Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Australian Public Assessment Report for Comirnaty JN.1 COVID-19 vaccine

Active ingredient: Bretovameran

Sponsor: Pfizer Australia Pty Ltd

March 2025

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
ARTG	Australian Register of Therapeutic Goods
BNT162b2	Pfizer BioNTech COVID-19 vaccine
CMI	Consumer Medicines Information
COVID-19	Coronavirus disease 2019
DS	Drug Substance
DP	Drug Product
GMP	Good Manufacturing Practice
LN	Lymph nodes
LNP	Lipid nanoparticle
mAb	Monoclonal antibody
mRNA	Messenger ribonucleic acid
NAb	Neutralising antibodies
PCR	Polymerase chain reaction
PFS	Pre-filled syringe
PI	Product Information
RAT	Rapid antigen test
TGA	Therapeutic Goods Administration

Comirnaty JN.1 COVID-19 Vaccine (bretovameran) submission

Product name:	Comirnaty JN.1 COVID-19 Vaccine (bretovameran)
Type of submission:	Minor variation
Decision and date of decision:	Approved 10 October 2024
Approved therapeutic use for the current submission:	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.
Date of entry onto ARTG:	11 October 2024
ARTG numbers:	457685, 457688, 457690, 457677, 457680, 457686. 459385, 457679, 459366
, *Black Triangle Scheme*	Yes
Sponsor's name and address:	Pfizer Australia Pty Ltd, Level 17, 151 Clarence Street Sydney NSW 2000
Dose form:	Bretovameran is a single-stranded, 5'-capped messenger RNA (mRNA). Comirnaty JN.1 (Grey, Orange and Maroon cap) is a white to off-white frozen suspension. Comirnaty JN.1 (Blue and yellow cap) is a clear to slightly opalescent solution. Comirnaty JN.1 – Single dose Glass Prefilled Syringes and Single dose Plastic Prefilled Syringes, 30 micrograms, for 12 years and older is a white to off-white suspension.
Strengths:	See table below
Containers and pack sizes:	Comirnaty JN.1 Grey or Blue cap: Suspension for injection 2 mL clear vial (Type I glass) with a stopper (synthetic bromobutyl rubber) and a Grey or

Age group	**12 years and older**		**5 to <12 years**			**6 months to <5 years**	
Cap & Label colour code	Light Grey	Dark Grey	Orange	Light Blue	Dark Blue	Maroon	Yellow
Strength per dose	30 micrograms (0.3 mL dose)		10 micrograms (0.2 mL dose)	10 micrograms (0.3 mL dose)		3 micrograms (0.2 mL dose)	3 micrograms (0.3 mL dose)
Fill volume	0.48 mL	2.25 mL	1.3 mL	0.48 mL	2.25 mL	0.4 mL	0.48 mL
No. of doses per vial	1	6	10	1	6	10	3
Dilution	Do not dilute		Requires dilution	Do not dilute		Requires dilution	

Blue flip-off plastic cap with aluminium seal. Each vial contains either 1 or 6 doses.

- Light Grey or Light Blue cap: single dose vial
- Dark Grey or Dark Blue cap: 6 dose multidose vial

Comirnaty JN.1 Orange or Maroon or Yellow cap: Concentrated Suspension for injection: 2 mL clear multidose vial (Type I glass) with a stopper (synthetic bromobutyl rubber) and an Orange or a Maroon or a Yellow flip-off plastic cap with aluminium seal. Each vial contains 10 or 3 doses after dilution.

Orange or Maroon cap: 10 dose multidose vial after dilution Yellow cap: 3 dose multidose vial after dilution

Pack size: 10 vials, 195 vials

Comirnaty JN.1 Prefilled Glass Syringe: 1 mL clear glass syringe (Type I glass) with polypropylene rigid cap with a 1 mL plunger stopper (bromobutyl elastomer). Each prefilled glass syringe contains 1 dose.

