Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Australian Public Assessment Report for Comirnaty

Active ingredient: Tozinameran

Sponsor: Pfizer Australia Pty Ltd

September 2023

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Aged Care and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
- To report a problem with a therapeutic good, please see the information on the TGA website.

About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

Contents

List of abbreviations

Abbreviation	Meaning
ACV	Advisory Committee on Vaccines
ATC	Anatomical Therapeutic Chemical (code)
CI	Confidence interval
COVID-19	Coronavirus disease 2019
EU	European Union
PI	Product Information
RMP	Risk Management Plan
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
TGA	Therapeutic Goods Administration
US(A)	United States (of America)

Product submission

Submission details

Type of submission:	Major variation (change in dosage)
Product name:	Comirnaty
Active ingredient:	Tozinameran
Decision:	Approved
Date of decision:	23 August 2023
Date of entry onto ARTG:	6 September 2023
ARTG numbers:	346290 and 377110
, *Black Triangle Scheme*	Yes
for the current submission:	As a provisionally registered product, this medicine will remain in the Black Triangle Scheme for the duration of its provisional registration
Sponsor's name and address:	Pfizer Australia Pty Ltd Level 17 151 Clarence Street Sydney, NSW, 2000
Dose form:	Suspension for injection
Strength:	30 µg/0.3 mL
Container:	Vial
Pack sizes:	10 and 195
Approved therapeutic use for the current submission:	*Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARSCoV-2, in individuals 12 years of age and older.* *The use of this vaccine should be in accordance with official recommendations.*
Route of administration:	Intramuscular
Dosage:	Comirnaty is administered intramuscularly after dilution as a primary course of 2 doses at least 21 days apart. A first booster dose of Comirnaty may be administered intramuscularly at least 6 months after the completion of a COVID-19 vaccine primary series in individuals 12 years of age and older. Subsequent doses of Comirnaty may be administered to individuals 18 years of age and older at least 3 months after a previous booster dose of Comirnaty. For further information regarding dosage, refer to the Product Information.
Pregnancy category:	B1

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of fetal damage.

The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. This must not be used as the sole basis of decision making in the use of medicines during pregnancy. The TGA does not provide advice on the use of medicines in pregnancy for specific cases. More information is available from obstetric drug information services in your State or Territory.

Product background

This AusPAR describes the submission by Pfizer Australia Pty Ltd (the sponsor) to change the dose regimen for the following provisionally registered medicines:[1]

- Comirnaty (tozinameran) COVID-19 vaccine 30 μg/ 0.3 mL suspension for injection, vial
- Comirnaty (tozinameran) COVID-19 vaccine 30 μg/ 0.3 mL concentrated suspension for injection, vial.

At the time of this submission, the Comirnaty COVID-19 vaccine presentations described above were provisionally approved for the following indication:[2]

> *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 12 years of age and older.*
>
> *The use of this vaccine should be in accordance with official recommendations.*

In adults and children over the age of 5 years, the Comirnaty COVID-19 vaccine is typically administered as a two-dose primary series (Doses 1 and 2);[3] with Dose 2 given at least 21 days after Dose 1.

Doses after the primary series are referred to as booster doses. At the time of this submission, the approved dosage regimen allows for adults and children over the age of 5 years to receive a

[1] At the time this submission was considered by the TGA Comirnaty (tozinameran) was provisionally registered in Australia. Full registration was obtained for Comirnaty (tozinameran) on 13 July 2023.

[2] Note that other presentations of Comirnaty (tozinameran) COVID-19 vaccine have been provisionally registered for use in younger age groups (from 6 months of age). No changes to the following presentations or dosage changes to the indicated populations are proposed in this submission:

- Comirnaty (tozinameran) COVID-19 3 μg/0.2 mL concentrated suspension for injection vial (ARTG R 393433) has provisional registration, indicated for: *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 6 months of age to less than 5 years of age.*
- Comirnaty (tozinameran) COVID-19 10 μg/0.2 mL concentrated suspension for injection vial (ARTG R 377111) has provisional registration, indicated for: *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 5 years of age to less than 12 years of age.*

[3] A variation of the primary series consisting of three doses, with the third dose (Dose 3) given at least 28 days after Dose 2 may be given to individuals with severe immunocompromise.

booster dose of vaccine (Dose 3). This is to be given at least 6 months after completion of the primary series (Dose 2).

This AusPAR discusses a submission where the sponsor has proposed a change in dosage regimen for individuals aged from 12 years and older, allowing for administration of an additional booster dose (Dose 4), at least 4 months after Dose 3.

The sponsor has proposed these changes in dosage regimen through making changes to the Product Information (PI). There are no proposed changes to the wording of the approved indications.

Coronavirus disease 2019

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The SARS-CoV-2 virus is a member of the coronavirus family and it is characterised as an enveloped, positive sense, single stranded RNA virus that first appeared in late 2019. COVID-19 is predominantly a respiratory illness resulting from SARS-CoV-2 infection that also has systemic manifestations and may affect other organs. Disease symptoms and severity vary, with many people presenting with asymptomatic or mild disease and some progressing to severe respiratory tract disease including pneumonia and acute respiratory distress syndrome, leading to multi-organ failure and death. All ages may present with the disease, but notably, case fatality rates are elevated in persons over 60 years of age. Comorbidities are also associated with increased case fatality rates, including cardiovascular disease, diabetes, hypertension, and chronic respiratory disease.

COVID-19 continues to be a significant public health issue to Australians. In Australia, as of 15 August 2023, 5,150 cases of COVID-19 were reported over the previous 7 days (an average of 736 cases per day), of which 986 people were hospitalised, 25 people were admitted to intensive care and there were ten deaths.[4] Cumulatively, there have been 11,576,428 confirmed cases and 22,696 deaths in Australia due to COVID-19 up to 16 August 2023.[5]

Current treatment options

As of 16 August 2023, over 68.5 million total vaccine doses have been administered since the COVID-19 vaccination program began in February 2021, with 37,000 doses administered over the last 7 days.[4]

The benefits of receiving COVID-19 vaccine have been well established.[6] These include protection from SARS-CoV-2 infection as well as progression to severe COVID-19 and death. At the time that this submission was considered, there were 5 monovalent vaccines (see Table 1

[4] Department of Health and Aged Care (2023), Coronavirus (COVID-19) case numbers and statistics. Available at: https://www.health.gov.au/health-alerts/covid-19/case-numbers-and-statistics (accessed on 24 August 2023).
[5] World Health Organization (2023) WHO Health Emergency Dashboard WHO (COVID-19) Homepage, Australia Situation. Available at: https://covid19.who.int/region/wpro/country/au (accessed on 24 August 2023).
[6] Centers for Disease Control and Prevention (2022) Benefits of Getting A COVID-19 Vaccine. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/vaccine-benefits.html (accessed on 28 February 2023).

below) and 4 bivalent (see Table 2 below) COVID-19 vaccines that were either provisionally approved or fully registered in Australia.[7,8]

Table 1: Approved monovalent COVID-19 vaccines in Australia

Monovalent COVID-19 vaccines approved in Australia	
Comirnaty COVID-19 Vaccine (provisional registration) Active ingredient: tozinameran; formerly known as BNT162b2 (mRNA) Sponsor: Pfizer Australia Pty Ltd	
25 February 2021 (initial registration)	Primary series: for individuals aged 16 years and over (AusPAR) New product: 30 µg/0.3 mL concentrated suspension for injection ARTG number: 346290
22 July 2021	Primary series: for individuals aged 12 years and over (AusPAR)
26 October 2021	Booster dose: for individuals aged 18 years and over (AusPAR)
3 December 2021	Primary series: for individuals aged 5 years and over (AusPAR) New strength/formulation: (Tris/sucrose buffer formulation), 10 µg/0.2 mL, 30 µg/0.3 mL ARTG numbers: 377110, 377111
27 January 2022	Booster dose: for individuals aged 16 to 17 years old (AusPAR)
7 April 2022	Booster dose: for individuals aged 12 to 15 years old (AusPAR)
20 September 2022	Booster dose: for individuals aged 5 to 11 years old (AusPAR)
29 September 2022	Primary series: for individuals aged 6 months and over (AusPAR) New strength: 3 µg/0.2 mL concentrated suspension for injection (Tris/sucrose formulation) ARTG number: 393433
Vaxzevria COVID-19 vaccine (provisional registration) (formerly AstraZeneca COVID-19 vaccine) Active ingredient: ChAdOx1 (viral vector) Sponsor: AstraZeneca Pty Ltd	
15 February 2021 (initial registration)	Primary series: for individuals aged 18 years and over (AusPAR) New product: 1 x 10^{11} viral particles/mL, solution for injection ARTG number: 349072
8 February 2022	Booster dose: for individuals aged 18 years and over (AusPAR)
COVID-19 Vaccine Janssen (provisional registration) Active ingredient: Ad26.COV2.S (viral vector) Sponsor: Janssen-Cilag Pty Ltd	

[7] As part of the **provisional approval pathway**, the provisional registration process will allow certain medicines to be provisionally registered in the Australian Register of Therapeutic Goods (ARTG) for a limited duration. These medicines are registered on the basis of preliminary clinical data, where there is the potential for a substantial benefit to Australian patients. The TGA will re-assess risks related to the absence of evidence through data provided at a later stage, as part of the confirmatory data. Confirmatory data should confirm the relationship between outcomes predicted by the surrogate endpoint, or other preliminary data, and the clinical benefit as demonstrated by direct clinical outcomes.
The sponsor may apply to transition to full registration at any time up until the provisional registration lapse date, once they have completed the obligations outlined for the provisional registration period and complete confirmatory data on safety and efficacy are available.

