HSA's COVID-19 Vaccine Safety Update #12
(30 December 2020 – 31 May 2022)

This is HSA's 12th safety update of the COVID-19 vaccines covering the period from the roll-out of the vaccines on 30 December 2020 to 31 May 2022. It provides an overview of the reports by healthcare professionals of ***suspected* adverse events[1] (AEs)** associated with COVID-19 vaccines to the Health Sciences Authority (HSA) and our current assessment of these AEs.

2 The COVID-19 vaccines* used in Singapore are:

- mRNA vaccines: Pfizer-BioNTech/Comirnaty, Moderna/Spikevax
- Protein subunit vaccine: Nuvaxovid
- Inactivated vaccines: Sinovac-CoronaVac, Sinopharm

3 Vaccination is the most effective way to reduce deaths and severe illness from COVID-19 infection. Based on the local reports received, **HSA has assessed that the reporting rates of AEs (0.12%) and serious AEs (0.007%) of administered doses the cOVID-19 vaccines have remained stable. The benefits of the Pfizer-BioNTech/Comirnaty, Moderna/Spikevax, Nuvaxovid and Sinovac-CoronaVac COVID-19 vaccines continue to outweigh the known risks when used in a pandemic.** HSA and MOH will continue to monitor the safety profile of the COVID-19 vaccines closely, take the necessary regulatory actions and update members of the public of any significant safety concerns detected with the vaccines.

** Pfizer-BioNTech/Comirnaty is registered as a therapeutic product by HSA. Moderna/Spikevax, Nuvaxovid, Sinovac-CoronaVac are authorised under the Pandemic Special Access Route whereas Sinopharm is supplied via HSA's Special Access Route. The authorised mode of administration for COVID-19 vaccines is through the intramuscular injection route. Alternative routes such as subcutaneous injections are not encouraged as there are no robust clinical studies to support it.*

Key Updates (as of 31 May 2022)

i) mRNA COVID-19 Vaccines

Table 1. Overview of vaccination data and no. of suspected AE reports reported by healthcare professionals for mRNA COVID-19 vaccines

	Pfizer-BioNTech/Comirnaty	Moderna/Spikevax	Total
No. of persons who have received the first dose	4,060,694	1,083,966	**5,144,660**
No. of persons who received two doses*	4,004,622	968,640	**4,973,262**
No. of persons who received booster doses	3,103,484	1,209,050	**4,312,534**

[1] An adverse event is any untoward medical occurrence in a patient administered a pharmaceutical product (including vaccines) but does not necessarily have a causal relationship with this treatment/vaccination.

	Pfizer-BioNTech/Comirnaty	Moderna/Spikevax	Total
Total no. of doses administered	11,168,800	3,261,656	**14,430,456**
No. of suspected AE reports	14,236 (0.13% of doses administered)	3,077 (0.09% of doses administered)	**17,313 (0.12% of doses administered)**
No. of suspected serious[2] AE reports	841 (0.008% of doses administered)	191 (0.006% of doses administered)	**1032 (0.007% of doses administered)**

*The primary vaccination regimen for Pfizer-BioNTech/Comirnaty and Moderna/Spikevax COVID-19 vaccines comprise 2 doses. The number of persons who received two doses includes those who had received the first dose.

- The incidence rates of adverse events of interest (AESIs), namely, anaphylaxis, myocarditis (inflammation of heart muscles), pericarditis (inflammation of the outer lining of the heart) and cerebral venous thrombosis (CVT) with the mRNA vaccines have stabilized. There are no new findings since the last update in February 2022 (please refer to the previous HSA's COVID-19 Vaccine Safety Update for details).