Pack size: 10 Prefilled glass syringes

Comirnaty JN.1 Prefilled Plastic Syringe: 1 mL transparent plastic (cyclic-olefin copolymer plastic) syringe with polycarbonate rigid cap with a 1 mL plunger stopper (bromobutyl elastomer). Each prefilled plastic syringe contains 1 dose.

Pack size: 10 prefilled plastic syringes

Routes of administration

In individuals **5 years of age and older**, administer the vaccine intramuscularly in the deltoid muscle.

In individuals 1 to **<5 years of age and older**, administer the vaccine intramuscularly in the anterolateral aspect of the thigh or the deltoid muscle.

In individuals from **6 to <12 months of age**, administer the vaccine intramuscularly in the anterolateral aspect of the thigh.

The vaccine should NOT be injected intravascularly, subcutaneously or intradermally.

Dosage:

Age group	12 years and older	5 to <12 years	6 months to <5 years
Strength/dose	30 micrograms	10 micrograms	3 micrograms

For further information regarding dosage, such as dosage modifications to manage adverse reactions, refer to the Product Information.

Pregnancy category:

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. The pregnancy database 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.

The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. The pregnancy database 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.

Comirnaty JN.1 – proposed indication

This AusPAR describes the evaluation of the submission by Pfizer Australia Pty Ltd (the Sponsor) to register Comirnaty JN.1 COVID-19 Vaccine (bretovameran). No changes are proposed to the formulation, other than the active ingredient, nucleoside modified mRNA (modRNA), which is adapted to target the SARS-CoV-2 Omicron JN.1 variant. The proposed indication is:

> *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.*

COVID-19

There has been a significant number of COVID-19 cases since the emergence of the Omicron variants in Australia: 5,357,128 PCR-confirmed and 6,229,346 RAT probable COVID-19 cases from 15 December 2021 to 10 March 2024. Nationally, since the emergence of Omicron BA.2.86 + sub-lineages (including JN.1), there has been an increasing trend in hospitalisation, reflecting the start of a new Omicron wave of SARS-CoV-2 transmission.

COVID-19 burden persists among individuals of all ages and a variant-adapted vaccine that improves immune responses to currently circulating variants may help restore higher levels of protection against infection, and thus transmission, similar to that observed at earlier stages in the pandemic. Currently, a COVID-19 vaccine adapted to the World Health Organization recommended SARS-CoV-2 Omicron JN.1 is not available in Australia.

Clinical rationale for the use of the Comirnaty JN.1 Vaccine

Given the genetic and resulting antigenic differences in currently circulating Omicron JN.1 sublineages of SARS-CoV-2 (e.g., JN.1, JN.1.6.1, JN.1.7, JN.1.13.1, JN.1.16.1, KP.1.1, KP.2 and KP.3) compared to the original (wildtype) or Omicron XBB.1.5 strains, the Omicron JN.1 adapted vaccine is needed to ensure adequate protection. Implementation of the Omicron JN.1 adapted vaccine would expand vaccine protection and add another important layer of community

protection against symptomatic infection and severe cases of COVID-19, particularly in the current setting of Omicron JN.1 sublineages dominance and with multiple lines of evidence that wild-type or Omicron XBB.1.5 based vaccines likely offer significantly reduced protection against JN.1-related disease, including severe illness, compared to prior variants.

Regulatory status

Australian regulatory status

This product is considered a new biological entity medicine for Australian regulatory purposes.

International regulatory status

Applications for a JN.1 strain update of Comirnaty monovalent COVID-19 vaccine and introduction of new presentations have been filed in the European Union.

Registration timeline

This submission was evaluated under the standard prescription medicines registration process.

Table 1: Timeline for Comirnaty JN.1 COVID-19 Vaccine (bretovameran), submission PM-2024-02578-1-2.

