NEW ZEALAND DATA SHEET

1. PRODUCT NAME

COMIRNATY™ COVID-19 VACCINE 0.5 mg/mL concentrated suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial and must be diluted before use.

One vial (0.45 mL) contains 6 doses of 0.3 mL after dilution, see Section 4.2 Dose and method of administration and Section 6.6 Special precautions for disposal and other handling.

1 dose (0.3 mL) contains 30 micrograms of BNT162b2 [mRNA] (embedded in lipid nanoparticles).

The active ingredient is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Concentrated suspension for injection (sterile concentrate).

COMIRNATY is a white to off-white frozen suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

COMIRNATY has provisional consent (see section 5.1) for the indication below:

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.

4.2 Dose and method of administration

Dose

Individuals 12 years of age and older

COMIRNATY is administered intramuscularly after dilution as a course of 2 doses at least 21 days apart. See dosing instructions below.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination course. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination course.

Elderly population

No dosage adjustment is required in elderly individuals ≥ 65 years of age.

Method of administration

COMIRNATY should be administered intramuscularly after dilution (see Section 6.6 Special precautions for disposal and other handling).

After dilution, vials of Comirnaty contain six doses of 0.3 mL of vaccine. In order to extract six doses from a single vial, low dead-volume syringes and/or needles should be used. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

The preferred site of administration is the deltoid muscle of the upper arm.

Do not inject COMIRNATY intravascularly, subcutaneously or intradermally.

COMIRNATY should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering COMIRNATY, see Section 4.4 Special warnings and precautions for use.

For instructions regarding thawing, handling and disposal of COMIRNATY, see Section 6.6 Special precautions for disposal and other handling.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 List of excipients.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

General recommendations

Hypersensitivity and anaphylaxis

Events of anaphylaxis have been reported. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of COMIRNATY.

The individual should be kept under close observation for at least 15 minutes following vaccination. A second dose of COMIRNATY should not be given to those who have experienced anaphylaxis to the first dose of COMIRNATY.

Myocarditis and pericarditis

Very rare cases of myocarditis and pericarditis have been observed following vaccination with COMIRNATY. These cases have primarily occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vacination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Stress-related responses

Some individuals may have stress-related responses associated with the process of vaccination itself. Stress-related responses are temporary and resolve on their own. They may include dizziness, fainting, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, tingling sensations, sweating and/or anxiety. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation and precautions should be in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, COMIRNATY should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy, safety and immunogenicity of COMIRNATY has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COMIRNATY may be lower in immunosuppressed individuals.

Duration of protection

The duration of protection afforded by COMIRNATY is unknown as it is still being determined by ongoing clinical trials.

Limitations of vaccine effectiveness

As with any vaccine, vaccination with COMIRNATY may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of COMIRNATY.

Use in the elderly

Clinical studies of COMIRNATY include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy. See Section 5.1 Pharmacodynamic properties, Clinical trials, Efficacy against COVID-19. No dosage adjustment is required in elderly individuals ≥ 65 years of age.

The data for use in the frail elderly (>85 years) is limited. The potential benefits of vaccination versus the potential risk and clinical impact of even relatively mild systemic adverse events in the frail elderly should be carefully assessed on a case-by-case basis.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

No interaction studies have been performed.

Concomitant administration of COMIRNATY with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Fertility

In a combined fertility and developmental toxicity study, female rats were intramuscularly administered COMIRNATY prior to mating and during gestation (4 full human doses of 30 µg each, spanning between pre-mating day 21 and gestation day 20). SARS-CoV-2 neutralising antibodies were present in maternal animals from prior to mating to the end of the study on postnatal day 21 as well as in fetuses and offspring. There were no vaccine related effects on female fertility and pregnancy rate.

Pregnancy

There is limited experience with use of COMIRNATY in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition or post-natal development (see Fertility). Administration of COMIRNATY in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Lactation

It is unknown whether BNT162b2 [mRNA] is excreted in human milk. A combined fertility and developmental toxicity study in rats did not show harmful effects on offspring development before weaning (see Fertility).

4.7 Effects on ability to drive and use machines

COMIRNATY has no, or negligible, influence on the ability to drive and use machines. However, some of the effects mentioned under Section 4.8 Undesirable effects may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of safety profile

The safety of COMIRNATY was evaluated in participants 12 years of age and older in 2 clinical studies that included 22,875 participants (comprised of 21,744 participants 16 years of age and older and 1,131 adolescents 12 to 15 years of age) that have received at least one dose of COMIRNATY.

