PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

COMIRNATY®

COVID-19 Vaccine, mRNA

Suspension for Intramuscular Injection

Multiple Dose Vial

For 12 Years of Age and Older (after dilution each vial contains 6† doses of 0.3 mL)

For Age 5 Years to <12 Years (after dilution each vial contains 10* doses of 0.2 mL)

Active Immunizing Agent

BioNTech Manufacturing GmbH
An der Goldgrube 12
Mainz, Rhineland-Palatinate, Germany
55131

Imported and distributed by:
Pfizer Canada ULC
17,300 Trans-Canada Highway
Kirkland, Quebec, Canada H9J 2M5

Date of Initial Authorization:
September 16, 2021

Date of Revision:
November 19, 2021

Submission Control Number: 257698

† Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a 6th dose from a single vial.

* Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.

RECENT MAJOR LABEL CHANGES

1. INDICATIONS	11/2021
4. DOSAGE AND ADMINISTRATION	11/2021
7. WARNINGS AND PRECAUTIONS	11/2021

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

COMIRNATY (COVID-19 Vaccine, mRNA) is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) in individuals 5 years of age and older.

1.1 Pediatrics

The safety and efficacy of COMIRNATY in children under 5 years of age have not yet been established (see **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

1.2 Geriatrics

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 **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

The safety and immunogenicity of a booster dose of COMIRNATY in individuals 65 years of age and older is based on safety and immunogenicity data in adults 18 through 55 years of age (see **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

2 CONTRAINDICATIONS

COMIRNATY is contraindicated in individuals who are hypersensitive to the active substance or to any ingredient in the formulation. For a complete listing see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.**

3 SERIOUS WARNINGS AND PRECAUTIONS

At the time of authorization, there are no known serious warnings or precautions associated with this product.

4 DOSAGE AND ADMINISTRATION

The storage, preparation and administration information differ depending on which presentation of the vaccine is considered. Careful attention should be paid to the vial cap colour and the appropriate corresponding instructions must be followed.

Dosage Form	Vial Cap Colour	Age Range	Dilution Information	Doses Per Vial	Dose Volume
COMIRNATY* Multiple Dose Vial (for 12 years of age and older)	Purple	12 years and older	Dilute with 1.8 mL 0.9% Sodium Chloride Injection, USP prior to use	6	0.3 mL
COMIRNATY* Multiple Dose Vial (for age 5 years to <12 years)	Orange	5 to <12 years	Dilute with 1.3 mL 0.9% Sodium Chloride Injection, USP prior to use	10	0.2 mL

*May be labeled as Pfizer-BioNTech COVID-19 vaccine

4.1 Dosing Considerations

12 Years of Age and Older:
COMIRNATY is a suspension for intramuscular injection which must be diluted prior to administration. After preparation, a single dose is 0.3 mL.

Age 5 Years to <12 Years:
COMIRNATY is a suspension for intramuscular injection which must be diluted prior to administration. After preparation, a single dose is 0.2 mL.

4.2 Recommended Dose and Dosage Adjustment

Vaccination Schedule for Individuals 12 Years of Age and Older
COMIRNATY is administered intramuscularly after dilution as a primary series of two doses (0.3 mL each) 3 weeks apart in individuals 12 years of age and older.

A booster dose of COMIRNATY may be administered intramuscularly at least 6 months after completion of the primary series in individuals 18 years of age or older.

There are currently no data available from Pfizer and BioNTech clinical trials on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the primary vaccination series or for a booster dose.

COMIRNATY and the Interim Order authorized Pfizer-BioNTech COVID-19 Vaccine, for use in individuals 12 years of age and older, have the same formulation and can be used interchangeably to provide the COVID-19 vaccination series.

Vials of COMIRNATY intended for individuals 12 years of age and older (purple cap) cannot be used to prepare doses for individuals aged 5 years to <12 years.

Vaccination Schedule for Individuals Aged 5 Years to <12 Years
COMIRNATY is administered intramuscularly after dilution as a series of two doses (0.2 mL each) 3 weeks apart.

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

Vials of COMIRNATY intended for individuals aged 5 years to <12 years (orange cap) cannot be used to prepare doses for individuals 12 years of age and older.

Vials of COMIRNATY intended for individuals 12 years of age and older (purple cap) cannot be used to prepare doses for individuals aged 5 years to <12 years.