[8] Department of Health and Aged Care (2023) COVID-19 vaccine: Provisional registrations. Available at: https://www.tga.gov.au/products/covid-19/covid-19-vaccines/covid-19-vaccine-provisional-registrations

Monovalent COVID-19 vaccines approved in Australia	
25 June 2021 (initial registration)	Primary series: for individuals aged 18 years and over (AusPAR) New product: 5 x 10^{10} virus particles/ 0.5 mL, suspension for intramuscular injection ARTG number: 350150
Spikevax COVID-19 vaccine (full registration 21 April 2023) Active ingredient: elasomeran (mRNA) Sponsor: Moderna Australia Pty Ltd	
9 August 2021 (initial registration)	Primary series: for individuals aged 18 years and over (AusPAR) New product: 0.2 mg/mL, suspension for injection ARTG number: 370599
3 September 2021	Primary series: for individuals aged 12 years and over (AusPAR)
7 December 2021	Booster dose: for individuals aged 18 years and over (AusPAR)
17 February 2022	Primary series: for individuals aged 6 years and over (AusPAR)
19 July 2022	Primary series: for individuals aged 6 months and over (AusPAR) New strength: 0.1 mg/mL suspension for injection ARTG numbers: 388244, 388245
19 October 2022	Booster dose: for individuals aged 12 years and over (AusPAR)
21 April 2022	Conversion of provisional registration to full registration (AusPAR)
Nuvaxovid COVID-19 vaccine (provisional approval) Active ingredient: SARS-CoV-2 rS vaccine with Matrix-M1 adjuvant (protein vaccine) Sponsor: Biocelect Pty Ltd (on behalf of Novavax Inc)	
19 January 2022 (initial registration)	Primary series: for individuals aged 18 years and over (AusPAR) New product: 5 µg/0.5mL, suspension for injection ARTG number: 355139
9 June 2022	Booster dose: for individuals aged 18 years and over as homologous vaccination (AusPAR)
22 July 2022	Primary series: for individuals aged 12 years and over (AusPAR)

Abbreviations: AusPAR = Australian Public Assessment Report; ARTG = Australian Register of Therapeutic Goods; COVID-19 = coronavirus disease 2019; mRNA = messenger ribonucleic acid; TGA = Therapeutic Goods Administration.

A primary vaccine series involves the vaccine doses needed for initial protection against COVID-19 disease. Typically, a primary COVID-19 vaccine series of 2 doses of the vaccine given 8 to 12 weeks apart. In most situations, the primary course consists of two doses of the same vaccine. In certain age groups or situations, the number of vaccine doses in a primary series may vary. For people with severe immunocompromise, a primary course is defined as 3 doses of a COVID-19 vaccine. 'Third' doses are not booster doses, but an additional dose given such as to those considered to be severely immunocompromised.

A booster dose refers to an additional vaccine dose given after the primary vaccine course. The first booster will refer to the first additional vaccine dose given after completing a 2-dose (or sometimes 3-dose) primary vaccine course.

Note: The single dose COVID-19 Vaccine Janssen has been provisionally approved, but isn't currently being used in Australia.

Further information on vaccines can be found on the TGA website at COVID-19 vaccines, The Australian Immunisation Handbook or at the Australian Government Department of Health and Aged Care website.

Table 2: Approved bivalent COVID-19 vaccines in Australia

Bivalent COVID-19 vaccines provisionally approved in Australia	
Spikevax Bivalent Original/Omicron COVID-19 vaccine (provisional Active ingredients: elasomeran and imelasomeran (mRNA) Sponsor: Moderna Australia Pty Ltd	
29 August 2022 (initial registration)	Booster dose: for individuals aged 18 years and over (AusPAR) New product: 0.1 mg/mL suspension for injection. Each 0.5 mL dose contains 25 µg of elasomeran and 25 µg of imelasomeran ARTG number: 389513
Spikevax Bivalent Original/Omicron BA.4-5 COVID-19 vaccine Active ingredients: elasomeran and davesomeran Sponsor: Moderna Australia Pty Ltd	
20 February 2023 (initial registration)	Booster dose: for individuals aged 12 years and over (AusPAR) New product: 0.1 mg/mL suspension for injection. Each 0.5 mL dose contains 25 µg of elasomeran and 25 µg of davesomeran ARTG number: 399552
Comirnaty Original/Omicron BA.1 COVID-19 vaccine Active ingredients: tozinameran and riltozinameran (mRNA) Sponsor: Pfizer Australia Pty Ltd	
28 October 2022 (initial registration)	Booster dose for individuals aged 18 years and over (AusPAR) New Product: 30 µg/0.3 mL suspension for injection. Each 0.3 mL dose contains 15 µg of tozinameran and 15 µg of riltozinameran ARTG number: 394890
Comirnaty Original/Omicron BA.4-5 COVID-19 vaccine Active ingredients: tozinameran and famtozinameran (mRNA) Sponsor: Pfizer Australia Pty Ltd	
20 January 2023 (initial registration)	Booster dose: for individuals aged 12 years and over (AusPAR) New Product: 30 µg/0.3 mL suspension for injection. Each 0.3 mL dose contains 15 µg of tozinameran and 15 µg of famtozinameran ARTG number: 400874

Abbreviations: AusPAR = Australian Public Assessment Report; ARTG = Australian Register of Therapeutic Goods; COVID-19 = coronavirus disease 2019; mRNA = messenger ribonucleic acid; TGA = Therapeutic Goods Administration.

Comirnaty (tozinameran) COVID-19 vaccine

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to cause substantial morbidity and mortality globally. This is despite the widespread availability of effective vaccination. Vaccine effectiveness wanes over time necessitating further doses be administered.

Real-world data including data from the United States of America (USA);[9] Sweden;[10] Canada;[11] and Israel;[12,13] have shown that after the initial booster dose of Comirnaty (also referred to as BNT162b2), in the presence of the now predominant Omicron variant, vaccine effectiveness against symptomatic COVID-19 is lower and wanes more quickly post Dose 3 compared to prior variants. This underscores the need and potential benefit of an additional booster.

Comirnaty is a vaccine containing mRNA embedded in lipid nanoparticles that belongs to World Health Organisation Anatomical Therapeutic Chemical (ATC) drug class J07 (vaccines), ATC code J07BX03 (COVID-19 vaccines). It induces active immunity to the spike protein of SARS-CoV-2, which is the causative agent of COVID-19.

Comirnaty has provisional approval in Australia for the following indication:[1]

> *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals 6 months of age and older.*
>
> *The use of this vaccine should be in accordance with official recommendations.*
>
> *The decision has been made on the basis of short term efficacy and safety data. Continued approval depends on the evidence of longer term efficacy and safety from ongoing clinical trials and post-market assessment.*

This submission seeks approval for individuals 12 year of age or older to receive an additional booster dose (Dose 4) of Comirnaty (tozinameran) COVID-19 vaccine (that is, a second booster vaccine.

This is supported by Study C4591031, a Phase III master study evaluating BNT162b2 boosting strategies in healthy individuals previously vaccinated with BNT162b2.

This submission also included proposed changes to the Product Information (PI; see Table 3) to reflect the proposed change in dosage regimen.

[9] Link-Gelles R, Levy ME, Gaglani M, et al. Effectiveness of 2, 3, and 4 COVID-19 mRNA vaccine doses among immunocompetent adults during periods when SARS-CoV- 2 Omicron BA.1 and BA.2/BA.2.12.1 sublineages predominated - VISION Network, 10 US states, December 2021-June 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71(29):931-939.

[10] Nordström P, Ballin M, Nordström A. Effectiveness of a fourth dose of mRNA COVID- 19 vaccine against all-cause mortality in long-term care facility residents and in the oldest old: A nationwide, retrospective cohort study in Sweden. *Lancet Reg Health Eur.* 2022;100466.

[11] Grewal R, Kitchen SA, Nguyen L, et al. Effectiveness of a fourth dose of covid-19 mRNA vaccine against the omicron variant among long term care residents in Ontario, Canada: test negative design study. BMJ. 2022;378:e071502.

[12] Bar-On YM, Goldberg Y, Mandel M, et al. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. *N Engl J Med.* 2022 May 5;386(18):1712-1720.

[13] Magen O, Waxman JG, Makov-Assif M, et al. Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. *N Engl J Med.* 2022 Apr 28;386(17):1603- 1614.