Participants 16 years of age and older

In Study C4591001, a total of 22,026 participants 16 years of age or older received at least 1 dose of COMIRNATY and a total of 22,021 participants 16 years of age or older received placebo (including 138 and 145 adolescents 16 and 17 years of age in the COMIRNATY and placebo groups, respectively). A total of 20,519 participants 16 years of age or older received 2 doses of COMIRNATY.

At the time of the analysis of Study C4591001 with a data cut-off of 13 March 2021 for the placebo-controlled blinded follow-up period up to the participants' unblinding dates, a total of 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older were followed up for ≥4 months after the second dose. This included a total of 15,111 (7,704 COMIRNATY and 7,407 placebo) participants 16 to 55 years of age and a total of 10,540 (5,327 COMIRNATY and 5,213 placebo) participants 56 years and older.

The most frequent adverse reactions in participants 16 years of age and older were injection site pain (>80%), fatigue (>60%), headache (>50%), myalgia (>40%), chills (>30%), arthralgia (>20%), pyrexia and injection site swelling (>10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

The safety profile in 545 subjects receiving COMIRNATY, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Study C4591001 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. The safety profile of the participants receiving COMIRNATY (n=100) in the individuals with stable HIV infection was similar to that seen in the general population.

Adolescents 12 through 15 years of age

In an analysis of Study C4591001, 2,260 adolescents (1,131 COMIRNATY; 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 adolescents (660 COMIRNATY and 648 placebo) have been followed for at least 2 months after the second dose of COMIRNATY. The safety evaluation in Study C4591001 is ongoing.

The most frequent adverse reactions in adolescents 12 through 15 years of age were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).

Tabulated list of adverse reactions from clinical studies and post-authorisation experience

Adverse reactions observed during clinical studies are listed below according to the following frequency categories:

Very common (≥ 1/10),

Common (≥ 1/100 to < 1/10),

Uncommon (≥ 1/1,000 to < 1/100),

Rare (≥ 1/10,000 to < 1/1,000),

Very rare (< 1/10,000),

Not known (cannot be estimated from the available data).

Table 1: Adverse reactions from COMIRNATY clinical trials

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy		
Metabolism and nutrition disorders			Decreased appetite		
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache		Lethargy	Acute peripheral facial paralysis[a]	
Gastrointestinal disorders		Nausea;			
Skin and subcutaneous tissue disorders			Hyperhidrosis; Night sweats		
Musculoskeletal and connective tissue disorders	Arthralgia; Myalgia				

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
General disorders and administration site conditions	Injection site pain; Fatigue; Chills; Pyrexia[b]; Injection site swelling	Injection site redness	Asthenia; Malaise;		

[a] Through the clinical trial safety follow-up period to 14 November 2020, acute peripheral facial paralysis (or palsy) was reported by four participants in the COMIRNATY group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group.

[b] A higher frequency of pyrexia was observed after the second dose.

Post-marketing experience

Although the events listed in Table 2 were not observed in the clinical trials, they are considered adverse drug reactions for COMIRNATY as they were reported in the post-marketing experience. As these reactions were derived from spontaneous reports, the frequencies could not be determined and are thus considered as not known.

Table 2:Adverse reactions from COMIRNATY post marketing experience

System Organ Class	Adverse Drug Reaction
Immune system disorders	Anaphylaxis Hypersensitivity reactions (e.g. rash, pruritis, urticaria, angioedema)
Cardiac disorders	Myocarditis Pericarditis
Gastrointestinal disorders	Diarrhoea Vomiting
Musculoskeletal and connective tissue disorders	Pain in extremity (arm)

Reporting suspected adverse effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions at https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Overdose data is available from 52 study participants included in the clinical trial that due to an error in dilution received 58 micrograms of COMIRNATY. The COMIRNATY recipients did not report an increase in reactogenicity or adverse reactions.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, other viral vaccines, ATC code: J07BX03.

Mechanism of action

The nucleoside-modified messenger RNA in COMIRNATY is formulated in lipid nanoparticles, which enable delivery of the non-replicating RNA into host cells to direct transient expression of the SARS-CoV-2 spike (S) antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. COMIRNATY elicits both neutralising antibody and cellular immune responses to the antigen, which may contribute to protection against COVID-19.