4.3 Reconstitution

For 12 Years of Age and Older (Purple Cap)

Preparation for Administration

Prior to Dilution:

- The COMIRNATY multiple dose vial has a purple cap and contains a volume of 0.45 mL. It is supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator (2°C to 8°C [35°F to 46°F]) or at room temperature (up to 25°C [77°F]) (see **11 STORAGE, STABILITY AND DISPOSAL**).
- Prior to dilution, the thawed suspension may contain white to off-white opaque amorphous particles.
- Refer to thawing instructions in the panels below.

Dilution:

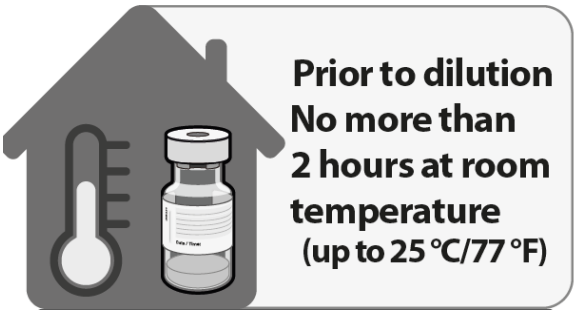
- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- After dilution, one vial contains 6[†] doses of 0.3 mL.
- After dilution, the vaccine will be an off-white suspension. Inspect vials to confirm there are no particulates and no discolouration is observed.
- Strict adherence to aseptic techniques must be followed.
- Refer to dilution and dose preparation instructions in the panels below.

[†] Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a 6th dose from a single vial.

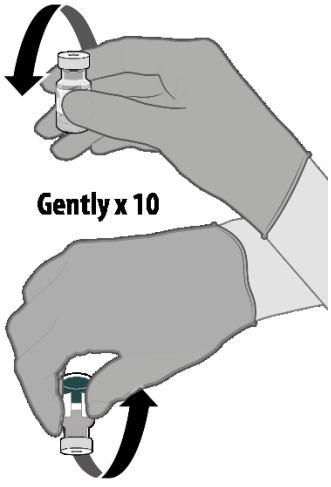
VIAL AND DOSE VERIFICATION
(Individuals 12 Years of Age and Older)

- Verify that the vial has a purple plastic cap. If the vial has an orange plastic cap and orange label border, do not use to prepare doses for individuals 12 years of age and older. product.

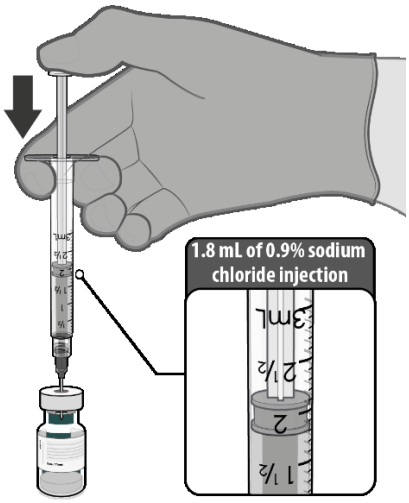
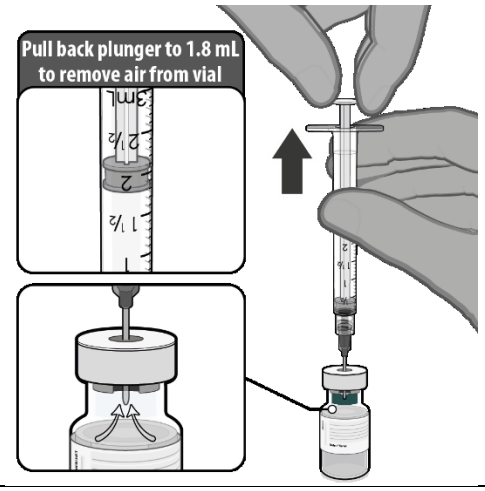
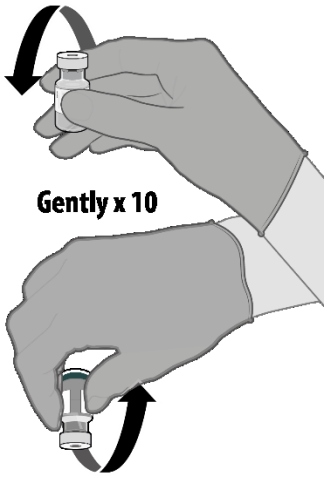
THAWING PRIOR TO DILUTION
(Individuals 12 Years of Age and Older)