Table 3: Proposed changes to the Product Information

Booster dose in individuals 12 years of age and older
A booster dose of Comirnaty Ready To Use Multidose (For Age 12 Years and Above, Do Not Dilute) may be administered intramuscularly at least 6 months after the completion of COVID-19 vaccine primary series in individuals 12 years of age and older. Subsequent doses of Comirnaty Ready To Use Multidose (For Age 12 Years and Above, Do Not Dilute) may be administered to individuals 12 years of age and older at least 4 months after a previous booster dose of Comirnaty The decision when and for whom to implement a booster dose of Comirnaty Ready To Use Multidose (For Age 12 Years and Above, Do Not Dilute) should be made based on available vaccine safety and effectiveness data (see Sections 4.4 Special warnings and precautions for use and 5.1 Pharmacodynamic properties), in accordance with official recommendations.

The sponsor proposes to amend the Product Information, as shown by the text in bold font.

Comirnaty (tozinameran) COVID-19 vaccine is currently provisionally registered in several different formulations indicated for populations of different ages requiring different doses.[1] These are presented in Table 4 and Table 5, below. Note that the proposed change to dosage regimen applies only to those aged 12 years and older, and the 30 µg/ 0.3mL strength presentations that are approved in this age group. The Comirnaty 10 µg/ 0.2 mL strength presentation (for individuals from 5 to less than 12 years of age) and 3 µg/ 0.2 mL strength presentation (for individuals from 6 months to less than 5 years of age) are unaffected by the proposed changes to dosage regimen.

Table 4: Comirnaty COVID-19 vaccine dosage forms and strengths

AUST R	Active ingredient	Tradename	Strength	Dosage form	Pack/ container
346290	Tozinameran	Comirnaty (tozinameran) COVID-19 vaccine 30 micrograms/ 0.3 mL concentrated suspension for injection vial	30 µg/ 0.3 mL	Injection, concentrated suspension (PBS buffer)	195 vials
377110	Tozinameran	Comirnaty (tozinameran) COVID-19 vaccine 30 micrograms/ 0.3 mL suspension for injection vial	30 µg/ 0.3 mL	Injection, suspension (Tris/sucrose buffer)	10 195 vials
377111	Tozinameran	Comirnaty (tozinameran) COVID-19 vaccine 10 micrograms/0.2 mL concentrated suspension for injection vial	10 µg/ 0.2 mL	Injection, concentrated suspension (Tris/sucrose buffer)	10 195 vials
393433	Tozinameran	Comirnaty (tozinameran) COVID-19 vaccine 3 micrograms/0.2 mL concentrated suspension for injection vial	3 µg/ 0.2 mL	Injection, concentrated suspension (Tris/sucrose buffer)	10 195 vials

Table 5: Comirnaty COVID-19 vaccine presentations and indication age group

AUST R	Product name	Age group
346290	Comirnaty (tozinameran) COVID-19 vaccine 30 micrograms/ 0.3 mL concentrated suspension for injection vial	individuals 12 years of age and older
377110	Comirnaty (tozinameran) COVID-19 vaccine 30 micrograms/ 0.3 mL suspension for injection vial	individuals 12 years of age and older
377111	Comirnaty (tozinameran) COVID-19 vaccine 10 micrograms/ 0.2 mL concentrated suspension for injection vial	individuals 5 years of age to less than 12 years of age
393433	Comirnaty (tozinameran) COVID-19 vaccine 3 micrograms/ 0.2 mL concentrated suspension for injection vial	individuals 6 months of age to less than 5 years of age

Regulatory status

Australian regulatory status

The product received provisional registration on the Australian Register of Therapeutic Goods (ARTG) on 25 January 2021 At the time that this submission was considered it was provisionally approved for the following indication:

> *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 16 years of age and older.*
>
> *The use of this vaccine should be in accordance with official recommendations*

Comirnaty was initially included on the register on 25 January 2021 (AUST R 346290) with provisional registration, for individuals aged 16 years and older. Since this time provisional registration for primary vaccination has been granted for individuals aged at least 6 months old. A first booster dose (that is, Dose 3) was provisionally approved for individuals 18 years of age or older on 26 October 2021 followed by approvals for a third dose for individuals aged at least 5 years of age or older. (Table 6).

Table 6: Timeline of provisional registration events for Comirnaty (tozinameran)

Date	Application
25 January 2021	For individuals aged 16 years and over
22 July 2021	For individuals aged 12 years and over
26 October 2021	Booster dose for individuals 18 years and over
3 December 2021	For individuals 5 years and over
27 January 2022	Booster dose for individuals 16-17 years old
7 April 2022	Booster dose for individuals aged 12-15 years old
20 September 2022	Booster dose for individuals aged 5-11 years old
29 September 2022	For individuals aged 6 months and over

International regulatory status

At the time the TGA considered this submission, a similar submission had been approved in the European Union (EU) on 27 October 2022 and in the United States of America (USA) on 29 March 2022.

The following table summarises these submissions and provides the indications where approved.

Table 7: International regulatory status

Region	Submission date	Status	Approved indications
European Union	14 September 2022	Approved on 27 October 2022	Changes to indication: None Changes to dosage: Fourth dose in individuals 12 years of age and older.
United States of America	14 March 2022	Authorised 29 March 2022	Changes to indication: None Changes to dosage: Second booster dose for older (50 years or older) and immunocompromised individuals (12 years or older).

The sponsor stated that similar applications have not been deferred, withdrawn or rejected in any of the above countries/jurisdictions.

Product Information

The Product Information (PI) approved with the submission which is described in this AusPAR can be found as Attachment 1. For the most recent PI and Consumer Medicines Information (CMI), please refer to the TGA PI/CMI search facility.

Registration timeline

The following table captures the key steps and dates for this submission.

This submission was evaluated under the provisional registration process for COVID-19 vaccines.

Data were provided as a rolling submission. Under normal circumstances, TGA's assessment (for both provisional and general registration) begins once all information to support registration is available. As part of the Department of Health and Aged Care's response to the pandemic, the TGA has agreed to accept rolling data for COVID-19 vaccines and treatments, to enable early evaluation of data as it becomes available.

Table 8: Timeline for Submission PM-2022-04970-1-2.

Description	Date
Submission dossier accepted and first round evaluation commenced	9 January 2023
Evaluation completed	1 May 2023

Description	Date
Delegate's Overall benefit-risk assessment and request for Advisory Committee advice	25 May 2023
Sponsor's pre-Advisory Committee response	1 June 2023
Advisory Committee meeting	7 June 2023
Registration decision (Outcome)	23 August 2023
Administrative activities and registration on the ARTG completed	6 September 2023
Number of working days from submission dossier acceptance to registration decision*	156

*Statutory timeframe for standard submissions is 255 working days

Submission overview and risk/benefit assessment

A summary of the TGA's assessment for this submission is provided below.

Quality

A new quality evaluation is not required for this submission as there are no proposed changes to the quality of the currently approved products available in Australia. The quality of the currently approved product is suitable for the proposed changes in this submission. A full quality evaluation was conducted at the time the Comirnaty COVID-19 vaccine received initial registration.[14, 15]

Nonclinical

No new nonclinical data or further nonclinical evaluation were required for this submission. The TGA considers that previously submitted and evaluated data satisfactorily address nonclinical aspects of safety/efficacy relating to this submission.

Clinical

Summary of clinical studies

The sponsor has presented the following clinical data in support of this submission:

- Study C4591031, Substudy D:
  - Phase III, randomised, observer blind clinical trial.

[14] AusPAR for Comirnaty (tozinameran/BNT162b2 (mRNA)) new biological entity, published on 25 January 2021. Available at: AusPAR: BNT162b2 (mRNA) - COMIRNATY | Therapeutic Goods Administration (TGA)

[15] AusPAR for Comirnaty (tozinameran/BNT162b2 (mRNA)). Approved: 25 January 2021; published on 13 December 2021. Available at: https://www.tga.gov.au/resources/auspar/auspar-tozinameran-mrna-covid-19-vaccine

  - Provided data from approximately 640 participants (Cohort 2) aged from 18 to 55 years of age who received a second booster (Dose 4) of Comirnaty (tozinameran) COVID-19 vaccine.

- Study C4591031 Substudy E:
  - Phase III, randomised, observer blind clinical trial.
  - Provided data from approximately 1840 participants (expanded cohort) aged 55 year or older from Study C4591031 Substudy E (expanded cohort) who received a second booster (Dose 4) of Comirnaty (tozinameran) COVID-19 vaccine.

Data from these studies has been previous evaluated in other submissions to the TGA.[16,17]

Relevant data from Study C4591044 and real-word evidence data were also provided and are discussed below.