Clinical efficacy and safety

Efficacy

Study C4591001 is a multicentre, multinational, Phase 1/2/3 randomised, placebo-controlled, observer-blind dose-finding, vaccine candidate selection and efficacy study in participants 12 years of age and older. Randomisation was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥ 56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalisation for worsening disease during the 6 weeks before enrolment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV).

Efficacy in participants 16 years of age and older

In the Phase 2/3 portion of Study C4591001, based on data accrued through 14 November 2020, approximately 44,000 participants were randomised equally and were to receive 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a minimum interval of 14 days before and after administration of an influenza vaccine in order to receive either placebo or COMIRNATY. In the clinical study, participants were required to observe a minimum interval of 60 days before or after receipt of blood/plasma products or immunoglobulins through to conclusion of the study in order to receive either placebo or COMIRNATY.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second

dose. In addition, 134 participants were between the ages of 16 to 17 years of age (66 in the COMIRNATY group and 68 in the placebo group) and 1616 participants 75 years of age and older (804 in the COMIRNATY group and 812 in the placebo group).

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID19 for in total 2,214 person-years for the COMIRNATY group and in total 2,222 person-years for the placebo group.

There were no meaningful clinical differences in overall vaccine efficacy in participants who were at risk of severe COVID-19 including those with 1 or more comorbidities that increase the risk of severe COVID-19 (e.g. asthma, body mass index (BMI) ≥ 30 kg/m^2, chronic pulmonary disease, diabetes mellitus, hypertension).

COMIRNATY efficacy information is presented in Table 3.

Table 3: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of infection prior to 7 days after Dose 2 – evaluable efficacy (7 days) population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY** **N[a] = 18,198 Cases** n1[b] Surveillance time[c] (n2[d])	**Placebo** **N[a] = 18,325 Cases** n1[b] Surveillance time[c] (n2[d])	**Vaccine efficacy** % (95% CI)[f]
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.0, 97.9)
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 [*Case definition: (at least 1 of) fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhoea or vomiting.]

* Participants who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by nucleic acid amplification tests (NAAT) [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in adolescents 12 to 15 years of age.
f. Two-sided confidence interval (CI) for vaccine efficacy (VE) is derived based on the Clopper and Pearson method adjusted to the surveillance time. CI not adjusted for multiplicity.

In the second primary analysis, efficacy of COMIRNATY in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 94.6% (95% credible interval of 89.9% to 97.3%) in participants 16 years of age and older with or without evidence of prior infection with SARS-CoV-2.

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through 13 March 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 4.

Table 4: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of infection and participants with or without evidence of infection prior to 7 days after Dose 2 – evaluable efficacy (7 days) population during the placebo-controlled follow-up period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhoea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

Efficacy against severe COVID-19

Secondary efficacy analyses suggested benefit of the COVID-19 mRNA Vaccine in preventing severe COVID-19.

As of 14 November 2020, efficacy against severe COVID-19 (as defined by the study protocol) occurring after the first dose was 88.9% (95% CI: 20.1, 99.7) (1 case in COVID-19 mRNA Vaccine group and 9 cases in placebo group), with an estimated vaccine efficacy of 75.0% (95% CI: -152.6, 99.5) (1 case in COVID-19 mRNA Vaccine group and 4 cases in placebo group) against severe COVID-19 occurring at least 7 days after Dose 2.

Efficacy against severe COVID-19, defined by the Centers for Disease Control and Prevention as hospitalisation, admission to the Intensive Care Unit, intubation or mechanical ventilation, or death occurring after the first dose, was 92.9% (95% CI: 53.2, 99.8) (1 case in COVID-19 mRNA Vaccine group and 14 cases in placebo group).

Efficacy and immunogenicity in adolescents 12 to 15 years of age

An analysis of Study C4591001 has been performed in adolescents 12 to 15 years of age up to a data cutoff date of 13 March 2021.

The vaccine efficacy information in adolescents 12 to 15 years of age is presented in Table 5.

