COVID-19

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

Thirteenth report

WASHINGTON, DC
Updated: 10 May 2021

CANADA

- As of 30 April 2021, 13,420,198 doses of the COVID-19 vaccines of Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, and the vaccine Covishield (AstraZeneca manufactured by the Serum Institute of India), had been administered.
- A total of 4,548 individual reports of one or more adverse events (0.034% of doses administered) were received. Of these, 748 were considered serious events (0.006% of doses administered), with anaphylaxis being the one most frequently reported.
- Of total reports, there were 2,072 non-serious and 520 serious events associated with the Pfizer-BioNTech vaccine. For the Moderna vaccine, 1,457 non-serious and 103 serious events were reported; for Covishield, there were 201 non-serious and 48 serious events, and for Oxford-AstraZeneca, 65 non-serious events and 62 serious events.
- A total of 13,596 adverse events following immunization (AEFI) were reported, with 4,548 reports with one or more events. The most frequently reported non-serious adverse events were injection-site reactions, paresthesia, itching, hives, headache, hypoesthesia, and nausea. There were 61 reports of anaphylaxis.
- Although 55% of vaccine doses were administered to women as of 30 April, and 45% to men, most of the reported adverse events were in women (84.3% of total doses). At the same time, 43.0% of total events were reported for people between the ages of 18 and 49, who account for 24% of people vaccinated.
- As of 30 April, there were eight reports of thrombosis with thrombocytopenia syndrome following vaccination with the Covishield/AstraZeneca vaccine. Symptoms occurred between 6 and 24 days after vaccination in three women (between the ages 54 and 72) and five men (ages 34 to 71).
- A total of 50 reported cases of adverse events resulted in post-vaccination deaths. Following a medical review, it was determined that 22 of these deaths were unconnected with administration of the COVID-19 vaccine, while the other 25 are still being investigated. One of these was possibly attributable to vaccination (a case of thrombosis with thrombocytopenia syndrome) and two were not able to be classified, due to insufficient information

Link: https://health-infobase.canada.ca/covid-19/vaccine-safety/

CHILE

- Between 24 December 2020 and 10 March 2021, a total of 5,770,172 doses of vaccine were administered – 5,350,038 doses of the CoronaVac and 420,134 doses of the Pfizer-BioNTech vaccine.
- The National Pharmacovigilance Center received 5,410 reports of AEFI (0.09% of doses administered), of which 2,712 were from the Pfizer-BioNTech vaccine, 2,584 were from the CoronaVac vaccine, while in 114

cases the brand was not specified. For both the Pfizer-BioNTech and the CoronaVac vaccines, the events reported were among the adverse events described in clinical trials.

- Of total AEFI, 79% occurred in women. Among this total, 86.9% of reports were for people under 60 years of age.
- A total of 166 AEFI were classified as serious (3.1% of total AEFI), 43 cases with the Pfizer-BioNTech vaccine (10.2 per 100,000 doses administered) and 122 with the CoronaVac vaccine (2.3 per 100,000 doses administered). The serious AEFI were similar to those reported in the country's previous (third) report, in which anaphylaxis was the most frequently reported serious event. The cumulative reporting rate for this event in that report was 1.69 cases per 100,000 doses administered.

Link: https://bit.ly/2QT8vBg

COSTA RICA

- As of 26 April 2021, the Directorate of Epidemiological Sub-Surveillance of the Costa Rican Social Security Fund reported that, of the total doses of COVID-19 vaccines administered (818,884 doses), 815,857 were with the Pfizer-BioNTech vaccine and 3,027 were with the AstraZeneca vaccine.

For the Pfizer-BioNTech vaccine:

- From 24 December 2020 to 25 April 2021, there were 3,291 reports of AEFI.
- From 16 April to 23 April, 156 AEFI were analyzed, of which 74% were in women. Of AEFI analyzed during this period, 99.4% were classified as non-serious and all but one as mild. A total of 20% of reported events involved pain at the injection site, 10% fever, and 8% headache. A single case was reported as severe, and involved an anaphylactic reaction.
- For this period, there were no reported cases of adverse event of special interest (AESI).

