HSA's COVID-19 Vaccine Safety Update #14
(30 December 2020 – 31 December 2022)

This is HSA's 14th safety update of the COVID-19 vaccines covering the period from the roll-out of the vaccines on 30 December 2020 to 31 December 2022. With the recent roll-out of COVID-19 vaccination in young children aged 6 months to 4 years, booster vaccination in children aged 5 to 11 years, and bivalent Original/Omicron mRNA COVID-19 vaccines, this report provides updates on the **suspected adverse events (AEs)**[1] reported in these subgroups. Based on our current assessment of local and overseas data, no new safety signals have been identified with the use of the vaccines in these subgroups.

2 The COVID-19 vaccines[2] used in Singapore are:

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

3 As of 31 December 2022, a total of 17,191,955 doses of COVID-19 vaccines have been administered. The majority of the doses administered were the monovalent mRNA vaccines (91.6%; 15,743,615 doses) as these were the first vaccines that were made available and recommended for use in Singapore. This was followed by the inactivated COVID-19 vaccines (4.2%; 722,419 doses), bivalent Original/Omicron mRNA vaccines (4.0%; 685,048 doses) and Nuvaxovid vaccine (0.2%; 40,873 doses).

4 Vaccination has been demonstrated to be the most effective way to reduce deaths and severe illness from COVID-19 infection and has enabled Singapore to ease most of the safe management measures. **The benefits of Pfizer-BioNTech/Comirnaty, Moderna/Spikevax, Nuvaxovid and Sinovac-CoronaVac COVID-19 vaccines continue to outweigh the known risks.**

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[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.

[2] Pfizer-BioNTech/Comirnaty vaccine is registered as a therapeutic product by HSA. Moderna/Spikevax, Nuvaxovid and Sinovac-CoronaVac vaccines are authorised under the Pandemic Special Access Route (PSAR) whereas Sinopharm vaccine is supplied via HSA's Special Access Route.

HSA extended the use of Pfizer-BioNTech/Comirnaty vaccine to adolescents aged 12 to 15 years on 18 May 2021 and to children aged 5 to 11 years old on 10 December 2021.

HSA extended the use of Moderna/Spikevax vaccine to children aged 6 months to 17 years old on 24 August 2022 and authorised the use of Pfizer-BioNTech/Comirnaty vaccine in those aged 6 months to 4 years old on 28 September 2022.

Moderna/Spikevax Bivalent Original/Omicron COVID-19 vaccine was authorised as a booster vaccine for individuals aged 18 years and above and Pfizer-BioNTech/Comirnaty Bivalent Original/Omicron COVID-19 vaccine was authorised as a booster vaccine for individuals aged 12 years and above under PSAR on 14 September 2022 and 11 October 2022 respectively.

Key updates (as of 31 December 2022)

i) mRNA COVID-19 vaccines

- A total of 10,506,824 primary doses, 4,682,058 first booster doses and 1,239,781 second booster doses of the mRNA vaccines have been administered.

- **The reporting rates of AEs and serious[3] AEs for the mRNA vaccines (monovalent and bivalent versions) remained rare at 0.11% (17,741 reports) and 0.007% (1,119 reports) respectively. The serious AE reporting rates for the first and second booster doses were at 0.004% (173 reports) and 0.001% (17 reports), respectively, which were lower compared to the primary doses at 0.009% (934 reports).**

- There were no new safety findings on the monovalent Pfizer-BioNTech/Comirnaty and Moderna/Spikevax vaccines since the update published in September 2022 (please refer to the previous HSA's COVID-19 Vaccine Safety Update for details).

Adverse events in children aged 6 months to 11 years with the monovalent mRNA COVID-19 vaccines

- Moderna/Spikevax vaccine was rolled out as primary vaccination to children aged 6 months to 4 years and Pfizer-BioNTech/Comirnaty vaccine was rolled out as booster doses to children aged 5 to 11 years on 25 October 2022. There were 16,448 doses of Moderna/Spikevax vaccine and 81,477 doses of Pfizer-BioNTech/Comirnaty vaccine administered in the respective age groups.