Description	Date
Submission dossier accepted and first round evaluation commenced	2 August 2024
Evaluation completed	8 October 2024
Registration decision (Outcome)	10 October 2024
Registration in the ARTG	11 October 2024
Number of working days from submission* dossier acceptance to registration decision	71

*Statutory timeframe for standard submissions is 255 working days

Evaluation overview

Quality evaluation summary

The manufacture of the JN.1 DS and DP relies on the same manufacturing processes used for the Original and Omicron variant vaccine DP with no changes to lipid nanoparticle (LNP) formation and stabilisation, bulk DS/DP formulation, thawing and pooling of DS/DP intermediates, DS/DP filling, or packaging processes, including facilities, filling lines and components for the updated vaccine compared to the previously authorised Original and/or variant vaccines. The DS/DP specifications are identical to the original DS/DP vials and recent XBB.1.5 vial and PFS

presentations and are considered acceptable for the control of the JN.1 DP (Vial and PFS presentations).

GMP clearance for listed manufacturers

All relevant manufacturing sites require approved and current Good Manufacturing Practise (GMP) clearances prior to Australian supply. A commitment is required from the Sponsor that they maintain the validity of all manufacturer GMP Clearances for the duration of product supply to Australia. Additionally, that adherence to the conditions of GMP Clearance approval is upheld. All manufacturing sites responsible for all steps of the Omicron JN.1 DS and Omicron JN.1 drug product manufacture are performed by previously authorised GMP facilities, and all clearances are up to date.

Post-approval stability protocol and stability commitment

The manufacturer has provided a commitment to continue the ongoing stability studies presented in the stability studies protocol. Additionally, one batch of DP per year for all relevant products will be placed on long term stability program and on accelerated stability testing where significant changes are made to the manufacturing process. The manufacturer has committed to communicate any out of specifications stability test results to the TGA.

Batch analysis (DS and DP)

While it is usual practice of providing three batch analysis to demonstrate batch to batch consistency to demonstrate the manufacturing process performs in a state of control, it should be noted that the JN.1 DS and DP is produced according to the same manufacturing processes and controls as the Original and subsequent variant DS/DP. As such, the Sponsor submitted release data for a single confirmatory batch manufactured on the 9 March 2024 at the commercial scale (112.8 L). The batch met the pre-determined release acceptance criteria.

The Sponsor has committed to provide batch analysis data for additional DS and DP batches manufactured at the commercial scale once they become available to support batch-to-batch consistency.

Stability (DS and DP)

The Sponsor has demonstrated the DS is stable for 6 months when stored at the intended storage condition of –20±5°C, that the DP is stable for 18 months stored at -90°C to -60°C for vial presentations, 12 months for plastic pre-filled syringe (PFS) presentations at -90°C to -60°C, and 8 months for glass PFS when stored at 2-8°C.

The Sponsor has committed to:

- Provide the results from ongoing stability studies performed on Omicron JN.1 DS lots when stored at -20±5°C and 5±3°C for each time point in accordance with the stability testing protocols to support the shelf life of the DS.
- Provide the results from ongoing stability studies performed on JN.1. Variant DP (vial) lots when stored at -90°C to -60°C and 5±3°C for each time point in accordance with the stability testing protocols to support the shelf life of the DP vial lots.
- Provide the results from ongoing stability studies performed on JN.1. Variant DP (PFS – Frozen Plastic) lots when stored at -90°C to -60°C and 5±3°C for each time point in

accordance with the stability testing protocols to support the shelf life of the DP PFS – Frozen Plastic lots.

- Provide the results from ongoing stability studies performed on JN.1. Variant DP (PFS – Refrigerated Glass) lots when stored at 2-8°C and 25±2°C for each time point in accordance with the stability testing protocols to support the shelf life of the DP PFS – Refrigerated Glass lots.
- There are no significant issues identified from the quality evaluation of the submitted data that would indicate the product should not be registered on the basis of quality, or safety-related issues arising from the quality of the product. The manufacturing quality information submitted by the Sponsor support the registration of bretovameran.

Nonclinical evaluation summary

The nonclinical data comprised 2 immunogenicity studies with BNT162b2 (Pfizer BioNTech COVID-19 vaccine) JN.1 and 2 tissue distribution studies with LNP/luciferase-encoding modRNA or LNP/BNT162b2 mRNA.

