Memo

Decision to use a primary course of the Novavax COVID-19 vaccine: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	10 February 2022
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Cc:	Astrid Koornneef, Director, National Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the decision to use a primary course (two doses) of the Nuvaxovid COVID-19 Vaccine with Matrix-M Adjuvant ('the Novavax vaccine').

Background and Context

2. In February 2021, CV TAG advice was sought about the use of the Pfizer COVID-19 vaccine for people who were 16 years and over, following Medsafe provisional approval. Cabinet agreed that the COVID-19 Vaccine Immunisation Programme proceed with the rollout of the Pfizer vaccine. It was noted that further advice would be provided to Cabinet on each of New Zealand's four vaccine candidates as they became available for use (following Medsafe approval), without knowing if a future vaccine was going to be more suitable or effective. In order to make decisions given the uncertainty, a Decision to Use framework was developed.
3. In July 2021, CV TAG advice was sought about the use of the Janssen COVID-19 vaccine for people aged 18 years and over, following Medsafe provisional approval. CV TAG advised that there was no current indication for wide use of the Janssen vaccine, however, it could be considered at an individual level where the Pfizer vaccine was not suitable e.g., anaphylaxis or other rare side effects following the first dose of the Pfizer vaccine.
4. In October 2021, CV TAG advice was sought about the use of the AstraZeneca COVID-19 vaccine for people aged 18 years and over. CV TAG advised that the AstraZeneca vaccine should be used as a second-line vaccine, with Pfizer remaining the first-line and preferred vaccine. It was recommended that the AstraZeneca vaccine be restricted to people who have a contraindication to the Pfizer vaccine, or people who would prefer to get the AstraZeneca vaccine. For example, those currently under a Vaccination Order, people who are unvaccinated or have only received one dose, and people who are hesitant about getting the Pfizer vaccine.

5. The Novavax vaccine was granted provisional approval by Medsafe for use in people aged 18 and over in New Zealand on 4 February 2022, under section 23(1) of the Medicines Act 1981, with conditions. It is a two-dose recombinant spike protein nanoparticle vaccine containing the Matrix-M adjuvant, with the second dose approved to be administered at least 3 weeks after the first dose [1].

6. The Ministry's Policy team sought clinical and scientific advice from CV TAG on the use of the Novavax vaccine in New Zealand.

Data on a primary course of the Novavax vaccine

7. The overall efficacy and safety of the Novavax vaccine is based on analysis of data from clinical trials conducted in the UK, South Africa, the US and Mexico (PREVENT-19 trial).

8. *UK phase III trial*[2]*:* Per protocol efficacy against symptomatic, laboratory-confirmed COVID-19 (in an Alpha-variant-dominant setting) ≥7 days post-second dose was 89.7% [95% CI: 80.2-94.6]. Solicited local adverse events were reported more frequently in the vaccine group than in the placebo group after both the first dose (57.6% vs. 17.9%) and the second dose (79.6% vs. 16.4%). Solicited systemic adverse events were also reported more frequently in the vaccine group than in the placebo group after both the first dose (45.7% vs. 36.3%) and the second dose (64.0% vs. 30.0%). Overall, reactogenicity was generally mild to moderate and transient. The frequency of unsolicited adverse events was higher among vaccine recipients than among placebo recipients (25.3% vs. 20.5%), with similar frequencies of severe adverse events (1.0% vs. 0.8%) and serious adverse events (0.5% vs. 0.5%) between the two groups. There was one case of myocarditis that occurred three days after the second dose, which was considered possibly immune related, however, it was adjudicated to most likely be viral myocarditis.

9. *US and Mexico phase III trial (PREVENT-19)*[3]: Per protocol efficacy against PCR-confirmed, symptomatic COVID-19 (in an Alpha-variant-dominant setting) ≥7 days post-second dose was 90.4% (95% CI: 82.9-94.6) and against moderate or severe disease was 100% (95% CI: 87-100). Similar to the results from the UK phase III trial, reactogenicity was mostly mild to moderate and transient but was more frequent among Novavax recipients compared to placebo recipients and was more frequent after the second dose (local adverse events: 58.0% vaccine vs. 21.1% placebo after dose 1, and 78.9% vaccine and 21.7% placebo after dose 2; systemic adverse events: 47.7% vaccine and 40.0% placebo after dose 1, and 69.5% vaccine and 35.9% placebo after dose 2). Serious adverse events were balanced between the vaccine and placebo groups (0.9% vs. 1.0%). No episodes of the Guillain–Barré syndrome and there were no differences reported in myocarditis, pericarditis or in vaccine-induced immune thrombosis with thrombocytopenia observed between groups in the two-month follow-up period.

10. *South Africa phase IIa–b trial*[4]: Per protocol efficacy against symptomatic, laboratory-confirmed COVID-19 (in a Beta-variant-dominant setting) among HIV-negative participants was 60.1% (95% CI: 19.9-80.1) but was lower when HIV-positive participants were included (49.4% [95% CI: 6.1-72.8]). Solicited local and systemic adverse events, which were predominantly mild to moderate and transient, were more common in the vaccine group than in the placebo group. Serious adverse events were rare in both groups.

11. *Heterologous schedules:* Data are still emerging on the efficacy and safety of heterologous ("mixed dose") vaccine schedules incorporating approved vaccines in New Zealand. Results from the UK Com-CoV2 trial found that immunogenicity following a Novavax dose in

participants primed with Pfizer was inferior to those who received a homologous schedule of Pfizer. However, immunogenicity following a Novavax dose in those who were primed with AstraZeneca was superior to immunogenicity in those who received a homologous AstraZeneca course. Novavax did not increase reactogenicity when administered following a first dose of either Pfizer or AstraZeneca [5].