Study C4591031

This is a Phase III master study to evaluate Comirnaty (tozinameran/BNT162b2) COVID-19 vaccine boosting strategies in healthy individuals previously vaccinated with Comirnaty (tozinameran) vaccine. Substudies D and E have been designed to assess the safety, tolerability, and immunogenicity of monovalent and bivalent Omicron variant modified vaccine in BNT162b2 experienced participants enrolled to receive booster dose(s) of either the BNT162b2 prototype vaccine or an Omicron BA.1 variant modified vaccine (BNT162b2 OMI).

Substudy D (Cohort 2) evaluated an additional booster dose (Dose 4) of BNT162b2 30 μg and the Omicron variant specific BNT162b2 OMI 30 μg to approximately 640 BNT162b2 experienced participants in Cohort 2 who have received three doses of BNT162b2, with their last dose 90 to 180 days prior to randomisation at a ratio of 1:1. Randomisation was stratified by age (18 to 30 years, and 31 to 55 years of age).

In Substudy E there were approximately 1840 participants who were 55 years of age or older and who had received three prior doses of BNT162b2 (30 μg doses). The most recent dose was given 5 to 12 months prior to the substudy and participants were randomised into six equal sized groups to receive BNT162b2 as follows:

- BNT162b2 (30 μg);
- BNT162b2 (60 μg);
- BNT162b2 OMI (30 μg);
- BNT162b2 OMI (60 μg);
- a combination of BNT162b2 and BNT162b2 OMI (30 μg total; 15 μg each); or
- a combination of BNT162b2 and BNT162b2 OMI (60 μg total; 30 μg each) as a fourth dose.

Immunogenicity analyses were conducted based on the evaluable and all available immunogenicity populations. The BNT162b2 30 μg vaccine group was used as the control group for all immunogenicity endpoints in Substudy D and E. Immunogenicity results were reported as:

[16] AusPAR for Comirnaty Original / Omicron BA.1 COVID-19 Vaccine (tozinameran and riltozinameran); available at: https://www.tga.gov.au/resources/auspar/auspar-comirnaty-original-omicron-ba1-covid-19-vaccine

[17] AusPAR for Comirnaty Original / Omicron BA.4 5 COVID-19 Vaccine (tozinameran and famtozinameran); available at: https://www.tga.gov.au/resources/auspar/auspar-comirnaty-original-omicron-ba4-5-covid-19-vaccine

- Geometric mean titres (GMTs)
- Geometric mean ratio of GMTs (BNT162b2 OMI/BNT162b2)
- Percentages/difference in percentages with seroresponse (BNT162b2 OMI/BNT162b2)
- Geometric mean-fold rises (GMFRs) in titres

Efficacy results

Substudy D

Substudy D included 436 participants (208 in the BNT162b2 OMI group and 228 in the BNT162b2 group) without evidence of infection up to one month after Dose 4.

SARS-CoV-2 50% neutralising GMTs for the reference strain and the Omicron (BA.1) variant increased from pre-vaccination to one month post-Dose 4 for participants who received BNT162b2 30 µg or the BNT162b2 OMI (Table 9).

Table 9: Study C4591031 (Substudy D) Geometric mean titres in participants without evidence of infection up to 1 month after vaccination (Dose 4) (full expanded set; evaluable immunogenicity population)

		Vaccine Group (as Randomized)			
		BNT162b2 OMI (30 µg)		BNT162b2 (30 µg)	
Assay	Dose/Sampling Time Point[a]	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
SARS-CoV-2 neutralization assay - Omicron BA.1 - NT50 (titer)	1/Prevax	206	374.1 (315.8, 443.2)	226	315.0 (269.0, 368.9)
	1/1 Month	208	2086.7 (1812.7, 2402.0)	228	1063.2 (935.8, 1207.9)
SARS-CoV-2 neutralization assay - reference strain - NT50 (titer)	1/Prevax	205	4430.2 (3852.0, 5095.3)	226	3999.0 (3529.5, 4531.0)
	1/1 Month	207	11997.1 (10553.5, 13638.3)	227	12009.9 (10744.3, 13424.6)

Abbreviations: GMT = geometric mean titre, LLOQ = lower limit of quantitation, N-binding = SARS-CoV-2 nucleoprotein binding, NAAT = nucleic acid amplification test, NT50 = 50% neutralising titre, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Full expanded set = Cohort 2 excluding the sentinel group.

Note: Participants who had no serological or virological evidence (prior to the 1 month post first study vaccination blood sample collection) of past SARS-CoV-2 infection (that is, N-binding antibody (serum) negative at the first study vaccination and the 1 month post first study vaccination visits, negative NAAT (nasal swab) at the first study vaccination visit, and any unscheduled visit prior to the 1 month post first study vaccination blood sample collection) and had no medical history of COVID-19 were included in the analysis.

a. Protocol specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 x LLOQ.

For participants without prior evidence of infection up to 1 month after Dose 4 vaccination:

- Geometric mean titres (GMTs) for the Omicron (BA.1) variant increased from 315.0 (pre-vaccination) to 1063.2 at one month post-Dose 4 for those who received BNT162b2 30 µg. For the reference strain, GMTs were also higher at one month post-Dose 4 compared to pre-vaccination (12009.9 versus 3999.0) (see Table 9).

- Geometric mean-fold rises (GMFRs) from Dose 4 to one month post-Dose 4 for the Omicron variant were 3.4 (95% confidence interval (CI): 3.0, 3.8) in the BNT162b2 group. For the reference strain, the GMFRs from Dose 4 to one month post Dose 4 were 3.0 (95% CI 2.7, 3.3) for BNT162b2 group.
- The proportion of participants in the BNT162b2 group, who achieved seroresponse at one month post-Dose 4 for the Omicron variant was 40.3% (2-sided 95% CI: 33.8%, 47%) and 27% for the reference strain.

There were no clinically meaningful differences between subgroups for neutralising GMTs and seroresponse rates, for the Omicron variant except for baseline SARS-CoV-2 status.

Geometric mean titres (GMTs), GMFRs and seroresponse rates at one month post-Dose 4 were generally higher for participants who were positive for SARS-CoV-2 at Baseline.

Confirmed COVID-19 cases: There were four confirmed cases in the BNT162b2 group and five in the BNT162b2 OMI group up to the data cut-off date. There were no cases meeting severe criteria.

Substudy E

The evaluable immunogenicity population (those without evidence of infection up to one month post-Dose 4) included a total of 1112 participants. These were as follows:

- 182 and 198 participants in the BNT162b2 30 μg and BNT162b2 60 μg, respectively;
- 180 and 185 participants in the BNT162b2 OMI 30 μg and BNT162b2 OMI 60 μg, respectively; and
- 186 and 181 participants in the BNT162b2 and BNT162b2 OMI 15 μg each (30 μg total) and BNT162b2 and BNT162b2 OMI 30 μg each (60 μg total), respectively

See Table 10 (below) for results in these groups.

Table 10: Study C4591031 (Substudy E) Geometric mean titres in participants without evidence of infection up to one month after study vaccination (Dose 4) (full expanded set; evaluable immunogenicity population)

		Vaccine Group (as Randomized)											
		BNT162b2 (30 µg)		BNT162b2 (60 µg)		BNT162b2 OMI (30 µg)		BNT162b2 OMI (60 µg)		BNT162b2 (15 µg) + BNT162b2 OMI (15 µg)		BNT162b2 (30 µg) + BNT162b2 OMI (30 µg)	
Assay	Sampling Time Point[a]	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
SARS-CoV-2 neutralization assay - Omicron BA.1 - NT50 (titer)	Prevax	167	67.5 (52.9, 86.3)	188	96.6 (76.7, 121.7)	174	70.8 (57.4, 87.4)	176	68.6 (54.3, 86.8)	177	76.7 (61.1, 96.1)	168	81.9 (63.9, 104.9)
	1 Month	163	455.8 (365.9, 567.6)	185	727.3 (606.0, 872.9)	169	1014.5 (825.6, 1246.7)	174	1435.2 (1208.1, 1704.8)	178	711.0 (588.3, 859.2)	175	900.1 (726.3, 1115.6)
SARS-CoV-2 neutralization assay - reference strain - NT50 (titer)	Prevax	179	1389.1 (1142.1, 1689.3)	197	1429.0 (1193.4, 1711.0)	176	1083.7 (896.1, 1310.7)	182	1345.6 (1120.1, 1616.3)	186	1387.1 (1158.9, 1660.2)	179	1396.7 (1149.9, 1696.3)
	1 Month	182	5998.1 (5223.6, 6887.4)	198	7708.8 (6772.3, 8774.7)	180	5539.0 (4715.0, 6506.9)	184	6726.3 (5832.9, 7756.6)	186	5933.2 (5188.2, 6785.2)	180	7816.9 (6820.7, 8958.6)

Abbreviations: GMT = geometric mean titre, LLOQ = lower limit of quantitation, N-binding = SARS-CoV-2 nucleoprotein–binding, NAAT = nucleic acid amplification test, NT50 = 50% neutralising titre, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Immunogenicity subset = a random sample of 230 participants in each vaccine group selected from the expanded cohort.