Immunogenicity

In the immunogenicity study with the BNT162b2 JN.1 vaccine as a primary 2-dose series immunisation in naïve mice, robust neutralising antibody responses were elicited 1 month after a 2nd injection against JN.1 and its sublineages including JN.1, JN.1.6.1, JN.1.7, JN.1.13.1, JN.1.16.1, KP.1.1, KP.2 and KP.3. Compared to the BNT162b2 XBB.1.5 vaccine, BNT162b2 JN.1 resulted in 6 to 196-fold higher neutralising antibody titres against JN.1 and sublineages, and 100 fold lower titres against XBB.1.5. Additionally, in spleens collected from immunised mice one month after the 2nd dose, BNT162b2 JN.1 induced strong spike specific CD4+ and CD8+ T cell cytokine responses that were highly cross-reactive to peptide pools (representing the full-length of spike protein) of all variants tested (Wuhan [WT], BA.4/5, JN.1, XBB.1.5). The BNT162b2 JN.1 vaccine elicited more robust T cell response against JN.1 peptide pools than the BNT162b2 XBB.1.5 vaccine, particularly in terms of CD8+ T cell responses vs. CD4+ T cell responses.

The BNT162b2 JN.1 vaccine as a 5th booster dose after 1st and 2nd vaccination doses of BNT162b2 (Original), a 3rd dose of bivalent BNT162b2 (Original + Omicron BA.4/5) and a 4th dose of monovalent BNT162b2 XBB.1.5, induced neutralising antibody (NAb) responses against a panel of JN.1 sublineage pseudoviruses (JN.1, JN.1.6.1, JN.1.7, JN.1.13.1, JN.1.16.1, KP.1.1, KP.2 and KP.3). The NAb titres against JN.1 and sublineages JN.1.1.1 and JN.1.7 after the BNT162b2 JN.1 vaccine were 9-10 fold higher than the pre-5th dose titres (i.e. after the 4th XBB.1.5 vaccine dose) and 2-3 fold higher than the titres after the XBB.1.5 vaccine as the 5th dose.

The BNT162b2 JN.1 vaccine also induced strong antigen-specific CD4+ and CD8+ T cell responses, which were slightly lower than the responses by the XBB.1.5 variant vaccine. All CD4+ and CD8+ T cell responses were highly cross-reactive against the Wuhan strain and Omicron BA.4/5, XBB.1.5 and JN.1 variants.

Overall immunogenicity studies in mice indicate the BNT162b2 JN.1 vaccine as a primary series vaccination or as a booster dose after previous vaccination with COVD-19 vaccines targeting other variants induced both humoral and cellular immunity, which may confer protection against COVID-19 infection by JN.1 and sublineage variants.

Tissue distribution of mRNA and expressed protein

Tissue distribution of luciferase expressed from luciferase mRNA, and mRNA and/or expressed spike protein from injected BNT162b2 mRNA was studied in mice. The two mRNA-LNP formulations used in the studies contained the same functional lipids and structural lipids as those in BNT162b2 mRNA vaccines.

Bioluminescence whole body imaging and luciferase assay of individual tissues showed high luciferase expression at the injection site (muscle) and the draining lymph node (popliteal LN) on day 1 post-injection (higher at a dose of 1 µg cf. 0.2 µg), which decreased to low levels by day 6. Other organs with protein (luciferase) expression at very low levels were axillary and inguinal LN on the injection side, liver and spleen. By day 6 after injection, luciferase was only detected in the injected muscle, popliteal LN, and at very low levels, in inguinal LN. No luciferase was detected in liver and spleen on day 6. The findings were similar to a previous study provided in the submission of the original vaccine, in which luciferase was detected by whole body imaging largely at the injection site (which declined to the background level after 9 days), with some distribution to liver (not detectable by 48 h).

