

## **CONSIDERATIONS OF THE EXPERT COMMITTEE ON COVID-19, ON EXTENDING THE MAXIMUM MRNA COVID-19 VACCINE DOSING INTERVAL TO EIGHT WEEKS**

EC19V considered the emerging scientific evidence around whether a delayed second dose of mRNA vaccine might be feasible, in the light of the rising community COVID-19 incidence and the current state of the evidence. EC19V noted that vaccination with the HSA PSAR approved mRNA vaccines is already considered valid in situations where the second dose is administered up to six weeks after the first dose. EC19V is of the view that the maximum interval between mRNA COVID 19 vaccines could be extended to six weeks and possibly eight weeks to maximise vaccine coverage in special circumstances of need.

### **Background**

2. Given the rise in COVID-19 transmission in Singapore, there is a need to consider speeding up the pace of vaccination to maximise vaccine coverage. However, this is currently constrained by our vaccine supplies.

3. One strategy to overcome this would be to maximise first-dose vaccine coverage while deferring the second dose to beyond the recommended interval. This has been adopted by some countries such as the UK, Canada and Germany.

### **Scientific Considerations**

4. EC19V deliberated the scientific merits of using such an approach. The committee looked at the available data from the original mRNA trials and emerging information from both real-world data as well as laboratory studies and simulations.

### Extension of the maximum interval between doses to beyond 6 weeks

5. Currently, the PSAR-approved mRNA vaccines can already be administered at an interval of up to 6 weeks (42 days) apart to be valid. This is based on the maximum dosing interval that was adopted during the pivotal trials.

6. There are concerns that the effectiveness and durability of vaccine protection may be adversely affected by extension in the interval between vaccine doses. However, based on early evidence in persons aged above 80, such a delay of the second dose to 12 weeks resulted in higher antibody levels 2 weeks after the second dose.

7. The immunologists in EC19V also opined that based on knowledge and experience with other vaccines, the interval of six to eight weeks between first and second dose should not materially impact the eventual overall immune response, so long as we are assured that the second dose was given.

8. Given the nascent data, EC19V is of the view that a cautious extension of the interval between the first and second dose to six weeks is unlikely to be an issue but indicated concern if the delay were beyond eight weeks.

Other supporting information regarding the impact of the first vaccine dose

9. There has also been evidence that a single dose of the vaccine confers some protection against symptomatic and asymptomatic infection, with studies indicating single-dose vaccine effectiveness of between 46% to 92%. Moreover, with one dose, the antibody and T-cell responses were robust, and meaningful protection persisting to 42 days and beyond has been documented. These further suggest that maximising first-dose vaccine coverage in settings of significant community spread is a tenable approach in such situations. A simulation study indicated that, based on some assumptions, first-dose vaccine coverage, even if the second dose is delayed, may prevent infections, admissions, and deaths.

**Overall Assessment and Recommendations**

10. Overall, while the evidence is still tentative, in the setting of increased disease transmission, the approach of maximising first-dose vaccine coverage while extending the maximum interval between doses to eight weeks may be adopted.

11. This approach would be particularly important for subpopulations at risk of exposure and/or at risk for severe disease. EC19V and MOH had established the priority groups previously which have generally achieved good vaccination coverage. Examples of at-risk groups would be those in congregate accommodation such as migrant workers.

12. It is important to emphasize that vaccination requires two doses with our current available vaccines. Regardless of the interval between doses, it would be necessary to ensure that each vaccinated individual in the population receives two doses of the vaccine to derive maximal protection from COVID-19 and COVID-19 variants. Keeping to the established dosing intervals is still preferable outside the contingencies that we are faced with currently, particularly as there remain plausible unknowns over the impact there may well be to overall effectiveness and durability of immunity that can be derived from a single dose, as well as the protective efficacy against Variants of Concern.

**Conclusion**

13. EC19V is of the view that extending the maximum dosing interval to six to eight weeks, thereby maximising first-dose vaccine coverage, is a reasonable strategy in particular local settings if there is a compelling need. EC19V will continue to monitor the evolving evidence as it emerges and will refine its recommendations accordingly as necessary.