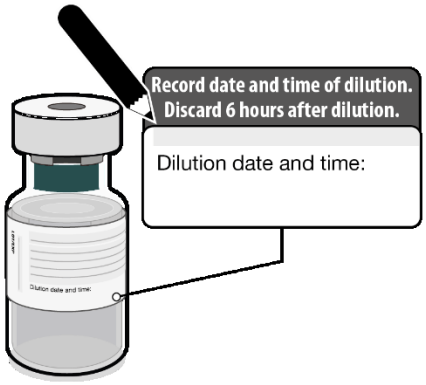


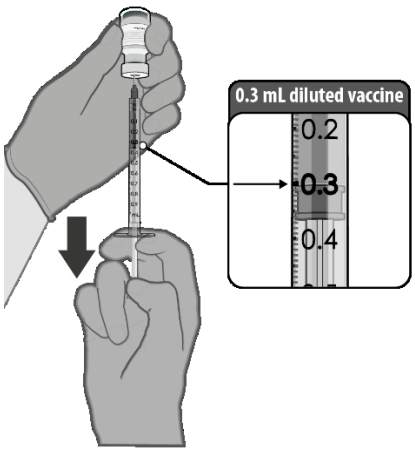
- Thaw vial(s) of COMIRNATY before use either by:
  - Allowing vial(s) to thaw in the refrigerator (2°C to 8°C [35°F to 46°F]). A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month.
  - Allowing vial(s) to sit at room temperature (up to 25°C [77°F]) for 30 minutes.
- Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours of exposure to room temperature.



- Before dilution, invert vaccine vial **gently** 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discoloured or if other particles are observed.

DILUTION **(Individuals 12 Years of Age and Older)**	
	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of 0.9% Sodium Chloride Injection, USP into a transfer syringe (using 21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• **Gently** invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discoloured or contains particulate matter.

	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY (Individuals 12 Years of Age and Older)	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY, preferentially using low dead-volume syringes and/or needles. • 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. • Administer immediately, and no later than 6 hours after dilution. • Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. In order to ensure consistent withdrawal of 6 doses of 0.3 mL, it is important to adhere to minimizing volume loss during dose extraction.

For Age 5 Years to <12 Years (Orange Cap and Orange Label Border)

Preparation for Administration

Prior to Dilution:

- The COMIRNATY multiple dose vial (for ages 5 years to <12 years) has an orange cap and an orange label border and contains a volume of 1.3 mL. It is supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials of COMIRNATY intended for 12 years or age or older with a purple cap cannot be used to prepare doses for individuals aged 5 years to <12 years.
- Vials may be thawed in the refrigerator at 2°C to 8°C [35°F to 46°F] or at room temperature (up to 25°C [77°F]) (see **11 STORAGE, STABILITY AND DISPOSAL**).

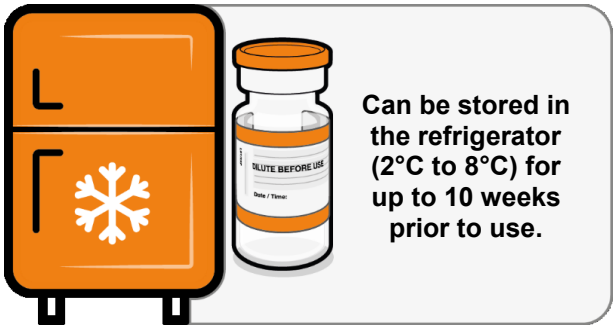
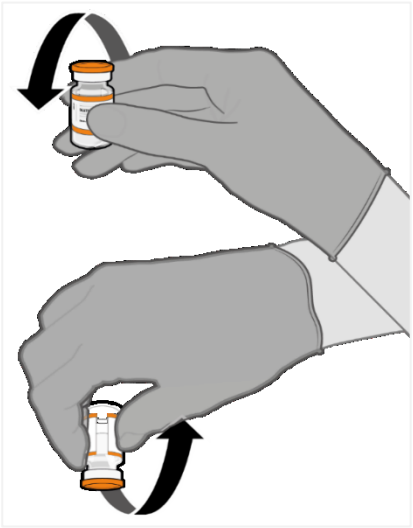
- Prior to dilution, the thawed suspension may contain opaque amorphous particles.
- Refer to thawing instructions in the panels below.

