANVISA announced that it had authorized the start of a new stage of the clinical trial for the COVID-19 vaccine candidate SpiN-Tec MCTI UFMG, developed by the Vaccine Technology Center (CTVacinas) of the Federal University of Minas Gerais (UFMG). SpiN-Tec is a recombinant chimeric protein that utilizes the SpiN protein, which is an association of the RBD portion of the Spike (S) protein with the nucleocapsid protein.

The clinical trial protocol for the SpiN-Tec vaccine is phase 1/2, and is subdivided into three parts.

The start of the first phase of the clinical trial was authorized by ANVISA in October 2022, and based on the preliminary safety and immunogenicity results obtained in that phase, ANVISA authorized continuation of the clinical trial for the following phases, which will include approximately 372 healthy volunteers of both sexes, between the ages of 18 and 85, who have completed the primary COVID-19 vaccination series with CoronaVac® or Covishield®, and have received one or two booster doses with Covishield® or Comirnaty® in at least the last six months.

Participants may have had a prior natural infection with SARS-CoV-2 at least six months prior to their clinical trial inclusion date.

Additional information available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2023/autorizado-o-inicio-da-fase-2-do-ensaio-clinico-da-vacina-spin-tec-para-covid-19.

Proposed International Nonproprietary Names: List 129 –COVID-19 (Special Edition)

WHO published the list of proposed international nonproprietary names (INNs) for the new adapted vaccines. The table below provides a summary.

International nonproprietary name	Description
Andusomeran	messenger RNA (mRNA), 5'-capped, encoding a full-length, codon-optimized pre-fusion stabilized conformation variant (K982P and V983P) of the SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) spike (S)glycoprotein (Omicron variant XBB.1.5; based upon GISAID: EPI_ISL_15948646)
Pitozinameran	messenger RNA (mRNA), 5'-capped, encoding a full-length, codon-optimized pre-fusion stabilized conformation variant (K982P and V983P) of the SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) spike (S) glycoprotein (Omicron sub-lineage XBB.1.16; based upon GISAID: EPI_ISL_16835403), flanked by 5' and 3' untranslated regions and a 3' polyadenylation (polyA) tail; contains N1-methylpseudouridine instead of uridine (all-U>m1Ψ).
Raxtozinameran	messenger RNA (mRNA), 5'-capped, encoding a full-length, codon-optimized pre-fusion stabilized conformation variant (K982P and V983P) of the SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) spike (S) glycoprotein (Omicron sub-lineage XBB.1.16; based upon GISAID: EPI_ISL_16835403), flanked by 5' and 3' untranslated regions and a 3' polyadenylation (polyA) tail; contains N1-methylpseudouridine instead of uridine (all-U>m1Ψ).
Tegrenmeran	messenger RNA (mRNA), 5'-capped, encoding the codon-optimized receptor binding domain (RBD) of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) glycoprotein (Omicron sub-lineages B.1.1.529.4 (BA.4) and B.1.1.529.5 (BA.5); based upon GISAID: EPI_ISL_12607996), with a cysteine 233 to serine substitution, expressed as a fusion protein with the S glycoprotein signal peptide derived from SARS-CoV-2 Wuhan-Hu 1 strain (GenBank: MN908947.3), flanked by 5' and 3' untranslated regions (UTRs) derived from the human β-globin gene and a 3' polyadenylation (polyA) tail; contains 5-methyluridine instead of uridine (all-U>5-Me-U) and 5-methylcytidine instead of cytidine (all-C>5-Me-C).
Upalsecovatein	severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) omicron lineage B.1.1.529.5 also known as BA.5 (GISAID: EPI_ISL_12097410) spike (S) glycoprotein (S glycoprotein) (1-1255), stable prefusion conformation variant (R664>Q, R665>Q, R667>Q, K968>P, V969>P), trimer, produced in Spodoptera frugiperda (Sf9) insect cells, glycoform alfa.
Vintesomeran	messenger RNA (mRNA), 5'-capped, encoding a full-length, codon-optimized pre-fusion stabilized conformation variant (K982P and V983P) of the SARSCoV-2 (severe acute respiratory syndrome coronavirus 2) spike (S) glycoprotein (Omicron variant XBB.1.16; based upon GISAID: EPI_ISL_16835403) further optimized by two additional stop codons, flanked by an artificial 5' untranslated region (UTR) and a 3' UTR derived from the human alpha globin gene (HBA1) modified to contain an identification and ratio (IDR) sequence to enable identification and relative ratio determination of individual RNA components in a multivalent mRNA vaccine and terminated by a 3' polyadenylation (polyA) tail; contains N1-methylpseudouridine instead of uridine (all-U>m1Ψ).

Additional information available from: https://cdn.who.int/media/docs/default-source/international-nonproprietary-names-(inn)/inn-pl-129-covid.pdf?sfvrsn=4ce4122c_3&download=true.

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