Note: Participants who had no serological or virological evidence (prior to the 1 month post study vaccination blood sample collection) of past SARS-CoV-2 infection (that is, N-binding antibody (serum) result negative at the study vaccination and the 1 month post study vaccination visits, negative NAAT (nasal swab) result at the study vaccination visit, and any unscheduled visit prior to the 1 month post study vaccination blood sample collection) and had no medical history of COVID-19 were included in the analysis.

a. Protocol-specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 x LLOQ.

The following was reported for participants without prior evidence of infection, up to one month after Dose 4 vaccine:

- Geometric mean titres (GMTs) for the Omicron (BA.1) variant increased from 1389 (pre-vaccination) to 5999 at one month post Dose 4 for those who received BNT162b2 30 µg. For the reference strain, GMTs were also higher at one month post-Dose 4 compared to pre-vaccination (67.5 versus 455.8) (Table 10).
- Geometric mean-fold rises (GMFRs) from Dose 4 to one month post-Dose 4 for the Omicron variant were 5.8 (2-sided 95% CI:4.6, 7.2) and 4.3 (2-sided 95% CI: 3.7, 5.0) for the reference strain in the BNT162b2 30 µg group.
- The proportion of participants who achieved seroresponse at one month post-Dose 4 for the Omicron variant was 57% and 49.2% for the reference strain in the BNT162b2 30 µg group.

There were no clinically meaningful differences between subgroups for neutralising GMTs and seroresponse rates for the Omicron variant except for baseline SARS-CoV-2 status.

Geometric mean titres (GMTs), GMFRs and seroresponse rates at one month post-Dose 4 were generally higher for participants who were positive for SARS-CoV-2 at Baseline.

Confirmed COVID-19 cases: There were a total of 30 confirmed cases across all vaccine groups up to the data cut-off date. These included:

- BNT162b2 30 μg and 60 μg groups: seven and six cases, respectively;
- BNT162b2 OMI 30 μg and 60 μg groups: seven and three cases, respectively; and
- BNT162b2 and BNT162b2 OMI 30 μg and 60 μg groups: one and six cases, respectively.

There were no severe cases.

Safety results

In Substudies D and E, adverse events were up to one month after the last dose administered, and serious adverse events were collected from study vaccination up to 6 months post dose.

Substudy D

Safety findings for the safety population of Substudy D are summarised as follows:

- The safety population included 640 participants (315 receiving BNT162b2 OMI, 325 receiving BNT162b2). No participants were excluded from the safety population.
- The median follow-up time after Dose 4 was 1.4 months (range: 1.0 to 1.7 months).
- Overall, the reactogenicity profile (local reactions, systemic events) within 7 days following a fourth dose (Dose 4) of either vaccination was similar to that observed after a third dose (Dose 3) of BNT162b2 vaccine.
- Injection site pain was the most frequently reported local reaction in participants in both the BNT162b2 and BNT162b2 OMI vaccine groups: 78.4% (2-sided 95% CI: 73.4%, 82.9%) and 77.9% (2-sided 95% CI: 72.7%, 82.5%), respectively. These events were severe in five participants (three in those receiving BNT162b2 vaccine, and two in those receiving BNT162b2 OMI vaccine).
- Systemic events reported within the 7 days following Dose 4 of vaccine were similar in the BNT162b2 OMI (77.6%) and BNT162b2 (72.9%) vaccine groups, and most were mild/moderate in severity. Most occurred within 1 to 2 days after dosing and resolved within 1 to 2 days. No Grade 4 systemic events were reported.[18]
- There were no reported events of myocarditis or pericarditis.
- No life threatening adverse events were reported in either group. No study participants had any adverse events leading to withdrawal from receiving Dose 4 to one month after Dose 4 of vaccine, and there were no deaths in this study period.

Substudy E

Safety findings for the safety population of Substudy E are summarised as follows:

- The safety population included 1841 participants as follows:
  - 305 and 302 in the BNT162b2 30 μg and BNT162b2 60 μg group, respectively;
  - 307 each in the BNT162b2 OMI 30 μg and BNT162b2 OMI 60 μg group; and
  - 305 in the BNT162b2 and BNT162b2 OMI 15 μg each (30 μg total); and
  - 316 in the BNT162b2 and BNT162b2 OMI 30 μg each (60 μg total) group, respectively.
- Median follow-up time after study vaccination was 1.7 to 1.8 months.

[18] Grades are based on Common Terminology Criteria for Adverse Events (CTCAE) available from nih.gov
Grade 4 events are characterised as Life-threatening consequences; urgent intervention indicated.

- The reactogenicity profile (local and systemic) within 7 days after BNT162b2 OMI and BNT162b2 as a fourth dose was similar to that previously observed after a third dose of BNT162b2 vaccine.
- At the injection site: pain occurred in 60.1% of participants, swelling in 6% and redness in 6.4%.
- Systemic reactions were as follows: fatigue 45.3%, headache 26.5%, muscle pain 19.8%, chills 16.4%, joint pain 9.1% and fever 3.7%.
- Most systemic events were mild/moderate in severity, and short-lived; with no Grade 4 events.[18]
- There were no cases reported of myocarditis/pericarditis, Bell's palsy (or facial paralysis/paresis), appendicitis, or vaccine related anaphylaxis.

Study C4591044

This is an ongoing randomised, active controlled, Phase II/III study investigating the safety, tolerability, and immunogenicity of BNT162b2 RNA-based Omicron BA.4/BA.5-adapted bivalent vaccine candidates as a booster dose in COVID-19 vaccine experienced healthy individuals. The study commenced in October 2022.

Immunogenicity results are shown in Table 11 and Table 12 (below); key findings include:

- A booster dose (Dose 4) of an Omicron BA.4/BA.5-adapted bivalent vaccine elicited substantially higher Omicron BA.4/BA.5-specific neutralisation titres and similar reference strain neutralisation titres one month post-vaccination in both those between 18 and 55 years of age, and those aged over 55 years. This was in comparison to an adult comparator group from Study C4591031 Substudy E (over 55 years of age) who received a booster dose of BNT162b2 at the 30 μg dose level.
- Irrespective of prior SARS-CoV-2 exposure, one month post-dose GMTs for the four variants were higher for the Omicron BA.4/BA.5-adapted bivalent vaccine (30 μg) groups compared to BNT162b2 vaccine treated groups.
- In terms of the seroresponse in the SARS-CoV-2 negative group, seroresponse were seen against Omicron subvariants BA.4.6, BA.2.75.2, BQ.1.1, and XBB in 94.1%, 70.6%, 76.5%, and 41.2% of participants respectively in the Omicron BA.4/BA.5-adapted bivalent vaccine 30 μg group but only 15%, 5%, 0%, and 0% in the BNT162b2 30 μg group.

In summary, descriptive immunogenicity analysis at one month post-dose compared BNT162b2 vaccine experienced adults (aged 18 to 55 years and over 55 years) in Study C4591044 (Cohort 2) who received an additional booster (Dose 4) of an Omicron BA.4/BA.5-adapted bivalent vaccine (30 μg); and BNT162b2 vaccine experienced adults over 55 years of age in Study C4591031 Substudy E who received BNT162b2 vaccine (30 μg) as a booster (Dose 4).

These data show that a booster dose (Dose 4) of bivalent Omicron BA.4/BA.5 modified variant vaccine elicited substantially higher Omicron BA.4/BA.5-specific neutralisation titres and similar reference strain neutralisation titres one month post-vaccination in both age groups of 18 to 55 years, and over 55 years, compared with an adult comparator group from Study C4591031 Substudy E (over 55 years of age) who received a booster dose of BNT162b2 vaccine at the 30 μg dose level. Note the different intervals from the last dose of BNT162b2 received (prior to study entry) to booster dose administration in the respective studies; the median interval was approximately 10 to 11 months in Study C4591044 Cohort 2 compared with approximately 6 months in Study C4591031 Substudy E. Dosing interval is a potential factor in observed booster elicited immune responses.