12. *Efficacy against variants of concern:* In the UK phase III trial, a post hoc analysis showed an efficacy of 86.3% (95% CI: 71.3-93.5) against the Alpha variant [2]. In the PREVENT-19 trial, efficacy against all variants of concern or interest circulating at that time of the trial was 92.6% (95% CI: 83.6 to 96.7) [3]. This included the Alpha, Beta, Gamma, Epsilon, and Iota variants that were predominant in the US and Mexico during the trial. In the South Africa phase IIa–b trial, post hoc efficacy against Beta was 51.0% (95% CI: -0.6-76.2) among the HIV-negative participants [4]. There are no efficacy data available for the Delta and Omicron variants.

13. *Co-administration with influenza vaccine[6]:* The UK phase III trial had a sub-study investigating co-administration of a licensed influenza vaccine (Flucelvax Quadrivalent for those aged 18-64 years and adjuvanted trivalent influenza vaccine Fluad for those ≥65 years) in 431 participants, given on the opposite deltoid to that of the first dose. The point estimate for efficacy against symptomatic PCR-confirmed COVID-19 was similar between the co-administration group at 87.5% (95% CI: -0.2-98.4) and the main study (Novavax only) at 89.8% (95% CI: 79.7-95.5). However, this observation was based on only nine cases in the co-administration sub-study.

Approval of the Novavax vaccine by other jurisdictions

14. The UK Medicines and Healthcare products Regulatory Agency (MHRA) approved the Novavax vaccine for use in over 18-year-olds on 3 February 2022 [9].

15. The European Medicines Agency approved the use of the Novavax vaccine on 20 December 2021 [7].

16. At the beginning of February 2022 Novavax filed for emergency use authorisation of its COVID-19 vaccine in the United States, however approval is yet to be granted.

17. The Novavax vaccine is provisionally approved by the Australian Therapeutics Goods Administration for use in a primary course of vaccination [11]. The Australian Technical Advisory Group on Immunisation (ATAGI) has recommended the Novavax vaccine be given in two doses, at least three weeks apart.

Recommendations

14. CV TAG met on 1 February 2022 and 8 February 2022 to discuss use of a primary course of the Novavax COVID-19 vaccine, noting the information provided in the vaccine Data Sheet.

15. CV TAG noted that:

15.1 The contraindications for the Novavax vaccine are anaphylaxis to a previous dose of Novavax COVID-19 vaccine or to a component of the vaccine, as outlined in the vaccine Data Sheet.

15.2 In general, the Novavax vaccine offers a high level of protection against symptomatic COVID-19 and severe disease. However, it is not known how effective the primary course is against variants of concern that have emerged recently, such as Delta and Omicron.

15.3 The Novavax vaccine is reactogenic, particularly after the second dose. Side effects are generally mild to moderate and transient, and the overall safety profile does not raise any significant concerns. Continued safety monitoring is essential to understand the long-term safety profile of this platform.

15.4 Data on efficacy and safety of the Novavax vaccine in people aged less than 18 years, in pregnant people, and in people who become pregnant after receiving the vaccine are limited.

15.5 Novavax has been trialled in heterologous primary schedules. It produced a stronger immune response in those primed with AstraZeneca as a first dose, and a slightly inferior immune response in those primed with Pfizer as a first dose. There was no increase in reactogenicity in the heterologous schedules.

15.6 There is a potential for Novavax to be used as a booster dose in the context of Omicron, however, at this stage data are limited and this item will be considered separately.

16. CV TAG recommends that:

16.1 The COVID-19 Vaccine Immunisation Programme use the Novavax vaccine as a second-line vaccine, with Pfizer remaining the first-line and preferred vaccine for a primary course.

16.2 Use of the Novavax vaccine should be restricted to people who:

a) have a contraindication to the Pfizer vaccine,

b) would prefer to get the Novavax vaccine and are currently under a Vaccination Order,

c) are unvaccinated or have only received one dose and are hesitant about getting the Pfizer vaccine, or

d) experienced anaphylaxis or other rare side effects following the first dose of the Pfizer vaccine.

16.3 There are currently insufficient data on the use of the Novavax vaccine to recommend it during pregnancy. Use in pregnancy should be based on an assessment of benefits and risks by the consumer and their healthcare professional.

16.4 With regard to timing:

a) two doses of the Novavax vaccine, given at least 3 weeks apart, are required for a primary vaccination course.

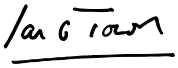
b) Novavax can be administered as part of a heterologous primary schedule to people who have received another COVID-19 vaccine as their first dose, and this should occur at least 28 days after the first dose of the other COVID-19 vaccine, to account for recommended intervals for other vaccine brands.

c) there should be no upper limit on time since the first dose.

d) the Novavax vaccine may be administered before, after, or at the same time as the influenza, MMR, HPV, diphtheria/tetanus/pertussis combination vaccine (Boostrix), and other vaccines. The only exception to this advice is for the live-attenuated shingles vaccine (Zostavax) where a 7-day interval, before or after administering the Novavax vaccine is advised.

17. Guidance on the use of a booster dose of the Novavax vaccine will be considered separately, pending any future Medsafe approval.

18. CV TAG will continue to monitor all relevant information (including vaccine effectiveness data against variants of concern and emerging evidence on the duration of immunity) and will update their recommendations as further evidence becomes available.



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