Table 5: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2 – participants without evidence of infection and with or without evidence of infection prior to 7 days after Dose 2 – adolescents 12 to 15 years of age evaluable efficacy (7 days) population

First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 to 15 years of age without evidence of prior SARS-CoV-2 infection*			
	COMIRNATY **N[a] = 1005** **Cases** **n1[b]** **Surveillance time[c] (n2[d])**	**Placebo** **N[a] = 978** **Cases** **n1[b]** **Surveillance time[c] (n2[d])**	**Vaccine efficacy % (95% CI[e])**
Adolescents 12 to 15 years	0 0.154 (1001)	16 0.147 (972)	100.0 (75.3, 100.0)
First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 to 15 years of age with or without* evidence of prior SARS-CoV-2 infection			
	COMIRNATY **N[a] = 1119** **Cases** **n1[b]** **Surveillance time[c] (n2[d])**	**Placebo** **N[a] = 1110** **Cases** **n1[b]** **Surveillance time[c] (n2[d])**	**Vaccine efficacy % (95% CI[e])**
Adolescents 12 to 15 years	0 0.170 (1109)	18 0.163 (1094)	100.0 (78.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 [*Case definition: (at least 1 of) fever, new or increased cough, new

or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhoea or vomiting).

* Participants who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (i.e, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by nucleic acid amplification tests (NAAT) [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. CI not adjusted for multiplicity.

In Study C4591001 an analysis of SARS-CoV-2 neutralising titres in a randomly selected subset of participants was performed to demonstrate non-inferior immune responses (within 1.5-fold) comparing adolescents 12 to 15 years of age to participants 16 to 25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection. The immune response to COMIRNATY in adolescents 12 to 15 years of age (n = 190) was non-inferior to the immune response in participants 16 to 25 years of age (n = 170), based on results for SARS-CoV-2 neutralising titres at 1 month after Dose 2. The geometric mean titres (GMT) ratio of the adolescents 12 to 15 years of age group to the participants 16 to 25 years of age group was 1.76, with a 2-sided 95% CI of 1.47 to 2.10, meeting the 1.5-fold non-inferiority criterion (the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] > 0.67), which indicates a statistically greater response in the adolescents 12 to 15 years of age than that of participants 16 to 25 years of age.

This medicine has been given a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use. Refer to the consent notice published in the New Zealand Gazette for the specific conditions.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Genotoxicity/Carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of COMIRNATY (lipids and mRNA) are not expected to have genotoxic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)

2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)

Distearoylphosphatidylcholine (DSPC)

Cholesterol

Potassium chloride

Monobasic potassium phosphate

Sodium chloride

Dibasic sodium phosphate dihydrate

Sucrose

Water for injections

This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially 'potassium-free'.

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in Section 6.6 Special precautions for disposal and other handling.

6.3 Shelf life

Unopened vial

6 months at -90°C to -60°C.

Unopened vials may be stored and transported at -25 C to -15°C for a total of 2 weeks on one occasion only and can then be returned to -90ºC to -60 C.

Once removed from the freezer, the unopened vial can be stored for up to 1 month at 2°C to 8°C. Within the 1 month shelf-life at 2°C to 8°C, up to 12 hours may be used for transportation.

Prior to use, the unopened vial can be stored for up to 2 hours at temperatures up to 30 C.

Once thawed, COMIRNATY should not be re-frozen.

Diluted medicinal product

Chemical and physical in-use stability, including during transportation, has been demonstrated for 6 hours at 2ºC to 30 C after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a freezer at -90°C to -60°C.

Store in the original package in order to protect from light.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thawed vials can be handled in room light conditions.

When you are ready to thaw or use COMIRNATY:

Transfers of frozen vials stored at ultra-low temperature (<-60°C)

- Closed-lid vial trays containing 195 vials removed from ultra-low temperature frozen storage (<-60°C) may be at temperatures up to 25°C for up to 5 minutes for transfer between ultra-low-temperature environments.
- Open-lid vial trays, or vial trays containing less than 195 vials removed from ultra-low temperature frozen storage (<-60°C) may be at temperatures up to <25°C for up to 3 minutes to remove vials or for transfer between ultra-low-temperature environments.
- After vial trays are returned to ultra-low temperature frozen storage following temperature exposure up to 25°C, they must remain in ultra-low temperature frozen storage for at least 2 hours before they can be removed again.

Transfers of frozen vials stored at -25°C to -15°C

- Closed-lid vial trays containing 195 vials removed from frozen storage (-25°C to -15°C) may be at temperatures up to 25 C for up to 3 minutes.
- Open-lid vial trays, or vial trays containing less than 195 vials, removed from frozen storage (-25°C to -15°C) may be at temperatures up to 25°C for up to 1 minute.