Table 11: Study C4591044/C4591031 One month immunogenicity analysis; Geometric mean titres, by baseline SARS-CoV-2 status up to one month after study vaccination (subset of Study C4591044 Cohort 2 and Study C4591031 Substudy E expanded cohort; evaluable immunogenicity population)

			Vaccine Group (as Randomized)					
			C4591044 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg				C4591031 BNT162b2 30 µg	
			18-55 Years		>55 Years		>55 Years	
Assay	Baseline SARS-CoV-2 Status	Sampling Time Point[a]	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
SARS-CoV-2 FFRNT - Omicron BA.4/BA.5 - NT50 (titer)	All	Prevax	38	63.7 (38.7, 104.9)	36	67.9 (39.7, 116.3)	40	82.1 (47.6, 141.8)
		1 Month	38	605.9 (413.3, 888.2)	36	896.4 (577.3, 1392.0)	40	236.3 (148.6, 375.7)
	Positive[d]	Prevax	20	197.0 (117.8, 329.4)	19	206.6 (115.9, 368.3)	20	226.3 (110.4, 463.8)
		1 Month	20	1173.8 (763.3, 1805.0)	19	1376.9 (820.1, 2311.6)	20	629.0 (371.2, 1066.0)
	Negative[e]	Prevax	18	18.2 (12.8, 25.9)	17	19.6 (12.4, 31.1)	20	29.8 (16.9, 52.5)
		1 Month	18	290.6 (180.6, 467.7)	17	554.9 (271.3, 1135.1)	20	88.8 (55.3, 142.6)
SARS-CoV-2 FFRNT - reference strain - NT50 (titer)	All	Prevax	38	558.2 (347.4, 896.8)	36	598.3 (372.2, 961.8)	40	874.3 (479.7, 1593.3)
		1 Month	38	2830.2 (2155.0, 3716.9)	36	3483.6 (2430.9, 4992.3)	40	2604.7 (1863.6, 3640.7)
	Positive[d]	Prevax	20	1371.9 (887.2, 2121.3)	19	1376.9 (854.0, 2219.9)	20	2516.0 (1291.8, 4900.4)
		1 Month	20	4231.4 (3002.9, 5962.6)	19	4847.4 (3228.6, 7277.6)	20	5120.0 (3465.6, 7564.2)
	Negative[e]	Prevax	18	205.5 (110.6, 381.8)	17	235.7 (126.8, 438.2)	20	303.8 (137.9, 669.3)
		1 Month	18	1810.2 (1276.0, 2568.1)	17	2408.1 (1310.7, 4424.5)	20	1325.1 (924.2, 1900.1)

Abbreviations: FFRNT = fluorescent focus reduction neutralisation test, GMT = geometric mean titre, LLOQ = lower limit of quantitation, N-binding = SARS-CoV-2 nucleoprotein–binding, NAAT = nucleic acid amplification test, NT50 = 50% neutralising titre, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Approximately forty participants (20 baseline SARS-CoV-2 positive status and 20 negative status) were selected from over 55 years age group in Study C4591044 Cohort 2 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg group and from Study C4591031 Substudy E expanded cohort (over 55 years) BNT162b2 30 µg group.

a. Protocol specified timing for blood sample.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the student t distribution). Assay results below the LLOQ were set to 0.5 x LLOQ.

d. Positive N-binding antibody result at Baseline, positive NAAT result at Baseline, or medical history of COVID-19.

e. Negative N-binding antibody result at Baseline, negative NAAT result at Baseline, and no medical history of COVID-19.

Table 12: Study C4591044/C4591031 New variant neutralisation/geometric mean titres by baseline SARS-CoV-2 status up to one month after study vaccination (subset of Study C4591044 Cohort 2 and Study C4591031 Substudy E expanded cohort; evaluable immunogenicity population)

			Vaccine Group (as Randomized)			
			C4591044 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg		C4591031 BNT162b2 30 µg	
Assay	Baseline SARS-CoV-2 Status	Sampling Time Point[a]	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
SARS-CoV-2 FFRNT - Omicron BA.4.6 - NT50 (titer)	All	Prevax	36	91.5 (52.5, 159.7)	40	101.1 (58.9, 173.5)
		1 Month	36	968.2 (623.3, 1503.9)	40	232.2 (149.3, 361.1)
	Positive[d]	Prevax	19	281.6 (159.5, 497.2)	20	283.4 (142.6, 563.2)
		1 Month	19	1564.4 (938.2, 2608.5)	20	586.9 (346.9, 993.0)
	Negative[e]	Prevax	17	26.1 (14.9, 45.6)	20	36.1 (20.4, 63.6)
		1 Month	17	566.3 (280.8, 1142.0)	20	91.9 (59.8, 141.1)
SARS-CoV-2 FFRNT - Omicron BA.2.75.2 - NT50 (titer)	All	Prevax	36	31.1 (20.1, 48.3)	40	48.0 (29.1, 79.0)
		1 Month	36	209.5 (131.6, 333.5)	40	99.3 (62.4, 158.1)
	Positive[d]	Prevax	19	62.0 (32.5, 118.0)	20	125.5 (62.1, 253.9)
		1 Month	19	325.9 (183.0, 580.5)	20	264.5 (146.3, 478.0)
	Negative[e]	Prevax	17	14.4 (10.1, 20.6)	20	18.3 (12.1, 27.7)
		1 Month	17	127.9 (61.5, 265.8)	20	37.3 (25.1, 55.4)
SARS-CoV-2 FFRNT - Omicron BQ.1.1 - NT50 (titer)	All	Prevax	36	30.8 (18.5, 51.3)	40	31.4 (21.4, 45.9)
		1 Month	36	266.5 (171.2, 415.0)	40	58.1 (39.2, 86.1)
	Positive[d]	Prevax	19	74.4 (34.7, 159.4)	20	59.6 (35.0, 101.5)
		1 Month	19	444.4 (259.4, 761.3)	20	132.2 (82.5, 212.0)
	Negative[e]	Prevax	17	11.5 (9.2, 14.5)	20	16.5 (11.0, 24.8)
		1 Month	17	150.5 (77.2, 293.4)	20	25.5 (17.4, 37.4)
SARS-CoV-2 FFRNT - Omicron XBB - NT50 (titer)	All	Prevax	36	18.2 (13.3, 24.8)	40	27.1 (18.9, 38.8)
		1 Month	36	89.8 (60.4, 133.5)	40	41.4 (27.5, 62.3)
	Positive[d]	Prevax	19	26.8 (16.2, 44.2)	20	54.6 (32.5, 92.0)
		1 Month	19	130.9 (80.0, 214.3)	20	98.5 (58.0, 167.3)
	Negative[e]	Prevax	17	11.8 (9.0, 15.4)	20	13.4 (10.3, 17.5)
		1 Month	17	58.9 (31.6, 109.9)	20	17.4 (12.6, 24.1)

Abbreviations: FFRNT = fluorescent focus reduction neutralisation test, GMT = geometric mean titre, LLOQ = lower limit of quantitation, N-binding = SARS-CoV-2 nucleoprotein–binding, NAAT = nucleic acid amplification test, NT50 = 50% neutralising titre, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Approximately forty participants (20 baseline SARS-CoV-2 positive status and 20 negative status) were selected from over 55 years age group in Study C4591044 Cohort 2 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg group and from Study C4591031 Substudy E expanded cohort (over 55 years) BNT162b2 30 µg group.

a. Protocol specified timing for blood sample.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 x LLOQ.

d. Positive N-binding antibody result at Baseline, positive NAAT result at Baseline, or medical history of COVID-19.

e. Negative N-binding antibody result at Baseline, negative NAAT result at Baseline, and no medical history of COVID-19.

Real-world effectiveness studies in adults

As part of this submission, the sponsor provided the TGA with studies and data evaluating the real-world effectiveness of Comirnaty (tozinameran/BNT162b2) vaccine when given as an additional booster dose (Dose 4). The following were provided:

- Clinical data from seven studies conducted in adults in Israel evaluating real-world effectiveness of an additional booster (Dose 4) of Comirnaty (tozinameran/BNT162b2) vaccine 30 μg given 4 months or more after the first booster (Dose 3) (see Table 13).
- Studies examining vaccine effectiveness of Comirnaty (tozinameran/BNT162b2) vaccine 30 μg and the Spikevax COVID-19 mRNA vaccine (Moderna) when an additional booster was given 4 months or more following a third dose to:
  - immunocompetent adults of 50 years of age or older (USA);[9]
  - long term care residents of 60 years of age or older (Canada);[11] and
  - long term care facility residents of 80 years of age or older (Sweden).[10]

  Note, these three studies were conducted in the Omicron era.

Table 13: Vaccine effectiveness from Israeli studies of a fourth dose of BNT162b2 30 μg (relative to 3 doses) administered 4 months or more after a third dose during the initial Omicron wave in 2021/2022

Publication/Population studied	Study vaccine doses (n)	Time period of Dose 4 administration	Relative vaccine efficacy (95% CI) and outcome(s)
Regev-Yochay G et al. (2022)[19]			
Healthcare workers 18 years of age or older Levels of pre-existing immunity in lowest 40th percentile	154	27 December 2021 to 30 January 2022	SARS-CoV-2 infection: 30% (-9, 55) Symptomatic COVID-19: 43% (7, 65)
Cohen MJ et al (2022)[20]			
Healthcare workers	4309	January 2022 onwards	Omicron-related infection: 39% (29, 46)
Bar-On YM et al. (2022)[12]			
Adults Israeli Ministry of Health data	623355	10 January 2022 to 2 March 2022 (infection) or 18 February 2022 (severe illness)	SARS-CoV-2 infection: 50% (47, 52) Severe COVID-19: 71% (63, 78)
Magen O et al (2022)[13]			

[19] Regev-Yochay, G. et al. Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron, *New England Journal of Medicine*, 2022; 386 (14): 1377-1380.

[20] Cohen, MJ. et al. Israeli-Hospitals 4th Vaccine Working Group. Association of Receiving a Fourth Dose of the BNT162b Vaccine With SARS-CoV-2 Infection Among Health Care Workers in Israel, *JAMA Network Open,* 2022; 5 (8).

