Australian Government
Department of Health
Therapeutic Goods Administration

Advisory Committee on Vaccines Meeting 30 Minutes on Item 2.2 Tozinameran (formerly BNT162b2 [mRNA])

Proprietary Product Name: Comirnaty

Sponsor: Pfizer Australia Pty Ltd

14 January 2022

TGA Health Safety Regulation

Contents

Submission details

Type of submission:	Major variation / PI change requiring evaluation – changes in population for booster dose
Product name:	Comirnaty
Active ingredient:	Tozinameran (formerly BNT162b2 [mRNA])
Submission:	PM-2021-04582-1-2
Dose form:	Concentrated suspension for injection
Strength:	30 microgram per 0.3 mL dose
Approved indication:	COMIRNATY (BNT162b2[mRNA]) COVID-19 Vaccine has **provisional approval** for the indication below: Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 5 years 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.
Approved dosage:	*Individuals 12 years of age and older* COMIRNATY is administered intramuscularly after dilution as a course of 2 doses at least 21 days apart. A booster dose (third dose) of COMIRNATY may be administered intramuscularly at least 6 months after the completion of a COVID-19 vaccine primary series in individuals 18 years of age and older. The decision when and for whom to implement a booster dose (third dose) of COMIRNATY should be made based on available vaccine safety and effectiveness data, in accordance with official recommendations. There are limited data on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the primary vaccination course or the booster dose (third 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.
Dosage initially proposed by sponsor:	A booster dose (third dose) of COMIRNATY may be administered intramuscularly approximately 6 months after the second dose in individuals 16 years of age and older.
Dosage proposed in pre-ACV response	A booster dose (third dose) of COMIRNATY may be administered intramuscularly at least 6 months after the completion of a COVID-19 vaccine primary series in individuals 16 years of age and older.

Documents considered by ACV

The ACV considered the following documentation, provided between 6 and 10 January 2022:

A1 Delegate - Request for ACV advice and overview – 'Delegate's Overview' – dated 5 January 2022
A2 Sponsor - application letter dated 12 October 2021
A2a Sponsor - application letter for supplementary data - dated 24 December 2021
A3 Sponsor – pre-ACV response
response
adverse reactions update
comments on PI
foreign regulatory status
comments on foreign PI
M5 TGA - Clinical - evaluation report – Round 2 draft dated 27 October 2021
M5a Sponsor – Synopsis of Interim Full Clinical Study report Protocol C4591031 Substudy A – dated 18 November 2021
PI Product Information – clean and annotated – BNT162b2 - from pre-ACV response
PI Product Information – clean and annotated – tozinameran / Tris formulation - from pre-ACV response
CMI Consumer Medicine Information – BNT162b2 - clean and annotated – from pre-ACV response
CMI Consumer Medicine Information – tozinameran / Tris formulation - clean and annotated – from pre-ACV response
CAN Canadian product monograph – dated 19 November 2021 - from pre-ACV response
EMA European summary of product characteristics – dated 3 November 2021 - from pre-ACV response
UK UK information for temporary supply authorisation – dated December 2021 - from pre-ACV response
USA USA fact sheet for vaccination providers – grey vial – dated 3 January 2022 September 2021 - from pre-ACV response
USA USA fact sheet for vaccination providers – purple vial – dated 3 January 2022 September 2021 - from pre-ACV response

Public materials discussed at the meeting included:

ACIP meeting material:

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/05-COVID-Twentyman-508.pdf

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/02-COVID-Su-508.pdf

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/06_COVID_Oliver_2022-01-05.pdf

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-09-22/02-COVID-Gruber-508.pdf

Preprints:

Buchan SA, Seo CY, Johnson C, et al. Epidemiology of myocarditis and pericarditis following mRNA vaccines in Ontario, Canada: by vaccine product, schedule and interval. https://doi.org/10.1101/2021.12.02.21267156; posted 5 December 2021.

Delegate's Overview

Delegate's summary of issues

Supplementary data have become available on a booster dose (third dose) of Comirnaty in individuals 16 years to 17 years of age.