Once a vial is removed from the vial tray, it should be thawed for use.

Transportation

If local redistribution of unopened vials is needed, and full trays containing vials cannot be transported at -90°C to -60°C, available data support physical and chemical stability during transportation of 1 or more thawed vials at 2°C to 8°C for up to 12 hours. Any hours used for transport of unopened vials at 2°C to 8°C count against the 1 month limit for storage at 2°C to 8°C.

If local redistribution of diluted medicinal product in vials or syringes is needed, available data support physical and chemical stability during transportation at 2°C to 30°C for up to 6 hours. Any hours used for transport of diluted medicinal product in vials or syringes at 2°C to 30°C count against the 6-hour limit for storage at 2°C and 30°C. Microbiological risks and package integrity, particularly for prepared dosing syringes, are the responsibility of the preparer during transportation of diluted medicinal product.

For storage conditions after thawing and dilution of the medicinal product, see Section 6.3 Shelf life.

For additional advice on storing COMIRNATY, contact Pfizer New Zealand on 0800 736 363.

6.5 Nature and contents of container

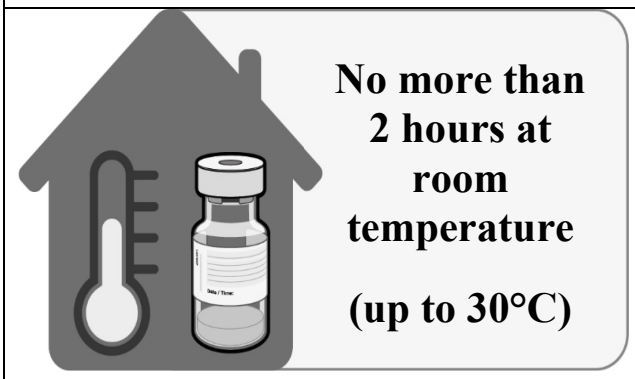
2 mL clear vial (Type I glass) with a stopper (synthetic bromobutyl rubber) and a flip-off plastic cap with aluminium seal. Each vial contains 6 doses, see Section 6.6 Special precautions for disposal and other handling.

Pack size: 195 vials

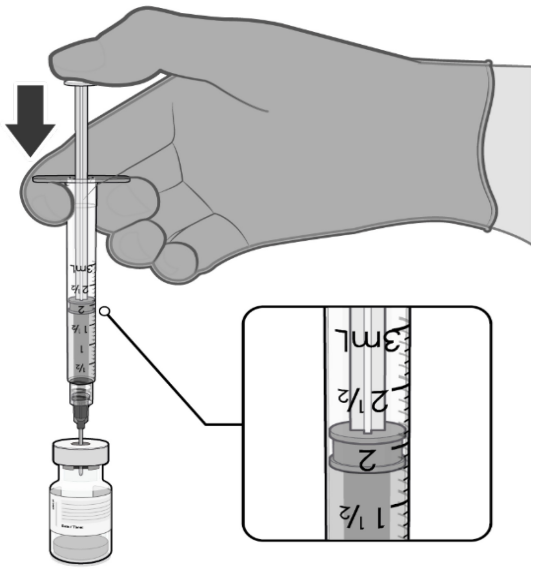
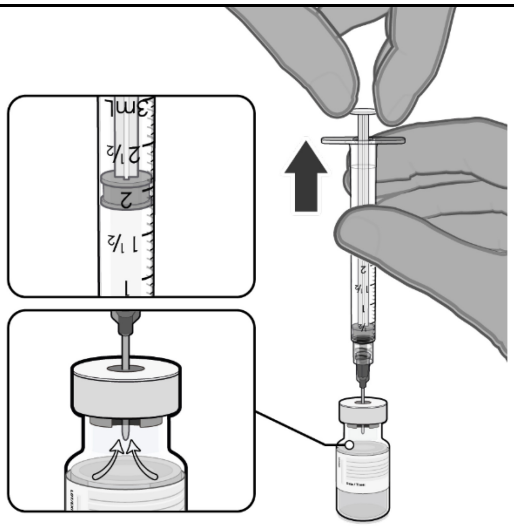
6.6 Special precautions for disposal and other handling