Publication/Population studied	Study vaccine doses (n)	Time period of Dose 4 administration	Relative vaccine efficacy (95% CI) and outcome(s)
Adults 60 years of age or older No prior SARS-CoV-2 infection Captures around 52% Israel population	182122	3 January 2022 to 18 February 2022	SARS-CoV-2 infection: 45% (44, 47) COVID-19: 55% (53, 58) Hospitalisation: 68% (59, 74) Severe illness; 62% (50, 74) Death: 74% (50, 90)
Arbel R et al. (2022)[21]			
Adults 60 to 100 years of age No known prior SARS-CoV-2 infection Captures around 67% older Israel population	328597	10 January 2022 to 20 February 2022	Death: 78% (72, 83); Hospitalisations: 64% (57, 69)
Gazit S et al (2022)[22]			
Adults 60 years of age or older Captures around 26.7% of population Israel	27876	10 January 2022 to 13 March 2022	65.1 (63.0, 67.1) SARS-CoV-2 infection in third week post-vaccine; 22 (4.9, 36.1) by end of 10th week; 86.5 (63.4, 95.0) severe illness between 6th and 9th weeks
Muhsen K et al (2022)[23]			
Long-term care residents 60 years of age or older	24088	10 January 2022 to 31 March 2022	34 (30, 37) SARS-CoV-2 infection; 64 (56, 71) hospitalisation mild-moderate COVID-19; 67 (57, 75) hospitalisation severe COVID-19; 72 (54, 83) death

Abbreviations: CI = confidence interval, VE = vaccine effectiveness.

[21] Arbel, R. et al. Effectiveness of a second BNT162b2 booster vaccine against hospitalization and death from COVID-19 in adults aged over 60 years, *Nature Medicine*, 2022.

[22] Gazit, S. et al. Short term, relative effectiveness of four doses versus three doses of BNT162b2 vaccine in people aged 60 years and older in Israel: retrospective, test negative, case-control study, *British Medical Journal*, 2022; 377.

[23] Muhsen, K. et al. Association of Receipt of the Fourth BNT162b2 Dose with Omicron Infection and COVID-19 Hospitalizations Among Residents of Long-term Care Facilities. *JAMA Internal Medicine*, 2022; 182 (8) :859-867.

The Link-Gelles et al. (2022);[9] study in the USA was notable for the following:

- Utilised data from the VISION network from 10 states between 18 December 2021 and 10 June 2022.[24]
- In adults 50 years of age or older during the period when Omicron BA.2/BA.2.12.1 subvariant predominated:
  - Compared to being unvaccinated, four doses of a COVID-19 mRNA vaccine was associated with a vaccine effectiveness against COVID-19 related hospitalisation of 80% (95% CI: 71, 85) 7 days or more after Dose 4.
  - Compared to being unvaccinated, three doses of a COVID-19 mRNA vaccine was associated with a vaccine effectiveness against COVID-19 related hospitalisation of 55% (95% CI:46, 62) 120 days or more after Dose 3.

The Grewel R et al. (2022) Canadian study;[11] was notable for the following:

- Utilised data between 30 December 2021 and 27 April 2022 (Omicron dominant period) from adults 60 years of age or older residing in 626 long term care facilities in Ontario.
- The effectiveness of a fourth dose (95% received mRNA-1273 (Moderna) as fourth dose) 7 or more days after vaccination versus third dose received 84 days or more earlier was 19% (95% CI 12% to 26%) against infection, 31% (20% to 41%) against symptomatic infection, and 40% (24% to 52%) against severe outcomes.

The Nordstrom P et al. (2022) study;[10] from Sweden was notable for the following:

- Utilised two datasets from Swedish nationwide registers during an Omicron dominant period:
  - residents of long term care facilities given a fourth dose of a COVID-19 mRNA vaccine (approximately 60% BNT162b2 30 μg and approximately 40% mRNA-1273 (Moderna)) from 1 January 2022 (matched 1:1 with residents given at least three doses);
  - all individuals 80 years of age or older given a fourth dose (matched 1:1 with individuals given at least three doses);
  - the outcome measure was all cause mortality.
- In the long term care facility cohort: During days 7 to 60, the vaccine effectiveness of the fourth dose was 39% (95% CI, 29 to 48), which declined to 27% (95% CI, -2 to 48) during days 61 to 126.
- In cohort of all individuals 80 years of age or older: During days 7 to 60, the vaccine effectiveness of the fourth dose was 71% (95% CI, 69 to 72), which declined to 54% (95% CI, 48 to 60) during days 61 to 143.
- The vaccine effectiveness of the fourth dose seemed stronger when it was compared to third dose recipients where at least four months had passed since vaccination ($p < 0.001$ for interaction).

[24] Established in 2019, the VISION Vaccine Effectiveness (VE) Network is a research collaboration between CDC, Westat, and multiple sites with integrated clinical, laboratory, and vaccination records in the United States that evaluate how well seasonal influenza (flu) vaccines protect people against flu and how well different COVID-19 vaccines protect against COVID-19. VISION Vaccine Effectiveness Network | CDC

Clinical data in the adolescent population

For use as an additional booster dose (Dose 4) in adolescent population, no immunogenicity, safety, or vaccine effectiveness data for a fourth dose were presented for adolescents from 12 to less than 18 years of age. Adolescent participants were not included in Study C4591031, nor in the real-world evidence provided. In relation to extending the age range for a fourth dose (Dose 4) to 12 years of age or older the sponsor provided the following rationale:

> 'Real-world effectiveness against symptomatic COVID-19 of two and three doses of BNT162b2 and the duration of protection post-Dose 2 have been shown to be similar among adolescents 12 to 15 years of age and adults ≥18 years of age during Omicron variant predominance.[25,26] Based on the available clinical and real-world data, it is therefore expected that the protection offered by BNT162b2 30 μg will be similar among adolescents and adults and supports an extension of the indication to ≥ 12 years of age.'

Risk management plan

The TGA decided a new risk management plan (RMP) was not required for this submission (see TGA's guidance on 'when an RMP is required'). Extensive risk management activities are already in place as a result of multiple previous submissions for this vaccine in Australia.

The sponsor is required to comply with product vigilance and risk minimisation requirements.

The TGA may request an updated RMP at any stage of a product's lifecycle, during both the pre-approval and post-approval phases. Further information regarding the TGA's risk management approach can be found in risk management plans for medicines and biologicals and the TGA's risk management approach. Information on the Australia specific annex (ASA) can be found on the TGA website.

Risk-benefit analysis

Delegate's considerations

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to cause substantial morbidity and mortality globally. Australia is experiencing ongoing COVID-19 cases, and hospitalisations, and further deaths as a result of Omicron subvariants. This leads to significant disruption to normal life and has health and economic implications for the country. Certain populations such as those aged 60 years of age or older, and people with immunosuppression and people with a range of comorbid conditions are at increased risk.

Real-world data have shown that after the initial booster dose of Comirnaty (tozinameran) COVID-19 vaccine, in the presence of the Omicron variant, vaccine effectiveness against symptomatic COVID-19 is lower and wanes more quickly post-Dose 3 compared to prior variants. This raises the potential need and likely benefit of an additional booster.

Clinical data from approximately 640 participants 18 to 55 years of age from Study C4591031 Substudy D (Cohort 2) and approximately 1840 participants over 55 years of age from Study C4591031 Substudy E (expanded cohort) who had received a fourth dose of Comirnaty

[25] Fleming-Dutra K,E, et al. Association of Prior BNT162b2 COVID-19 Vaccination With Symptomatic SARS-CoV-2 Infection in Children and Adolescents During Omicron Predominance, *Journal of the American Medical Association*, 2022; 327 (22): 2210-2219.

[26] Accorsi E.K, et al. Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants, *Journal of the American Medical Association*, 2022; 327 (7): 639-51.

COVID-19 vaccine 30 μg have been presented in this submission. Real-world data have been included.

Immunogenicity

Immunogenicity data are derived from Study C45981031 Substudies D and E, which enrolled healthy adult participants, who had previously received three doses of Comirnaty (tozinameran) COVID-19 vaccine 30 μg. Substudy D (Cohort 2) evaluated an additional booster (fourth) dose of Comirnaty (tozinameran) COVID-19 vaccine 30 μg and the Omicron variant-specific vaccine (BNT162b2 OMI) 30 μg to approximately 640 participants randomised at a ratio of 1:1. In Substudy E, 1840 participants over 55 years of age were randomised into 6 approximately equal sized groups to receive Comirnaty at 30 μg, Comirnaty at 60 μg, BNT162b2 OMI at 30 μg, BNT162b2 OMI at 60 μg, a combination of Comirnaty vaccine and BNT162b2 OMI at 30 μg (15 μg each), or a combination of Comirnaty and BNT162b2 OMI at 60 μg (30 μg each) as a fourth dose.