For the AstraZeneca vaccine:

- From 19 April 2021 to 23 April 2021, a total of 29 AEFI were reported; of those analyzed, three cases were classified as non-serious.

Source: Reportes de eventos supuestamente atribuibles a la vacunación e inmunización (ESAVI) 19 de abril al 25 de abril de 2021. Dirección de Regulación de productos de interés sanitario. Centro nacional de farmacovigilancia (CNFV). Ministerio de Salud de Costa Rica. [Reports of adverse events following administration (AEFI), 19 April 19 to 25 April 2021. Directorate for the Regulation of Health Products of Interest. National Pharmacovigilance Center; Costa Rican Ministry of Health.]

UNITED STATES

- Nearly 259 million doses of vaccine were administered between 14 December 2020 and 10 May 2021.

- Anaphylaxis following vaccination against COVID-19 remains very infrequent, with approximately two to five cases per million people vaccinated in the United States. When this occurs, it is approximately 30 minutes after vaccination, and is immediately and effectively treatable.
- As of 11 May, 9 million J&J/Janssen COVID-19 vaccines had been administered, with 28 cases of thrombosis with thrombocytopenia syndrome (TTS) reported. However, test results show that the benefits of the vaccine outweigh the known and potential risks. Tests indicate that women under the age of 50, in particular, should be informed of the risk of rare blood clots, accompanied by low platelet levels, following administration of the vaccine.
- The Vaccine Adverse Event Reporting System (VAERS) received 4,434 (0.0017%) reports of deaths among individuals vaccinated, though analysis failed to establish a link between these deaths and the vaccination. However, recent reports indicate the possibility of a causal link between the J&J/Janssen COVID-19 vaccine and TTS deaths. The U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) continue to investigate reports of these adverse reactions, including of deaths reported to VAERS.

Source: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html

MEXICO

- As of 5 May 2021, 19,340,234 total doses of Pfizer-BioNTech, AstraZeneca, Sinovac, CanSino, Sinovac, and Sputnik V vaccines had been administered.
- As of that date, 17,409 cases of AEFI (0.1% of doses administered) had been reported, of which 14,347 were associated with the Pfizer-BioNTech vaccine, 1,586 with the AstraZeneca vaccine, 732 with Sinovac, 269 with Sputnik V, and 461 with the CanSino vaccine.
- A total of 303 serious events were reported, representing 1.7% of total events reported. Of these serious events, 137 occurred with the Pfizer-BioNTech vaccine, 74 with the AstraZeneca vaccine, 56 with Sinovac, 9 with Sputnik V, and 25 with the CanSino vaccine. Of these events, 165 occurred in women and 138 in men; 105 cases remain hospitalized.

Source: https://www.gob.mx/salud/acciones-y-programas/versiones-estenograficas-conferencia-de-prensa

UNITED KINGDOM

- As of 28 April 2021, in the United Kingdom, an estimated 11.4 million first doses of the Pfizer-BioNTech vaccine, 22.6 million first doses of the Oxford-AstraZeneca vaccine, and approximately 8.1 million second doses of the Pfizer-BioNTech vaccine, 5.9 million second doses of the Oxford-AstraZeneca vaccine, and approximately 100,000 second doses of the Moderna vaccine had been administered.
- As of that date, there were 54,139 Yellow Card reports for the Pfizer-BioNTech vaccine, 160,543 for the Oxford-AstraZeneca vaccine, 683 for the Moderna vaccine, and 574 for which the brand was not specified. For the first two vaccines, the reporting rate was almost three to six Yellow Cards per 1,000 doses

administered. To be clear, Yellow Card data cannot be used to reach conclusions regarding adverse-event rates or to compare the safety profiles of different vaccines, since more information is required.