Pfizer data on time between the completion of the primary vaccine dose and the booster dose is limited to approximately 6 months. A recent NEJM publication [see below] reported on younger age groups who received a second dose at least 5 months earlier.

This Delegate is not aware that immunogenicity associated with a third dose against the Omicron (B.1.1.529) variant of interest have been submitted to TGA from Pfizer.

Summary of data

- Pfizer press release dated 17 December 2021 including a single booster dose to individuals 16 years of age and older in the FDA Emergency Use Authorization.
- An interim full CSR Version 1.0 (18 November 2021) for Study C4591031
- Bar-On YM, Goldberg Y, Mandel M, et al. Protection against Covid-19 by BNT162b2 Booster across Age Groups. N Engl J Med 2021;385:2421-30. DOI: 10.1056/NEJMoa2115926

Delegate's preliminary view

The Delegate is proposing to make a supplementary decision in relation to the previously considered booster submission, PM-2021-04582-1-2, for the 16-17 year old age group.

The Delegate propose to approve the registration of the product Comirnaty with a statement 'A booster dose (third dose) of Comirnaty may be administered intramuscularly approximately 6 months after the second dose in individuals 16 years of age and older'.

Advice sought by Delegate of the Secretary of the Department of Health

1. Does ACV agree that a booster dose (third dose) of Comirnaty may be administered in individuals 16 years of age and older?
2. Does ACV consider the time of the booster dose might be shortened to 5 months in light of the recent NEJM publication?
3. The Committee is also requested to provide advice on any other issues that it thinks may be relevant to this supplementary decision.

ACV discussion

Environment

The ACV noted that the vaccine was provisionally registered on the ARTG on 25 January 2021 for use in persons from 16 years of age. Continued approval is dependent on evidence of longer-term efficacy and safety from ongoing clinical trials and post-market assessment. (See ACV 18, held 15 January 2021, providing advice on new biological entity).

Supply of the vaccine commenced on 21 February 2021.

The ACV also noted the provisional registration on 22 July 2021 for use in persons from 12 years of age. (See ACV 22, held 16 June 2021, providing advice on extension of indication).

The ACV also noted the dosage and PI changes approved 26 October 2021 for use of third doses. (See ACV 26, held 25 October 2021, providing advice on booster dose for 18+ years and third primary dose in immunocompromised persons 12 years and older).

The ACV also noted the provisional registration on 3 December 2021 for use in persons from 5 years of age. (See ACV 27, held 1 December 2021, providing advice on extension of indication).

International regulatory status

The ACV noted the following in regard to the international regulatory status of a booster dose in 16 and 17 year olds:

- In the USA, emergency use authorization was amended on 3 January 2022 to recommend a booster dose at least 5 months after individuals received their second dose of the vaccine, including for children aged 12 to 17 years, citing rising infections in teens and young adults and an increase in paediatric hospitalisations.
- In the UK, temporary authorisation was amended on 3 January 2022 to permit a third dose at least 8 weeks after the second dose of an mRNA or adeno-virus-vectored COVID-19 vaccine when the potential benefits outweigh any potential risks, for individuals 12 years and older.

Booster doses are approved for 18 years and older in the EU, Canada and New Zealand.

Immunogenicity and efficacy

The ACV noted the C4591031 study included 90 subjects aged 16 and 17 years within the study of 10,136 subjects aged 18 years and over. The booster dose was administered at least 6 months after the primary series.[1] Efficacy in the 16-17 year age group was in line with the overall study population, within the limitations of the small sample size.

The Bar-On study showed reduction in confirmed infection rate in 16-29 year olds (population of 1.1 million) when the booster was administered a minimum of 5 months after the second dose. However, the ACV was unable to identify the distribution of time intervals between second and third doses for the 16-17 year olds.

Safety

Real world data from Israel indicate rare occurrences of myocarditis in people aged ≥16 years following a booster dose at 5 months occurred at less than half the rate observed following second doses.

US VAERS data from 47 thousand booster doses in 16-17 year olds show that most adverse event reports (95%) were non-serious and similar to primary series. Two reports meet the CDC cases definition of myocarditis, as at 19 December 2021, with 4 other cases under review.

