# In brief

Bivalent COVID-19 vaccines

16 November 2022



## Summary


- The bivalent COVID-19 vaccines have components that target both the original virus strain and the Omicron variant strain of the SARS-CoV-2 virus.[1]
- The Spikevax bivalent booster vaccine (Moderna, BA.1-adapted, data from an ongoing phase 2–3 trial) is found to induce stronger neutralising antibody activities against the Omicron variant (including BA.4/BA.5 subvariants) than the original booster version. It has a similar safety and reactogenicity profile to the original version.[2]
- The Comirnaty bivalent booster vaccine (Pfizer-BioNTech, BA.1-adapted, data from regulatory submission) is found to induce stronger neutralising antibody activities against the Omicron BA.1 subvariant than the original booster version.[3]
- According to data released by Pfizer, Comirnaty (Pfizer and BioNTech, BA.4/BA.5-adapted) bivalent booster vaccine provided better protection against BA.4/BA.5 compared to the original monovalent version. It had a safety and tolerability profile similar to that of the original version.[4]
- According to data released by Moderna, Spikevax (Moderna, BA.4/BA.5-adapted) bivalent booster vaccine provided better protection against BA.4/BA.5 compared to the original monovalent version. It had a safety and tolerability profile similar to that of the original version.[5]
- Safety monitoring data from the United States showed that in individuals aged 12 and over, bivalent booster vaccines (either Spikevax or Comirnaty, BA.4/BA.5-adapted) had similar frequencies of adverse reactions and health impacts to those previously described for monovalent booster vaccines.[6]
- Recent pre-print studies from laboratory testing suggested that bivalent mRNA boosters adapted for BA.4/BA.5 induce superior neutralising antibody response against emerging Omicron sublineages such as BQ.1, BQ.1.1 and XBB compared to monovalent mRNA boosters.[7, 8] For BA.4/BA.5 variants, however, the evidence is mixed with some suggesting non-superior results compared to the original monovalent boosters.[9, 10]


## Regulatory context: Australia

- 16 November 2022: The Therapeutic Goods Administration granted provisional determination to Pfizer's bivalent COVID-19 vaccine (Comirnaty bivalent original/Omicron BA.4/BA.5) for use as a booster dose in individuals aged 18 years and older.[11]
- 28 October 2022: The Therapeutic Goods Administration granted provisional approval to Pfizer's bivalent COVID-19 vaccine (Comirnaty bivalent original/Omicron BA.1) for use as a booster dose in adults 18 years and over.[12]
- 30 September 2022: The Therapeutic Goods Administration granted provisional determination to Moderna's bivalent COVID-19 vaccine (Spikevax bivalent original/Omicron BA.4/BA.5) for use as a booster dose in adults 18 years and over.[13]

- 12 September 2022: Australian Technical Advisory Group on Immunisation (ATAGI) recommended that Moderna bivalent vaccine (Spikevax bivalent original/Omicron BA.1 vaccine) can be used as an alternative vaccine for any booster dose in people aged 18 years or older.[14]
- 30 August 2022: the Therapeutic Goods Administration provisionally approved Moderna's bivalent COVID-19 vaccine (Spikevax bivalent original/Omicron BA.1 vaccine) for use as a booster dose in adults 18 years and over.[15]
- 6 July 2022: The Therapeutic Goods Administration granted provisional determination to Pfizer's bivalent COVID-19 vaccine (Comirnaty bivalent) and monovalent vaccine (Comirnaty Omicron) for active immunisation to prevent COVID-19.[16]

## Regulatory context: International

- 19 October 2022: The European Medicines Agency recommended approval of the Spikevax COVID-19 vaccine targeting the Omicron BA.4/BA.5 for adults and children from 12 years of age.[17]
- 12 October 2022: the U.S. Food and Drug Administration (FDA) authorised bivalent COVID-19 vaccines (Moderna and Pfizer-BioNTech vaccines adapted for BA.4/BA.5) for use as a booster dose in children down to six (five for Pfizer-BioNTech) years of age.[18]
- 7 October 2022: Health Canada authorised Pfizer-BioNTech bivalent COVID-19 vaccine booster adapted for BA.4/BA.5 subvariants for use in individuals 12 years of age and older.[19]
- 3 September 2022: The UK Medicines and Healthcare products Regulatory Agency approved Pfizer-BioNTech bivalent COVID-19 vaccine adapted for BA.1 for use in individuals aged 12 years and above.[20]
- 1 September 2022: Health Canada authorised Moderna bivalent COVID-19 vaccine booster adapted for BA.1 subvariant in individuals 18 years of age and older.[21]
- 31 August 2022: FDA authorized Moderna and Pfizer-BioNTech bivalent COVID-19 vaccines (adapted for BA.4/BA.5 subvariant) for use as a booster dose. Moderna bivalent vaccine was authorised for use in individuals 18 years of age and older and Pfizer-BioNTech in individuals 12 years of age and older.[3]
- 15 August 2022: The UK Medicines and Healthcare products Regulatory Agency approved Moderna bivalent COVID-19 vaccine adapted for BA.1.[22]