- For all vaccines, the vast majority of reports were related to injection-site reactions (arm pain) or general symptoms such as headaches, chills, fatigue, nausea, fever, weakness, muscle pain, tachycardia, and flu-like symptoms. These events usually occur close to the time of vaccination, and are not associated with more-serious or longer-lasting events.
- With regard to events of anaphylaxis (severe allergic reaction), the Medicines and Healthcare Products Regulatory Agency (MHRA) has received 283 spontaneous reports of these adverse events for the Pfizer-BioNTech vaccine.
- For the AstraZeneca vaccine, there were 590 spontaneous reports of adverse events involving anaphylaxis or anaphylactic reactions. Although these events are very rare, an update to the product information has been made, reflecting the fact that cases of anaphylaxis have been reported for the vaccine.
- In terms of Bell's palsy (facial paralysis) events, the MHRA is continuing to review reports of facial paralysis and compare these against randomly occurring cases in the unvaccinated populations (baseline rate). To date, the number of cases reported is similar to the baseline rate, and there is no indication that it will increase as a result of vaccination. These events continue to be monitored.
- With regard to thromboembolic events with thrombocytopenia, the MHRA received 242 Yellow Card reports of these events following administration of the AstraZeneca vaccine (141 in women and 100 in men), with a mortality rate of 20% (49 deaths). This event has a reporting frequency of 10.5 per million doses after the first dose, and suggests that there is a higher frequency in young adults. However, based on ongoing data, the authority continues to recommend that, for most of the population, the benefits of the vaccine outweigh the risks.
- Six cases of capillary filtration syndrome (a condition in which blood filters from small blood vessels to the body) have been reported, out of more than 20 million doses of the AstraZeneca vaccine administered. Current evidence does not suggest a causal link between this syndrome and the vaccine.

Link: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

PRAC meeting from 3 to 6 May 2021

As part of its pharmacovigilance work routine, PRAC reviewed a number of safety signals related to COVID-19 vaccines. The main details are as follows:

(a) Facial swelling with the Comirnaty COVID-19 vaccine (Pfizer-BioNTech). There is a reasonable possibility of an association between the vaccine and reported cases of facial swelling in people with previous histories of dermal fillers; it is therefore recommended that this possible adverse event be included in the summary of product characteristics.

(b) Unusual blood clots with low platelet counts with the Janssen COVID-19 vaccine: The need to refine the precautions regarding thrombosis with thrombocytopenia syndrome was highlighted. Thrombosis with thrombocytopenia syndrome will be added as a major risk in the vaccine risk plan.

(c) Unusual cases of blood clots with low platelet counts with the Comirnaty and Moderna COVID-19 vaccines: PRAC continues to monitor closely whether mRNA vaccines may be associated with rare and unusual cases of blood clots with low platelet counts, as has been reported with the Vaxzevria and Janssen COVID-19 vaccines. For the time being, there is no safety signal reported for these vaccines, since the observed cases occurred at a lower frequency than that occurring in the unvaccinated population. Monitoring will continue as necessary.

(d) PRAC is evaluating reported cases of Guillain-Barre Syndrome (GBS), following vaccination with the AstraZeneca COVID-19 vaccine. Since GBS was detected as a possible adverse event during the authorization process, the holder of the vaccine authorization had been asked to submit additional data, along with an analysis of the information collected to date.

(e) Reports of myocarditis and pericarditis are being evaluated with Comirnaty, but at present there is no indication that the cases are due to the vaccine. Nevertheless, PRAC has requested that the vaccine authorization holder provide additional detailed information in its next safety report, including an analysis of events that have occurred, disaggregated by gender and age. Consideration will be given at that time to whether regulatory action is needed. The authorization holder of the Moderna COVID-19 vaccine, since it too is an mRNA vaccine, has also been asked to conduct similar monitoring and present the results in its next safety report.

Source: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-3-6-may-2021

Pfizer-BioNTech COVID-19 vaccine authorization for children 12 to 15 years of age

On 5 May 2021, Health Canada authorized use of the Pfizer-BioNTech COVID-19 vaccine in children 12 to 15 years of age, after completing a comprehensive review of the evidence presented by Pfizer-BioNTech on preventing COVID-19 in children in this age group.