- Appendicitis (inflammation of the appendix) can be caused by various factors such as infections in the digestive tract or blockage of the opening of the appendix causing it to become sore and swollen. The background incidence of appendicitis is estimated to be about 100 per 100,000 persons per year. Rare cases of appendicitis have been reported following vaccination with COVID-19 vaccines globally. Locally, twenty-one cases of appendicitis following Pfizer-BioNTech/Comirnaty COVID-19 vaccination have been reported after more than 11 million doses were administered. HSA's analysis found a small increased incidence of appendicitis occurring within 21 days after the primary vaccination series of the Pfizer-BioNTech/Comirnaty vaccine, mainly in individuals 12 to 17 years old. This translates to 2 additional cases per 100,000 doses administered. No increased incidence of appendicitis has been observed with the booster dose of the vaccine. All the cases have been discharged after hospitalisation. Individuals who experience persistent or worsening of abdominal pain after vaccination are advised to seek prompt medical treatment.

ii) Nuvaxovid COVID-19 Vaccine

- The vaccination programme for Nuvaxovid COVID-19 vaccine was recently rolled out on 18 May 2022, with 2,792 doses being administered as of 31 May 2022.

- Locally, four non-serious AE reports were received, describing rash, vasculitis (inflammation of blood vessels), dizziness and chest pain. These are largely consistent with what was reported in the clinical studies and are known adverse effects associated with vaccines.

- An AESI which we are monitoring closely is myocarditis and pericarditis. While locally no AE reports of myocarditis have been received to date, a small number of reports were observed from ongoing global clinical trials. It is important to note that COVID-19 infection is also known to be associated with myocarditis. Based on published literature, 40 extra myocarditis events per million persons were observed following COVID-19

[2] An adverse event is classified as serious when the event resulted in hospitalisation/extended stay in hospital, resulted in a significant reduction in functioning level/disability, resulted in a life-threatening illness (e.g. anaphylaxis) or death, resulted in birth defects or is a medically important event.

infection.[3] HSA's assessment is that although the potential risk of myocarditis with Nuvaxovid COVID-19 vaccine cannot be excluded, the benefits of the vaccine continue to outweigh the risks in the Singapore context. As a precautionary measure, persons who are vaccinated with the Nuvaxovid vaccine should avoid strenuous physical activity or exercise for two weeks after vaccination to mitigate the potential risk of myocarditis. Strenuous activities refer to moderate to high intensity activities such as running, weightlifting, competitive sports and playing ball games. Light intensity activities where you can still speak without feeling out of breath such as casual walking, stretching, and housework can be continued.

iii) Sinovac-CoronoVac and Sinopharm COVID -19 Vaccine

- The incidence rates of AEs and SAEs with Sinovac-CoronaVac and Sinopharm COVID-19 vaccines have remained stable and there are no new safety updates with the vaccines (please refer to previous HSA's COVID-19 Vaccine Safety Update for details).

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Interpretation of the data

HSA reviews the submitted AE reports, in consultation with our expert panels[4].AEs are reported by healthcare professionals to HSA when they suspect that the AEs may be associated with the vaccine. This does not necessarily mean that the vaccine has caused the AEs. In some instances, these AEs are related to an underlying or undiagnosed disease or the natural progression of an underlying disease. It may be coincidental that the event occurred around the same time when the vaccine was given but is not caused by the vaccine. The causality based on isolated cases of individual events usually cannot be established as many illnesses cause the same symptoms and signs, and there are generally no confirmatory tests for diagnosing an AE. Hence, AEs are assessed and interpreted in the context of background incidence rates of such occurrences (i.e., historical rates in our general population unexposed to the COVID-19 vaccines). While each individual report is carefully reviewed, the totality of data from all sources (e.g., mechanistic actions, clinical assessments of local AE reports from healthcare professionals, public self-reported AEs, epidemiological studies, literature and overseas reports) has to be considered before drawing any evidence-based conclusions on the safety of the vaccine.

The type and number of reports received for the different COVID-19 vaccines are not directly comparable as the vaccines may have been used in the vaccination programme for different lengths of time, and may have been administered to different numbers of people with different underlying medical conditions and across different settings. Similarly, the AE numbers or rates between countries should not be directly compared as the usage of the vaccines may be different and the AE reporting systems are often also different.

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[3] Patone, M., Mei, X.W., Handunnetthi, L. et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med (2021)

[4] HSA has appointed seven Expert Panels to review neurological AEs, cardiac AEs, thromboembolic and haematological AEs, renal AEs, ear AEs, immunological AEs and severe hypersensitivity reactions such as anaphylaxis

The description of suspected AEs in this update reflects the available information known at the time by HSA. These data may undergo changes as more information on individual reports becomes available through follow-up, and as more data are reported and evaluated.