## Research evidence

- 14 November 2022: Moderna announced results from the phase 2/3 clinical trial of Omicron BA.4/BA.5-adapted bivalent booster (given as the second booster dose) in individuals 18 years and older.
    - The bivalent booster dose induced significantly higher neutralising antibody titers against BA.4/BA.5 than the original monovalent booster dose.
    - The bivalent booster dose showed neutralising titres against BQ.1.1.
    - Safety and tolerability profile of the bivalent booster was similar to the original monovalent booster and adverse events were generally lower than for the second dose of the primary series.[5]

- 4 November 2022: A Vaccine Adverse Event Reporting System surveillance report from the United States found that adverse events after the administration of the bivalent booster doses in persons aged ≥12 years are similar to those of monovalent vaccine booster vaccines.[6]
- 4 November 2022: Pfizer and BioNTech announced updated results from the clinical trial of Omicron BA.4/BA.5-adapted bivalent booster (given as the second booster dose) in individuals 18 years and older.
    - In individuals aged 55 and older, the bivalent booster dose induced four-fold higher neutralising antibody titers against BA.4/BA.5 than the original monovalent vaccine dose.
    - The magnitude of the increase of the neutralising antibody titres compared to the pre-booster level was also higher in the bivalent group.
    - Safety and tolerability profile of bivalent booster was similar to the original monovalent vaccine.[4]
- November 2022: Pre-print studies suggested that a fourth dose of BA.5-adapted bivalent vaccines induced stronger neutralising response against Omicron XBB, BQ.1, BQ.1.1 and BA.2.75.2.[7, 8] Previous infection enhanced the magnitude and breadth of BA.5-bivalent-booster-elicited neutralisation.[7]
- 25 October 2022: A pre-print study suggested that both the bivalent (adapted for BA.5) and monovalent mRNA boosters induced comparable neutralising antibody responses against BA.5 subvariant.[10] In this study, participants had a median of three (range 2-4) prior vaccine doses, and one third of the participants had documented SARS-CoV-2 infection history.
- 24 October 2022: A pre-print study looked at the mRNA bivalent vaccine adapted for BA.4/BA.5, when given as a second booster dose. The study found that the vaccine did not induce a superior neutralising antibody response against all variants tested (including Omicron BA.4/BA.5, BA.4.6, BA.2.75 and BA.2.75.2), compared to a second booster dose of the original monovalent mRNA vaccine.[9]
- 13 October 2022: Pfizer and BioNTech announced positive early results from the clinical trial of Omicron BA.4/BA.5-adapted bivalent booster dose (given as the second booster dose) in individuals 18 years and older.
    - A 30µg booster dose of the Omicron BA.4/BA.5-adapted bivalent vaccine induced a substantial increase in the Omicron BA.4/BA.5 neutralising antibody response above pre-booster levels.
    - Early data suggest a booster dose of the Omicron BA.4/BA.5-adapted bivalent vaccine is anticipated to provide better protection against the BA.4 and BA.5 sublineages than the original vaccine in younger and older adults.
    - The safety profile of the bivalent booster was similar to the original booster vaccine.[23]
- 6 October 2022: In an ongoing, phase 2–3 trial, interim results suggest the Spikevax bivalent vaccine (50ug, targeting BA.1) used as second booster dose elicited higher neutralising antibody responses against Omicron variant compared to that of Moderna original vaccine. The safety and reactogenicity profile of the bivalent booster was similar the original booster dose (50-µg).[2]
- 6 October 2022: Interim results from an ongoing, open-label phase 2/3 trial suggest that the Spikevax bivalent booster doses (50µg or 100µg, adapted for Beta variant) elicited higher neutralising antibody responses against the ancestral SARS-CoV-2, Beta, Omicron BA.1 and

Delta variants than that of after a 50ug original booster dose. The safety and reactogenicity profile of the bivalent booster (50-µg) was similar to the original booster dose (50-µg).[24]

- 13 September 2022: A study conducted in mice concluded that Spikevax bivalent booster (first booster) vaccines (targeting either BA.1 or BA4/BA.5) induced greater breadth of neutralising antibodies compared to an original Spikevax booster. Bivalent booster vaccines also resulted in stronger protection against BA.5 infection and inflammation in the mice's lung.[25]
- 31 August 2022: Data supporting the Pfizer-BioNTech bivalent (adapted for BA.1) authorization by the FDA suggest that when given as a second booster dose, the bivalent vaccine induced stronger immune response against BA.1 compared to the monovalent second booster dose.[3]

## Method

To inform this brief, PubMed and Google searches were conducted using terms related to bivalent COVID-19 vaccine on 24 and 31 October, and 16 November 2022.

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