The Pfizer-BioNTech vaccine was initially authorized by the Canadian authority on 9 December 2020, for use in people age 16 and older. The authorization issued on 5 May 2021 makes this COVID-19 vaccine the first in Canada to be authorized for use in children between the ages of 12 and 15.

Source: https://www.canada.ca/en/health-canada/news/2021/05/health-canada-authorizes-use-of-the-pfizer-biontech-covid-19-vaccine-in-children-12-to-15-years-of-age.html

Similarly, on 10 May, the FDA granted an extension of emergency use authorization to the Pfizer-BioNTech vaccine for adolescents ages 12 to 15, amending the initial authorization granted on 11 December 2021 for children age 16 and older.

The decision took into account the safety data of an ongoing randomized placebo-controlled clinical study that included 2,260 participants 12 to 15 years of age, including 1,131 who received the vaccine and were monitored for at least two months after the second dose was administered. Adverse events observed are consistent with events in the general population of those 16 years old and older.

The assessment of efficacy was based on immunogenicity and COVID-19 case data. In 120 adolescents between the ages of 12 and 15, when compared with 170 participants between 16 and 25 years of age, the immunogenicity response was no lower than (and at least as good as) in the older group. There were no cases of COVID-19 among the 1,005 participants ages 12 to 15 who received the vaccine, whereas there were 16 cases among the 978 participants in the placebo group. This represents 100% efficacy in preventing cases of COVID-19.

As part of the initial authorization, Pfizer Inc. presented a safety monitoring plan, which has been updated for the adolescent population in long-term trials, and for the population to be vaccinated.

Link: https://bit.ly/3fxs9vk

ANVISA recommended immediately suspending use of the AstraZeneca/Fiocruz COVID-19 vaccine in pregnant women

On Monday, 5 May 2021, Brazil's National Health Surveillance Agency (ANVISA) issued a statement recommending immediate suspension of the use of the AstraZeneca/Fiocruz COVID-19 vaccine in pregnant women. This recommendation is based on the results of ongoing monitoring of adverse events associated with COVID-19 vaccines being used in Brazil, as a precautionary measure. The action was taken after suspicion of a severe adverse event of hemorrhagic stroke that resulted in the death of the fetus. Up until 5 May, ANVISA had not received any other reports of serious adverse events in pregnant women.

According to the current package insert for the AstraZeneca COVID-19 vaccine, the vaccine is not recommended for use in pregnant women, absent a medical indication.

The ANVISA statement states that the use of this vaccine in situations not provided for in the package insert should only occur based on an individual evaluation by a health care professional that takes into account the comparative risks and benefits to the patient of receiving the vaccine. In addition, it provides guidance to pregnant women and health professionals on the issue.

Link: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2021/comunicado-suspensao-da-vacina-da-astrazeneca-para-gestantes

PAHO/WHO COVID-19 resources on vaccination

The PAHO Immunization Newsletter, vol. XLIII, no. 1, March 2021 presents a list of resources on COVID-19 vaccination, published by PAHO and WHO, at the regional and global levels. These resources are divided into categories, including ones related to the National Deployment and Vaccination Plan (PNDV); Vaccine and vaccination safety; Evaluation of the introduction of COVID-19 vaccines; and training resources.

This list can be consulted through the following link, which provides access to the Newsletter mentioned above: https://iris.paho.org/bitstream/handle/10665.2/53795/EPIv43n12021_eng.pdf?sequence=5&isAllowed=y

Unilateral axillary adenopathy in patients recently vaccinated against COVID-19

Several national mammography commissions, societies, and associations concerned with diagnostic radiology and imaging are making recommendations based on consultations with patients with axillary lymphadenopathies or reactive lymphadenitis who have recently received COVID-19 vaccinations.

According to these organizations, after the start of the COVID-19 vaccination campaigns, reactive lymphadenitis (enlarged axillary lymph nodes in women) is occurring more frequently in vaccinated women. In several of the cases, procedures ranging from biopsies to additional imaging have been recommended.