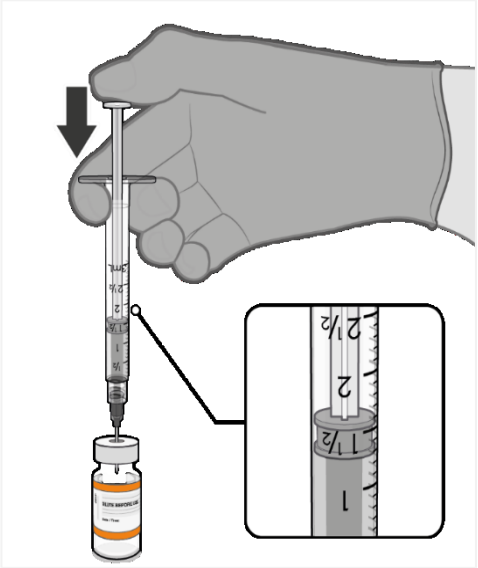
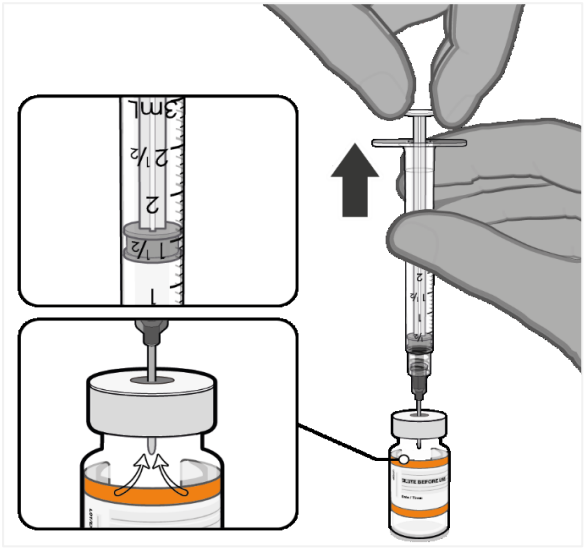
Dilution:

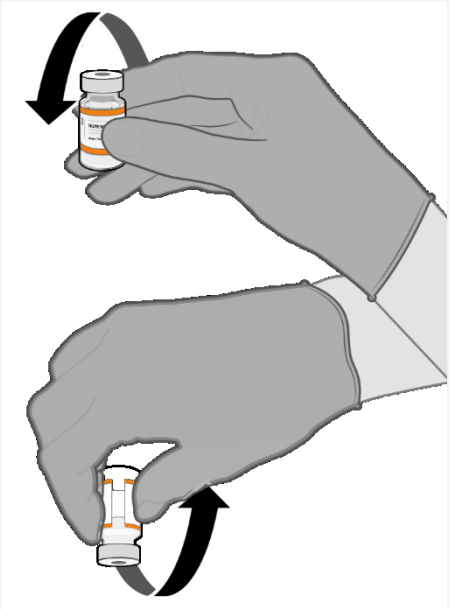
- Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.3 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- After dilution, one vial contains 10* doses of 0.2 mL.
- After dilution, the vaccine will be a white to off-white suspension. Inspect vials to confirm there are no particulates and no discolouration is observed.
- Strict adherence to aseptic techniques must be followed.
- Refer to dilution and dose preparation instructions in the panels below.

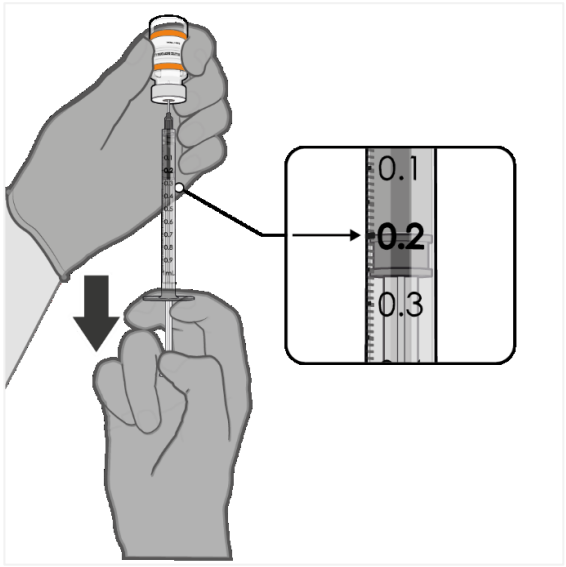
VIAL AND DOSE VERIFICATION (**Individuals aged 5 years to <12 years)**	
 ✓ **Orange plastic cap and orange label border.**	• Verify that the vial has an orange plastic cap and an orange label border. Do not use COMIRNATY vials with purple caps to prepare doses for individuals aged 5 years to <12 years. • The date printed on the vial and carton reflects the date of manufacture. The vaccine should not be used after 6 months from the date of manufacture printed on the vial and carton.

* Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.

<table>
<tr><td colspan="2">THAWING PRIOR TO DILUTION
(Individuals aged 5 years to <12 years)</td></tr>
<tr><td> 
</td><td>• Thaw vial(s) of COMIRNATY before use either by:
○ Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of 10 vials may take up to 4 hours to thaw, and thawed vials can be stored in the refrigerator for up to 10 weeks.
○ Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
○ Vials may be stored at room temperature [up to 25°C (77°F)] for up to 12 hours prior to dilution.</td></tr>
<tr><td> 
Gently × 10</td><td>• Before dilution, mix by inverting vaccine vial gently 10 times.
• Do not shake.
• Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
• Do not use if liquid is discoloured or if other particles are observed.</td></tr>
</table>

<table>
<tr><td colspan="2">DILUTION
(Individuals aged 5 years to <12 years)</td></tr>
<tr><td> 
1.3 mL of 0.9% sodium chloride injection</td><td>• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
• Using aseptic technique, withdraw 1.3 mL of diluent into a transfer syringe (using 21-gauge or narrower needle).
• Cleanse the vaccine vial stopper with a single-use antiseptic swab.
• Add 1.3 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.</td></tr>
<tr><td> 
Pull back plunger to 1.3 mL to remove air from vial.</td><td>• Equalize vial pressure before removing the needle from the vial by withdrawing 1.3 mL air into the empty diluent syringe.</td></tr>
</table>

 **Gently × 10**	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be a white to off-white suspension. Do not use if vaccine is discoloured or contains particulate matter.
 **Use within 12 hours after dilution.**	• Record the date and time of first vial puncture on the COMIRNATY (for age 5 years to <12 years) vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 12 hours after dilution.

PREPARATION OF INDIVIDUAL 0.2 mL DOSES (Individuals aged 5 years to <12 years)	
 **0.2 mL diluted vaccine**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.2 mL of COMIRNATY (for age 5 years to <12 years) preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.2 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.2 mL, discard the vial and any excess volume. • Administer immediately, and no later than 12[1] hours after dilution. • Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial. In order to ensure consistent withdrawal of 10 doses of 0.2 mL, it is important to adhere to minimizing volume loss during dose extraction.

4.4 Administration

For 12 Years of Age and Older (Vials with Purple Cap)

Visually inspect each dose in the dosing syringe prior to administration. The diluted vaccine will be an off-white suspension. During the visual inspection:

- Verify the final dosing volume of 0.3 mL.
- Confirm there are no particulates and that no discolouration is observed.
- Do not administer if vaccine is discoloured or contains particulate matter.

Administer COMIRNATY intramuscularly, preferably in the deltoid muscle.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. **Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial.** In order to ensure consistent withdrawal of 6 doses of 0.3 mL, it is important to adhere to minimizing volume loss during dose

[1] Vial labels and cartons may state that a vial should be discarded 6 hours after dilution. The information in this Product Monograph supersedes the number of hours printed on vial labels and cartons.

extraction. **If standard syringes and needles are used, there may not be sufficient volume to extract a 6th 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.

For Age 5 Years to <12 Years (Vials with Orange Cap and Orange Label Border)

Visually inspect each dose in the dosing syringe prior to administration. The diluted vaccine will be a white to off-white suspension. During the visual inspection:

- Verify the final dosing volume of 0.2 mL.
- Confirm there are no particulates and that no discolouration is observed.
- Do not administer if vaccine is discoloured or contains particulate matter.

Administer COMIRNATY intramuscularly, preferably in the deltoid muscle.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

After dilution, vials of COMIRNATY (for age 5 years to <12 years) contain 10 doses of 0.2 mL of vaccine. **Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial.** In order to ensure consistent withdrawal of 10 doses of 0.2 mL, it is important to adhere to minimizing volume loss during dose extraction. **If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.** Irrespective of the type of syringe and needle:

- Each dose must contain 0.2 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.2 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

5 OVERDOSAGE

In the event of suspected overdose, monitoring of vital functions and symptomatic treatment is recommended. Contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date (or manufacture date).