The ACV noted that 16-17 years is the age group likely at highest risk of myo/pericarditis following Comirnaty and likely to be most sensitive to shortening of the interval to the booster dose, although 5 months is unlikely to pose major issues.

The ACV noted that the ATAGI guidance on myocarditis and pericarditis after mRNA COVID-19 vaccines is under regular review.

General comments

The ACV noted that updating a vaccine for variant(s) of concern can occur after an earlier authorisation based on adequate data on quality, safety and efficacy from clinical trials.[2]

The ACV suggested that further data related to myocarditis (e.g. biomarkers of subclinical myocarditis) should be considered, if available.

[1] C4591031 Substudy A is part of the master protocol to evaluate BNT162b2 boosting strategies across different populations of participants (e.g., age groups). The pivotal Study C4591001 is the study number cited in the AusPAR for the Comirnaty booster dose for 18 years and older.

[2] Data requirements for second generation vaccines, active against SARS-CoV-2 variants of concern, are described in the ACCESS Consortium document. https://www.tga.gov au/points-consider-strain-changes-authorised-covid-19-vaccines-ongoing-sars-cov-2-pandemic

The ACV noted that official recommendations can take into account the most current data on epidemiologic context, vaccine effectiveness and post-marketing safety data, compared to what is published in the Product Information.

ACV advice to the Delegate

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

1. Does ACV agree that a booster dose (third dose) of COMIRNATY may be administered in individuals 16 years of age and older?

The ACV advised that there is sufficient evidence to support changes to the Product Information to include a booster dose (third dose) of Comirnaty for individuals 16 years of age and older given ≥ 6 months after the primary 2-dose series. Protection against COVID-19 in participants ≥16 years was shown irrespective of evidence of prior infection with SARS-CoV-2 and across various demographic subgroups.

The ACV were reassured that there were no significant differences between the 16-17 year age group and the 18+ years age group in the immunogenicity, reactogenicity or effectiveness of Comirnaty.

The ACV was of the view that the safety data, although with limited numbers, showed the Comirnaty booster was well tolerated, with similar frequencies and intensities of reactogenicity as experienced after the second dose of the primary series.

The ACV noted that immunogenicity associated with a third dose against the Omicron (B.1.1.529) variant of interest was not available.

2. Does ACV consider the time of the booster dose might be shortened to 5 months in light of the recent NEJM publication?

The ACV considered that the time interval from primary series to booster dose could be shortened to 5 months when warranted. However, the safety and efficacy of a time interval shorter than 5 months is not clear.

The ACV discussed the potential risk of myocarditis, particularly within the 16-17 year old age group, who appear to be at the highest risk of myocarditis. The ACV was reassured by early data indicating that the rate of myocarditis appears lower after booster (third dose) compared to after the second dose. There continues to be a need to communicate the risk of myocarditis to vaccine recipients.

3. The Committee is also requested to provide advice on any other issues that it thinks may be relevant to this supplementary decision.

The ACV noted that there is likely to be a minimum safe window between the second dose and the booster dose, but this is as yet undefined. The PI should include a statement such as:

> 'Data support an interval of 5 months. Safety for shorter intervals has not been established.'

The ACV noted Buchan et al, in a preprint paper, suggests that the reporting rates of myocarditis/pericarditis were higher when the interval between first and second doses was shorter (i.e., ≤30 days). This supported the view that the interval between doses is an important safety consideration.

The ACV advised that wording in the PI should clearly differentiate third dose as a booster dose from the three dose primary series for persons 12 years and over who are immunocompromised.

The ACV supported alignment of terminology used within dosage directions (e.g. the use of 'booster dose' or 'third dose') across all COVID-19 vaccines.

The use and timing of Comirnaty booster in 16-17 year olds should be in accordance with official recommendations.

ACV conclusion

The ACV recommended the approval of changes to the Product Information of Comirnaty to include a booster (third) dose for persons 16 years and older.

The use and timing of Comirnaty booster in 16-17 year olds should be in accordance with official recommendations.

Ratified and sent to the sponsor 1 pm on 21 January 2022

Therapeutic Goods Administration

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