Clinical studies of several of the approved vaccines highlighted the possibility of axillary node enlargement on palpation, with varying frequency, depending on the vaccine. For the Moderna vaccine, this effect has been seen in 11% of first-dose cases, and in 16% of cases after the second dose, occurring more frequently in young people, in the armpit on the side where the vaccination was administered. These events are less common with the Pfizer and AstraZeneca vaccines. The CDC has indicated that enlargement of the axillary node on palpation on the side where the vaccination was administered is the second-most common local adverse side effect. When lymph nodes become swollen, this generally begins on the second day after vaccination, persists for at least 10 days, and can be detected in diagnostic imaging for several weeks.

Given the possibility of these events occurring, especially in women, the following measures are recommended:

(a) It should be emphasized that swollen lymph nodes after vaccination is an expected event and is not unique to COVID-19 vaccines, as it is also seen with other vaccines such as influenza, human papilloma, measles, chickenpox, and BCG – vaccines that induce a strong immune response.
(b) Patients should not be alarmed if, within a few days of being vaccinated, lumps are noticeable in the armpits or neck, generally on the side where the vaccination was administered.
(c) No specific medical care or diagnostic imaging is considered indicated unless the enlargement of the nodes persists for more than six weeks with no apparent decrease in size.
(d) For patients with a personal history of breast cancer, it is recommended that the vaccine be administered on the side opposite to the side on which any medical intervention has occurred.
(e) For programs for early detection of breast cancer, it is recommended that detailed information on vaccination history, type of vaccine, vaccination date, and side where the vaccine was administered be recorded.

Sources:

Alvarez Benito M, et al. Recomendaciones de la Sociedad Española de Diagnóstico por Imagen de la Mama (SEDIM) para el manejo de mujeres con antecedente de vacunación para covid-19 reciente. [Recommendations of the Spanish Society of Breast Imaging (SEDIM) for the management of women with a recent history of COVID-19 vaccination.]

Lehman CD, Lamb LR, D'Alessandro HA. Mitigating the Impact of Coronavirus Disease (COVID-19). Vaccinations on Patients Undergoing Breast Imaging Examinations: A Pragmatic Approach. American Journal of Roentgenology, 2021, doi: 10.2214/AJR.21.25688

OTHER RELATED UPDATES

New vaccine included in WHO's Emergency Use Listing (EUL)

Name	Inactivated COVID-19 vaccine (Vero Cell)
Commercial name	N/A
WHO date of recommendation	7 May 2021
Platform/vaccine type	Inactivated virus
EUL holder	Beijing Institute of Biological Products Co., Ltd. (BIBP)
Manufacturers	Beijing, China.
Pharmaceutical form	Suspension for injection
Presentation	Pre-filled syringe (not auto-disposable) or one-dose vial
Diluent	N/A
Dose/Route of administration	0.5 mL intramuscular
Storage temperature/shelf life	2°C to 8°C for 24 months
Open vial/in use	Use immediately once the syringe or vial is opened

Source: https://extranet.who.int/pqweb/vaccines/who-recommendation-covid-19-vaccine-bibp

COVID-19 vaccines involved in incidents of breaks in the cold chain

The National Institute for Drug and Food Surveillance (INVIMA) of Colombia published on its website information on the six requests it has received so far from cold chain engineering professionals in the Expanded Immunization Program, under the country's Ministry of Health and Social Protection, to issue a recommendation on the use of COVID-19 vaccines involved in incidents of breaks in the cold chain.

The incidents were related to freezing temperatures above the recommended temperature for the vaccine involved, and in other cases, temperatures below the recommended refrigeration temperature for vaccine adjuvants.

The INVIMA notes that the recommendations issued are based on the analysis of information from reports of breaks in the cold chain, temperatures reached, and the transportation equipment and measuring instruments used, as well as the supporting information provided by each of the manufacturers in stability studies of the vaccines involved.

Source: https://bit.ly/3hHei82

Storage temperatures for COVID-19 vaccines

During the development and characterization phase of the vaccines, manufacturers perform different stability studies that include an evaluation of the appropriate storage conditions, in order to establish the vaccine's shelf life. Accelerated stability studies are also carried out to determine other storage conditions, and the maximum time of exposure to these temperatures (1).