- The number of doses of Moderna/Spikevax vaccine administered in children aged 6 months to 4 years and the number of booster doses of the Pfizer-BioNTech/Comirnaty vaccine administered in children aged 5 to 11 years are still relatively small. Serious AEs after COVID-19 vaccination in children aged 6 months to 11 years are rare. Based on our assessment of current local and overseas data, no new safety signals have been identified with the use of the vaccines in this age group.

- The AE reporting rate in **children 6 months to 4 years** is 0.05% (8 reports out of 16,448 doses of **Moderna/Spikevax vaccine**). There were five serious reports which included febrile seizures (fits), Kawasaki disease (swelling of blood vessels), fever and vomiting. Febrile seizures and Kawasaki disease are rare events that have been reported following childhood vaccination and can be associated with childhood illnesses. All the children have recovered or were recovering at the time of report.

- The AE reporting rate for booster doses in **children aged 5 to 11 years** is 0.03% (26 reports out of 81,477 doses of **Pfizer-BioNTech/Comirnaty vaccine**), which is lower than the AE reporting rate for the primary vaccination series in this age group (0.15%). These were mostly non-serious AEs such as fever, headache, musculoskeletal chest pain, palpitations, joint pain, rash and vomiting. There were two serious AEs, one describing myocarditis (inflammation of heart muscles) and the other was a drop in platelet count. Both were recovering at the time of report. There have also been overseas cases of myocarditis reported with the booster doses of the mRNA COVID-19 vaccines in this age group. The incidence remains rare and is generally lower compared

[3] 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.

to adolescents and adults. HSA is closely monitoring these AEs and assessing them in the context of their background incidence rate.

- It should be noted that the type and number of reports received for the different age groups may not be directly comparable as the vaccines have been used for different lengths of time in the different age groups.

Adverse events with the bivalent Original/Omicron mRNA COVID-19 vaccines

- Moderna/Spikevax Bivalent Original/Omicron COVID-19 vaccine and Pfizer-BioNTech/Comirnaty Bivalent Original/Omicron COVID-19 vaccine were rolled out on 14 October 2022 and 12 December 2022 respectively. There were 482,666 doses and 202,382 doses administered for these 2 vaccines respectively.

- HSA received 59 and 11 AE reports (reporting rate of 0.012% and 0.005%) for Moderna/Spikevax Bivalent vaccine and Pfizer-BioNTech/Comirnaty Bivalent vaccine respectively. The AEs reported for the bivalent mRNA vaccines were similar to those following the monovalent vaccines, describing mostly non-serious AEs such as allergic reactions, which included rash and eyelid swelling, fever, giddiness, chest discomfort or pain, syncope and increase in blood pressure.

- There were six serious AEs reported for Moderna/Spikevax Bivalent vaccine and two serious AEs for Pfizer-BioNTech/Comirnaty Bivalent vaccine. These reports include serious allergic reactions, anaphylaxis, myocarditis, hypotension with tachycardia (fast heartbeat) and hearing loss. **The serious AE** reporting rates for the two vaccines are similar, at 0.001%, which **is lower compared to the monovalent vaccines (0.007%)**. **For myocarditis, the reporting rate is 0.1 per 100,000 doses for the bivalent vaccines, which is lower compared to 1.1 per 100,000 doses for the primary vaccination series of the monovalent vaccines.**

ii) Nuvaxovid COVID-19 vaccine

- A total of 40,873 doses of the Nuvaxovid vaccine have been administered as of 31 December 2022. The serious AE reporting rate remained rare at 0.02% (9 reports).

iii) Sinovac-CoronaVac and Sinopharm COVID-19 vaccines

- A total of 722,419 doses of the inactivated vaccines have been administered as of 31 December 2022. The serious AE reporting rate remained rare at 0.006% (40 reports).

- As with the case of monovalent mRNA vaccines, there were no new safety findings for the inactivated vaccines since the last update published in September 2022 (please refer to the 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.

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.

[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.