New drugs

BNT162b2 COVID-19 vaccine

Approved indication: prevention of COVID-19

Comirnaty (Pfizer)
multidose vials containing 0.45 mL suspension for dilution

In March 2020, the World Health Organization declared that the COVID-19 outbreak was a pandemic. Since then, there have been over 111 million confirmed cases worldwide and over 2.4 million deaths resulting from SARS-CoV-2 viral infection (WHO COVID-19 dashboard).[1] In response, hundreds of vaccines are being rapidly developed in an effort to prevent further disease.[2]

The BNT162b2 COVID-19 vaccine was the first to be given provisional approval in Australia and is indicated for those aged 16 years and over. It is made up of single-stranded messenger RNA (mRNA) which encodes the viral spike protein of the SARS-CoV-2 virus. The RNA is encapsulated in lipid nanoparticles which allows uptake by antigen-presenting cells (e.g. dendritic cells). Once inside, the mRNA is translated into the spike protein by host-cell machinery and presented on the cell surface. These antigen-presenting cells then show the spike protein to other immune cells including B cells which produce anti-spike protein antibodies.

The approval of this vaccine is based on short-term efficacy and safety data from an ongoing global trial. In the phase I part of the study, basic safety data including reactogenicity and immunogenicity of the vaccine were established.[3] Two 30 microgram doses given intramuscularly 21 days apart were found to elicit high titres of neutralising antibodies to the SARS-CoV-2 virus and robust cell-mediated responses involving CD8 and CD4 T cells.[4] This dosing regimen was progressed into the phase II/III part of the trial,[5] which randomised 43,548 participants (aged 16–91 years) 1:1 to receive the vaccine or a matching placebo.

The primary outcome of the phase II/III study was efficacy against COVID-19 disease onset at least seven days after the second dose in participants who were naïve to the SARS-CoV-2 virus. During the surveillance period, there were eight cases of COVID-19 among those who received the vaccine and 162 cases among those who received placebo. This equates to a vaccine efficacy of 95% (confidence interval (CI) 90.3–97.6%). A subgroup analysis found that protective efficacy was similar regardless of age, sex, ethnicity, obesity and co-existing hypertension.[5]

There were also less COVID-19 cases with the vaccine compared to placebo after the first dose but before the second dose (39 vs 82 cases) indicating that one dose of the vaccine confers some protective efficacy (52%, CI 29.5–68.4%). Severe COVID-19 occurred in one person who received the vaccine after the first dose and nine people who received placebo.[5]

In a safety cohort of 21,744 people who received at least one vaccine dose, the most common adverse events were injection-site pain (>80% of patients), fatigue (>60%), headache (>50%), myalgia and chills (>30%), arthralgia (>20%) and fever and injection-site swelling (>10%). Most reactions were mild to moderate in severity and often occurred at a higher frequency after the second vaccine dose. In general, older participants reported fewer and less severe adverse events. There were four cases of Bell's palsy with the vaccine versus none with the placebo. In the phase II/III part of the study, there were two deaths in the vaccine group (from arteriosclerosis and cardiac arrest) and four in the placebo group (deemed not related to study intervention).

Anaphylaxis has been reported with this vaccine following its rollout in the UK and USA. Two cases in the UK were in people who had a history of severe allergic reactions. Close observation for at least 15 minutes after vaccine administration is recommended and the second dose should not be given to someone who had an anaphylactic reaction with the first dose. Vaccination is appropriate in those with minor infections or low-grade fevers but should be postponed in those with acute severe febrile illness.

There have so far been no interaction studies with the vaccine. It is unclear whether it can be given at the same time as other vaccines.

There are limited data on use of the vaccine during pregnancy and lactation. Studies in animals did not indicate any harmful effects. Given the low level of community transmission in Australia, routine use of COVID-19 vaccines during pregnancy is not currently recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists.[6] However, its guidance states that vaccination may be considered in some groups with a high risk of complications from COVID-19. Pregnant healthcare workers in an at-risk work environment should be

Aust Prescr 2021;44:57–8
https://doi.org/10.18773/austprescr.2021.008
First published 26 February 2021

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NEW DRUGS

allocated to lower-risk duties, work from home or take leave of absence. If this is not possible, they should be offered vaccination. The Australian Department of Health has published a guide to help women making decisions about vaccination during pregnancy and breastfeeding.

The vaccine is supplied in frozen multidose vials. Once thawed, the vaccine should be diluted with 1.8 mL of normal saline. This allows for administration of six 0.3 mL doses using low dead-volume syringes and needles. Opened vials should be discarded after six hours. Training modules for vaccination providers have been developed by the Department of Health in partnership with the Australian College of Nursing to ensure COVID-19 vaccines are administered safely.

The vaccine should be given by intramuscular injection into the deltoid muscle of the upper arm. The patient's name and the batch number of the vaccine must be recorded in the Australian Immunisation Register. Enhanced monitoring of adverse events following COVID-19 vaccination is in place at national and state and territory levels.[2]

This vaccine appears to be well tolerated and very effective at preventing COVID-19. Duration of protection is not currently known, and clinical trials are ongoing. Although the Australian Government's COVID-19 vaccination plan is for vaccines to be universally available, free and voluntary, they will initially be rolled out to priority groups including quarantine and border workers, frontline health workers, and staff and residents in aged care. Other vulnerable groups and high-risk workers will be targeted in later phases before the vaccine is rolled out to everyone.

T manufacturer provided the AusPAR and the product information

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.