Another distribution study in mice investigated BNT162b2 mRNA and spike protein biodistribution in mice 24 h after an IM injection of 1 µg BNT162b2 in the right hind muscle. Vaccine mRNA and expressed spike protein were both detected in the injected muscle and lymph nodes (popliteal, inguinal and axillary), and only mRNA (not spike protein) was detected in spleen and liver. No mRNA or spike protein was detected in lung, heart and brain (mRNA not analysed in brain), but the distribution of mRNA to these tissues cannot be completely ruled out due to limitation of the assay methods and occasionally detected weak signals in these tissues.

Highest BNT162b2 mRNA containing cells were found in injected muscle, liver and spleen. Lymph nodes (popliteal, inguinal and axillary) also contained detectable levels of mRNA. The injected muscle tissue also had the highest spike protein levels, followed by the popliteal, inguinal and axillary LN (in descending order).

In muscle tissue, spike protein and mRNA were located between muscle fibres, in adipocytes and in cells in close vicinity to blood vessels. In LNs, spike protein positive cells were located in the subcapsular sinus (SCS) macrophages (not in geminal centres), while mRNA was present in the SCS and germinal centres. mRNA was located in spleen white pulp and homogeneously distributed in liver tissues, suggesting uptake by hepatocytes.

BNT162b2 vaccination in mice showed dose- and time-dependent distribution of mRNA to the injection site (muscle of right hind leg), draining LN (popliteal), non-draining LNs (inguinal and axillary) and spleen. A strong modRNA signal corresponded to strong spike protein expression in muscle and LNs, but not in spleen (only a weak spike signal detected). Major cell populations expressing spike protein were fibroblasts and macrophages (in injected muscle) and subcapsular sinus macrophages (in LNs). Spike protein expression was also visible in dendritic cells to a lower extent. No mRNA or spike expression was observed in selected vital and reproductive organs (heart, kidney, lung, brain, uterus and ovary), with a weak to moderate mRNA signal in liver at all time points (6 h – 2 days post dose) at 1 and 5 µg and a few cells positive for spike protein at 1 day post dose at the high dose.

Conclusions and recommendations

A primary 2-dose series of the BNT162b2 JN.1 vaccine in naïve mice or as a 5th dose booster in BNT162b2 ‘vaccine ‘experienced’ mice induced higher neutralising antibodies against the JN.1 lineage and sublineages than BNT162b2 XBB.1.5 vaccine. Additionally, the BNT162b2 JN.1

vaccine induced T cell responses, which were highly cross-reactive to all spike antigens (WT, BA.4/5, XBB.1.5, JN.1 and sublineages).

In mice after an IM injection of the BNT162b2 mRNA vaccine, mRNA spread from the injection site to lymph nodes (popliteal, inguinal, and axillary), spleen and liver. Spike protein expression did not always correlate with mRNA biodistribution and was restricted to the injected leg muscle, popliteal, inguinal and axillary lymph nodes (not in liver and spleen). Similarly, high levels of luciferase were detected at the injection site (muscle) and draining lymph node (popliteal LN) after an IM injection of luciferase mRNA. Different from the BNT162b2 mRNA vaccine, luciferase was detected in liver and spleen.

There were no protection studies for the Comirnaty JN.1 monovalent vaccine. No toxicity studies on the JN.1 monovalent vaccine were submitted. This is acceptable since the new mRNA (bretovameran) uses the same backbone and manufacture platform as the original BNT162b2 mRNA and there are no changes to vaccine formulation.

There are no nonclinical objections to the approval of the Comirnaty JN.1 vaccine.

Outcome

Based on a review of quality, safety, and efficacy, the TGA decided to register Comirnaty JN.1 (bretovameran) COVID-19 Vaccine for the following indication:

> *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.*

This approval is based on the evaluation of the information and data provided with the original letter of application and with any subsequent correspondence and submissions relating to the application.

Product Information

The Product Information (PI) associated with this submission for Comirnaty JN.1 COVID-19 Vaccine (bretovameran) is available via the link on this AusPAR's webpage.

For the most recent PI and Consumer Medicines Information (CMI) associated with this medicine, query the medicine in the PI/CMI search facility.

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6203 1605
https://www.tga.gov.au