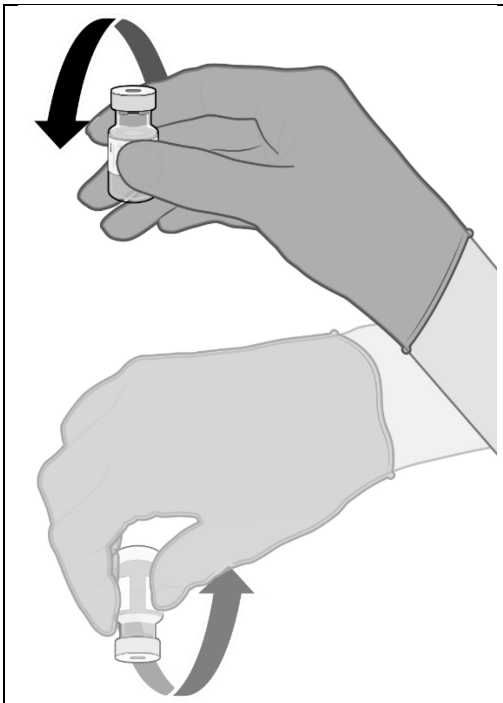
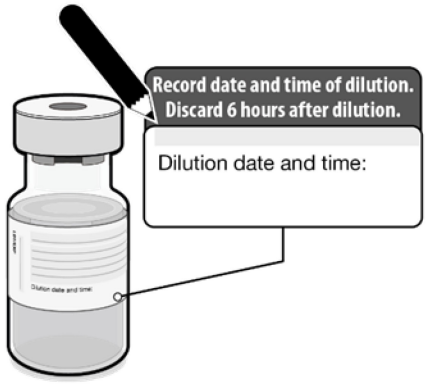
COMIRNATY should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared suspension.

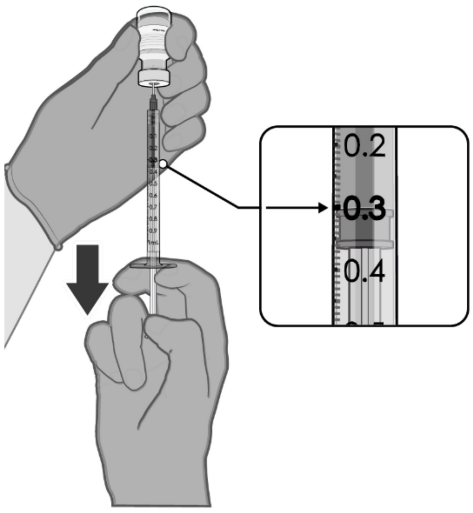
THAWING PRIOR TO DILUTION



- The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use.
- The unopened vial can be stored for up to 1 month at 2°C to 8°C. Within the 1-month shelf-life at 2°C to 8°C, up to 12 hours may be used for transportation.
- Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. **Do not shake.**
- Prior to dilution, the thawed suspension may contain white to off-white opaque amorphous particles.

DILUTION	
 **1.8 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques. Do not use any other diluent.
 **Pull back plunger to 1.8 mL to remove air from vial.**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

	• **Gently invert the diluted suspension 10 times. Do not shake.** • The diluted vaccine should present as an off-white suspension with no particulates visible. Discard the diluted vaccine if particulates or discolouration are present.
	• The diluted vials should be marked with the date and time of dilution. • Do not freeze or shake the diluted suspension. If refrigerated, allow the diluted suspension to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• After dilution, the vial contains 2.25 mL from which 6 doses of 0.3 mL can be extracted. • Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab. • Withdraw 0.3 mL of COMIRNATY. Low dead volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Verify a final injection volume of 0.3 mL prior to administration. • Discard syringe and needle after administration to a single patient. • Use a new, sterile needle and syringe to draw up each new dose. • Discard any unused vaccine 6 hours after dilution.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Pfizer New Zealand Limited
P O Box 3998
Auckland, New Zealand

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute this medicine:

03 February 2021

10. DATE OF REVISION OF THE TEXT

28 July 2021

Summary of Updates

Section	Update
4.4	Update for immunisation stress-related responses Update relating to reports of myocarditis and pericarditis
4.8	Update relating to reports of myocarditis and pericarditis Updated vaccine safety analyses data in participants followed up to 6 months after Dose 2
5.1	Updated vaccine efficacy analyses data in participants followed up to 6 months after Dose 2