ATAGI recommendations on use of the Pfizer bivalent (Original/Omicron BA.1) COVID-19 vaccine

Recommendations from the Australian Technical Advisory Group on Immunisation (ATAGI) the Pfizer bivalent (Original/Omicron BA.1) COVID-19 vaccine.

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On 27 October 2022, the Therapeutic Goods Administration of Australia provisionally approved the Pfizer (Comirnaty) Bivalent Original/Omicron BA.1 vaccine (subsequently referred to as Pfizer bivalent) for use as a booster COVID-19 vaccine in people aged 18 years and older. The

Australian Technical Advisory Group on Immunisation (ATAGI) has evaluated the immunogenicity, efficacy, and safety data on this vaccine.

Recommendations

ATAGI updates its existing recommendations regarding use of bivalent Original/Omicron BA.1 vaccines with the following:

- The Pfizer bivalent vaccine can be used as an alternative vaccine to any of the available mRNA COVID-19 vaccines (Pfizer original vaccine, Moderna bivalent vaccine or Moderna original vaccine) for any booster dose in people aged 18 years or older who are currently recommended to receive a COVID-19 booster.
- In those who are eligible for a booster dose, ATAGI does not have a preference for bivalent mRNA vaccines over original mRNA vaccines.
- Booster doses of COVID-19 vaccine should be given at least 3 months after the most recent COVID-19 vaccine dose or confirmed SARS-CoV-2 infection.
- As with other mRNA COVID-19 vaccines, the Pfizer bivalent vaccine can be co-administered with other non-COVID-19 vaccines.
- The Pfizer bivalent vaccine is not recommended for the primary course of vaccination (the first two doses in most people or first three doses in severely immunocompromised people).
- ATAGI does not currently recommend use of the Pfizer bivalent vaccine as a booster in anyone aged **under** 18 years as it is not registered for use in this age group.

Read the summary of current ATAGI recommended doses and vaccines.

Vaccine presentation

The Pfizer bivalent vaccine is presented as a grey-capped multi-dose vial containing six 0.3mL doses of 30 mcg. The vaccine does not require dilution.

Each dose should be administered intramuscularly, preferably in the deltoid.

Rationale

The original Pfizer and Moderna COVID-19 vaccine used mRNA from the ancestral (original) strain of SARS-CoV-2. Newer combination formulations of COVID-19 booster vaccines have been developed using mRNA encoding for the spike protein the BA.1 sublineage of the Omicron variant together with the mRNA encoding ancestral strain spike.

All mRNA COVID-19 booster vaccine doses (bivalent and original) result in an improvement in the immune response against Omicron subvariants BA.1 and BA.4/BA.5. The inclusion of BA.1 in bivalent vaccines is expected to provide a greater breadth of protection compared with ancestral vaccines against current and future Omicron sub-variants such as BQ.1 and XBB, though there are no published data yet to demonstrate this.

A clinical trial among people aged over 55 years has demonstrated that the Pfizer bivalent vaccine induces a modestly higher level of antibody response against BA.1 and BA.4/5 Omicron subvariants compared to the Pfizer COVID-19 original vaccine, when used as a second booster dose. There are no objective data to translate this directly to clinical protection.

Modelling suggests that differences in the additional protection against COVID-19 from a bivalent booster over an original booster are relatively small compared to the protection obtained from receiving any booster at all.[1]

The safety profile of the bivalent vaccine as a booster dose in adults aged over 55 years appears similar to the original vaccine.

There are no data yet on the immunogenicity or safety of the Pfizer bivalent vaccine in people under 55 years of age. Evidence from a monovalent Omicron BA.1 vaccine in people aged 18 to 55 years, showing improved immune response against BA.1, was used to infer protection. There are no data on the use of any Pfizer vaccine containing the Omicron variant in any population aged <18 years. There are no studies at present which compare the Pfizer bivalent vaccine head-to-head with the Moderna bivalent vaccine.

Vaccine immunogenicity

Evidence supporting use of the Pfizer bivalent vaccine is limited to immunogenicity and safety data from the C4591031 trial (substudy E) at 4 weeks after a second booster dose (fourth dose).[2] Participants aged >55 years received Pfizer bivalent vaccine as their second booster dose, 5 to 12 months following a Pfizer original primary course (30mcg) and Pfizer original first booster dose (30mcg).

The trial included 305 people who received the Pfizer bivalent vaccine and 305 people who received the Pfizer original vaccine as a second booster dose. Against the Omicron BA.1 variant, the Pfizer bivalent vaccine provided 1.6 times higher neutralising antibodies compared to the

original vaccine, in people without prior infection (95% CI: 1.17, 2.08).[2] Against the original virus, neutralising antibody titres were similar for the Pfizer bivalent and Pfizer original vaccine (Geometric mean ratio 0.99 [95% CI: 0.82, 1.20]).[2]

While immunogenicity data are not available for people aged ≤55 years, the C4591031 trial (substudy D) included a cohort of participants aged 18 to 55 years who received the Pfizer monovalent Omicron BA.1 vaccine (30mcg) as a second booster. The trial included 263 people receiving the Pfizer monovalent omicron vaccine and 280 people receiving the Pfizer original vaccine. Against the Omicron BA.1 variant, neutralising antibodies for the Pfizer monovalent vaccine were higher compared to the Pfizer original vaccine (unpublished company data) by a similar degree to that seen in the Pfizer bivalent study.

Cross-protection against variants/subvariants

Evidence from a small subgroup analysis of 20 participants in each group from the trial suggests that Pfizer bivalent vaccine may provide cross-protection against variants and subvariants not included in the vaccine. Neutralisation titres against BA.4 and BA.5 subvariants were higher for the bivalent vaccine (226.3 [95% CI: 120.7, 424.1) compared with the original vaccine (110.9 [95% CI: 67.9, 180.9]).[3] Pre-print studies, that have not yet been peer reviewed, have found that BA.4/5 bivalent vaccines induce an immune response against emerging sub-variants BQ.1.1 and XBB[4,5,6]. There are no published data on the immunogenicity of BA.1 bivalent vaccines against these newer sublineages.

Safety data from clinical trials[3]

The Pfizer bivalent trial and the Pfizer monovalent BA.1 trial suggest that the safety profile of these vaccines is similar to the Pfizer original vaccine.

The most commonly reported local and systemic adverse reactions following a second booster of the Pfizer bivalent vaccine in people aged over 55 years were injection site pain (58%), fatigue (49%), headache (34%) and myalgia (22%). The most commonly reported local and systemic adverse reactions following a second booster of the Pfizer monovalent vaccine in people aged 18 to 55 years were injection site pain (78%), fatigue (64%), headache (48%) and myalgia (34%). The risk of myocarditis or pericarditis (very rare adverse effects of COVID-19 vaccines) following the Pfizer bivalent vaccine has not yet been characterised as this vaccine has not been used extensively in large populations. However, evidence from booster doses with the original Pfizer mRNA vaccine, which has been used for longer and on more people, shows that the frequency of myocarditis is lower for booster doses compared with second doses, and this is not expected to be different with bivalent booster vaccines.

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