This information allows the regulatory authorities, in the event of variations in the storage temperature or a break in the cold chain, to determine whether the vaccine can be used (considering alternative storage temperatures, when applicable) or whether it should be discarded.

In the case of COVID-19 vaccines, each vaccine has different storage specifications. In the following table, summarizing the storage conditions for these vaccines, it can be seen that some have alternative storage temperatures applicable for a given period of time.

When storing a vaccine at the alternative storage temperature, where applicable, the new shelf life must be recalculated and recorded on the vaccine vial, taking into account the date on which storage at that temperature began; for example, five days for the Pfizer Tozinameran vaccine, from the moment the vaccine is kept between 2°C and 8 °C (36°F to 46°F).

Storage temperatures for COVID-19 vaccines					
Name	Type of vehicle	Temperature			Remarks
		Storage	Alternative storage	In use	
Tozinameran COVID-19 COMIRNATY® vaccine Pfizer-BioNTech	mRNA	From -90°C to -60°C (-112°F to -76°F) until the expiration date	From +2°C to +8°C (+36°F to +46°F) for five days maximum; or up to two hours at a temperature lower than +30°C (+86°F)	Once diluted, use within six hours of being stored between +2°C and +30°C (+36°F to +86°F)	Protect from light Do not shake Do not freeze the thawed vaccine
Moderna COVID-19 vaccine	mRNA	From -25°C to -15°C (-13°F to 5°F) until the expiration date	From +2°C to +8°C (+36°F to +46°F) for 30 days maximum	After the vial is opened, store between +2°C and +25°C (+36°F to +46°F) and use within six hours	Protect from light Do not shake Do not freeze the thawed vaccine
AstraZeneca SK/ BIO/ AstraZeneca AB COVID-19 vaccines	Non-replicating adenoviral vector	From +2°C to +8°C (+36°F to +46°F) until the expiration date	N/A	After the vial is opened, store between +2°C and +8°C (+36°F to +46°F) and use within six hours.	Protect from light Do not shake Do not freeze
COVISHIELD™ AstraZeneca/SK COVID-19 vaccine Serum Institute of India Pvt. Ltd.	Non-replicating adenoviral vector	From +2°C to +8°C (+36°F to +46°F) until the expiration date	N/A	After the vial is opened, store between +2°C and +8°C (+36°F to +46°F) and use within six hours	Protect from light Do not shake Do not freeze
CoronaVac/Sinovac (inactivated) COVID-19 vaccine	Inactivated virus	From +2°C to +8oC (+36°F to +46°F) until the expiration date	N/A	The one-dose vial should be used immediately once opened. The multidose vial, once opened, can be stored between +2°C and +8°C (+36°F to +46°F) for up to six hours.	Protect from light Do not shake Do not freeze Vaccine contains adjuvant ($Al(OH)_3$)
Sinopharm BBIBP COVID-19 vaccine	Inactivated virus	From +2°C to +8°C (+36°F to +46°F) until the expiration date	N/A	Use the one-dose vial immediately, once opened	Protect from light Do not shake Do not freeze Vaccine contains adjuvant ($Al(OH)_3$)
SPUTNIK V/ Gam-COVID-Vac vaccine	Non-replicating adenoviral vector (rAd26-S) and (rAd5-S)	From below -18°C (0°F) until the expiration date	N/A	Use within the first two hours of defrosting. Do not refrigerate; do not freeze the thawed vaccine.	Protect from light Do not shake Do not freeze the thawed vaccine
Janssen COVID-19 vaccine	Non-replicating adenoviral vector	From -25°C to -15°C (-13°F to +5°F) until the expiration date	From +2°C to +8°C (+36°F to +46°F) for 3 months maximum	After the vial is opened, store between +2°C and +8°C (+36°F to +46°F) and use within six hours	Protect from light Do not shake Do not freeze the thawed vaccine

Prepared by the authors based on published data on vaccines.

Source: (1) WHO. Stability evaluation of vaccines. Can be found at;

https://www.who.int/biologicals/areas/vaccines/stability/en/