These studies show that a fourth dose of Comirnaty (tozinameran) COVID-19 vaccine 30 μg elicits immune response against the reference strain and Omicron BA.1 variant. Substudy E also shows against other Omicron sublineages, Comirnaty 30 μg elicited neutralisation titres to other Omicron sublineages including the more recent circulating Omicron variants.

Vaccine efficacy

The clinical evidence for Comirnaty (tozinameran) COVID-19 vaccine effectiveness (greater than 95%; pre-Omicron era) includes induction of strong immune responses and high vaccine efficacy accompanied by a satisfactory safety profile associated with the primary series. Vaccine efficacy and the immune responsiveness both began to decline post-Dose 2, with previous submissions supporting a third dose (Dose 3 or booster Dose 1) where a booster dose of Comirnaty vaccine at the same dose level restored the vaccine efficacy to greater than 95% (median follow up time of 2.5 months post booster) in Phase III Study C4591031.

In this submission, vaccine efficacy was not the main endpoint in Study C4591031, however available data from Study C4591031 and real-world evidence show that four doses of Comirnaty vaccine (relative to only three doses) improves protection against the Omicron variant across a spectrum of COVID-19 outcomes, including infection, symptomatic disease, severe illness, hospitalisation, and mortality. It is noted that the vaccine efficacy in the real-world studies presented varies considerably, and this likely reflects study methodology, including the specific populations studied.

Safety

The safety profile of Comirnaty (tozinameran) COVID-19 vaccine 30 μg is known and has been documented previously and extensively when utilised as a primary vaccine series and as a first booster (third dose). Overall, the reactogenicity profile (local reactions, systemic events) within seven days following a fourth dose was similar to that observed after a third dose of Comirnaty vaccine. There were no cases reported of myocarditis/pericarditis, Bell's palsy (or facial paralysis/paresis), appendicitis, or vaccine related anaphylaxis and no deaths reported in Study C4591031. No new safety concerns were identified. However, follow up time following the fourth dose was short (less than two months), and the only data available was in adult populations. Furthermore, data for the first booster dose (Dose 3) only pertain to participants 16 years of age or older.

Data limitations

The following are considered limitations of the available data:

- Safety and immunogenicity data for second booster vaccine available only for less than two months post second booster dose.
- Immunogenicity data from booster dose against the currently circulating variants is limited.
- Data related to persistence of immune response was not available.
- No immunogenicity, safety, or real-world evidence for second booster dose in those 12 to less than 18 years of age.
- No safety data on pregnant women and breastfeeding women.
- Short term safety data may not provide information on rare adverse events and there may be adverse events that have a long latency period including adverse events of special interest.

Conclusions

From the currently available data, it can be concluded for many populations a second booster dose (Dose 4) of Comirnaty (tozinameran) COVID-19 vaccine 30 μg is efficacious in protecting individuals against symptomatic COVID-19. The safety profile is similar to that observed in adults previously; with no new safety signals identified. Thus, in individuals 18 years of age or older, it is expected that the known and potential benefits outweigh the known and potential risks at this time. However, given the lack of data pertaining to the adolescent population, the risk-benefit assessment is not possible.

Proposed action

The Delegate is of the view approval of the variation to the Comirnaty (tozinameran) COVID-19 vaccine 30 μg to be used as a second booster (that is, Dose 4) for individuals aged 18 years of age is appropriate.

The Delegate does not propose to approve the use of Comirnaty (tozinameran) COVID-19 vaccine 30 μg in individuals aged 12 to less than 18 years of age and will seek advice from the Advisory Committee on Vaccines (ACV) on this issue.

The final decision will be made following the ACV discussion and the satisfactory negotiation of the Product Information and the conditions of registration.

Advisory Committee considerations

The Advisory Committee on Vaccines (ACV), having considered the evaluations and the Delegate's overview, as well as the sponsor's response to these documents, advised the following.

Specific advice to the Delegate

The ACV advised the following in response to the Delegate's specific request for advice:

1. ***Does ACV consider that there is a favourable benefit-risk balance to recommend provisional approval of the Comirnaty (original) vaccine as a second booster (Dose 4) in individuals 18 years and older?***

The ACV advised that there is a favourable benefit-risk balance for provisional approval of Comirnaty (tozinameran) as a second and subsequent booster in individuals 18 years and older, at least 4 months after an earlier booster dose.

The ACV advice reflected:

- substantial real-world experience in Australia of Comirnaty used as a second booster dose prior to the availability of the bivalent vaccines
- real-world effectiveness on rates of severe infection, hospitalisation and mortality are supportive
- AusVaxSafety data on 1.1 million doses of Comirnaty Dose 3/boosters in adults, with less than 1% of patients reporting a medical attendance, and the adverse effect profile similar to that following Dose 2.

2. Does ACV consider that the indication for Comirnaty (original) vaccine as a second booster (Dose 4) should include individuals 12 to 17 years of age?

The ACV advised that as there was no clinical trial data on safety or reactogenicity after Dose 4 in adolescents it was not possible to find a favourable benefit-risk balance for provisional approval of Comirnaty (tozinameran) as a second booster in individuals 12 to 17 years of age.

The ACV noted that use of an additional dose has been recommended by the Australian Technical Advisory Group on Immunisation (ATAGI) for individuals in this age group who have underlying risk factors for developing severe COVID-19, for example immunocompromise, but this is not the indication proposed by the sponsor.

The ACV noted the unknown risk of myocarditis/ pericarditis following a second booster (Dose 4) in individuals 12 to 17 years of age.

3. Can the ACV comment on the real-world data influence (if any) on decision making regarding this submission?

The ACV advised that the real-world data is highly complementary to the immunogenicity and safety data from controlled trials.

Real-world effectiveness data against severe infection, hospitalisation and mortality, particularly in the elderly and people in residential care facilities, appears favourable, including data recently analysed from Australia.

While vaccine effectiveness estimates from real-world data do vary considerably, likely due to differences in study methodology, including the specific populations studied, and circulating strains at the time of the studies, they still indicate a positive benefit-risk profile.

4. Can the ACV comment on any specific risk mitigation strategies required for the booster dose?

The ACV advised that robust communication strategies continue to be needed for primary care as to the vaccines approved for which age groups and the interval since the prior dose and/or infection to ensure vaccines are delivered appropriately.

5. The committee is also requested to provide advice on any other issues that it thinks may be relevant to a decision on whether or not to approve this application.

The ACV noted that the use of ordinal numbers to describe additional COVID-19 vaccine doses (for example, third dose; Dose 4) is becoming problematic as, for example, the primary series may be 2 or 3 doses and the first dose of a bivalent vaccine may be the fifth dose of any COVID-19 vaccine. The use of the term 'booster' is also becoming dated. The ACV supported consistency in terminology across clinical and consumer documents, including with the official

guidelines mentioned in the approved indication, potentially using more generic terms such as additional or repeat doses.

The ACV comments on this point apply across the range of COVID-19 vaccines.

Conclusion

The ACV considered this vaccine to have an overall positive benefit-risk profile for the dosage:

> *Comirnaty COVID-19 vaccine 30 micrograms may be administered to individuals 18 years of age and older at least 4 months after a previous booster dose of any COVID-19 vaccine.*

Outcome

Based on a review of quality, safety, and efficacy, the TGA approved the registration of Comirnaty (tozinameran) 30 µg/ 0.3 mL suspension for injection, vial, change in dose regimen to:

> *Individuals 12 years of age and older*
>
> Comirnaty is administered intramuscularly after dilution as a primary course of 2 doses at least 21 days apart. See dosing instructions below.
>
> *Booster dose in individuals 12 years of age and older*
>
> A first booster dose of Comirnaty may be administered intramuscularly at least 6 months after the completion of a COVID-19 vaccine primary series in individuals 12 years of age and older.
>
> Subsequent doses of Comirnaty may be administered to individuals 18 years of age and older at least 3 months after a previous booster dose of Comirnaty.
>
> The decision when and for whom to implement a booster dose of Comirnaty should be made based on available vaccine safety and effectiveness data (see sections 4.4 Special warnings and precautions for use and 5.1 Pharmacodynamic properties), in accordance with official recommendations.
>
> *Interchangeability*
>
> There are limited data on the interchangeability of Comirnaty with other COVID-19 vaccines to complete the primary vaccination course or the booster dose. Individuals who have received 1 dose of Comirnaty should preferably receive a second dose of Comirnaty to complete the primary vaccination course and for any additional doses.
>
> *Severely immunocompromised aged 12 years and older*
>
> In accordance with official recommendations, a third dose may be given, as part of the primary series, at least 28 days after the second dose to individuals who are severely immunocompromised (see section 4.4 Special warnings and precautions for use).
>
> *Elderly population*
>
> No dosage adjustment is required in elderly individuals ≥ 65 years of age.

Attachment 1. Product Information

The PI for Comirnaty approved with the submission which is described in this AusPAR is at Attachment 1. For the most recent PI, please refer to the TGA PI/CMI search facility.

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Reference/Publication #