For 12 Years of Age and Older (Vials with Purple Cap)

COMIRNATY is supplied as a frozen suspension in multiple dose vials. Each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine, and contains 6[†] doses of 0.3 mL after dilution. Each 0.3 mL dose of COMIRNATY contains 30 mcg of a nucleoside modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 and the non-medicinal ingredients listed in Table 1 below.

Table 1 – Dosage Forms, Strengths, Composition and Packaging (For 12 Years of Age and Older)

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension (to be diluted before use) Multiple dose vial (after dilution, each vial contains 6[†] doses of 0.3 mL)	• ALC-0315 = ((4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) • ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide • 1,2-distearoyl-sn-glycero-3-phosphocholine • cholesterol • dibasic sodium phosphate dihydrate • monobasic potassium phosphate • potassium chloride • sodium chloride • sucrose • water for injection

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

COMIRNATY multiple dose vials are supplied in a carton containing 25 multiple dose vials or 195 multiple dose vials. Not all pack sizes may be available.

[†] Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a 6th dose from a single vial.

For Age 5 Years to < 12 Years (Vials with Orange Cap and Orange Label Border)
COMIRNATY is supplied as a frozen suspension in multiple dose vials with orange caps and an orange label border. Each vial must be diluted with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine, and contains 10* doses of 0.2 mL after dilution. Each 0.2 mL dose of COMIRNATY contains 10 mcg of a nucleoside modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 and the non-medicinal ingredients listed in Table 2 below.

Table 2 – Dosage Forms, Strengths, Composition and Packaging (For Age 5 Years to <12 Years)

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension (to be diluted before use) Multiple dose vial (after dilution, each vial contains 10* doses of 0.2 mL)	• ALC-0315 = ((4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) • ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide • 1,2-distearoyl-sn-glycero-3-phosphocholine • cholesterol • sodium chloride • sucrose • tromethamine • tromethamine hydrochloride • water for injection

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

COMIRNATY multiple dose vials are supplied in a carton containing 10 multiple dose vials or 195 multiple dose vials. Not all pack sizes may be available.

7 WARNINGS AND PRECAUTIONS

General

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

Fainting may occur in association with administration of injectable vaccines. Individuals should be advised to bring symptoms (e.g., dizziness, increases in heart rate, feeling short of breath, tingling sensations or sweating) to the attention of the vaccination provider for evaluation. Procedures should be in place to avoid injury from fainting.

As with any vaccine, vaccination with COMIRNATY may not protect all recipients.

Individuals may not be optimally protected until at least 7 days after their second dose of vaccine (see **14 CLINICAL TRIALS**).

* Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.

Acute Allergic Reactions

Anaphylaxis has been reported. As with all vaccines, training for immunizers, appropriate medical treatment and supervision after immunization should always be readily available in case of a rare anaphylactic event following the administration of this vaccine.

Vaccine recipients should be kept under observation for at least 15 minutes after immunization; 30 minutes is a preferred interval when there is a specific concern about a possible vaccine reaction.

A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of COMIRNATY.

Cardiovascular

Myocarditis and Pericarditis

Very rare cases of myocarditis and/or pericarditis following vaccination with COMIRNATY have been reported during post-authorization use. These cases occurred more commonly after the second dose and in adolescents and young adults. Typically, the onset of symptoms has been within a few days following receipt of COMIRNATY. Available short-term follow-up data suggest that the symptoms resolve in most individuals, but information on long-term sequelae is lacking. The decision to administer COMIRNATY to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances.

Healthcare professionals are advised to consider the possibility of myocarditis and/or pericarditis in their differential diagnosis if individuals present with chest pain, shortness of breath, palpitations or other signs and symptoms of myocarditis and/or pericarditis following immunization with a COVID-19 vaccine. This could allow for early diagnosis and treatment. Cardiology consultation for management and follow up should be considered.

Driving and Operating Machinery

COMIRNATY has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under **8 ADVERSE REACTIONS** may temporarily affect the ability to drive or use machines.

Fertility

It is unknown whether COMIRNATY has an impact on fertility. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility or reproductive toxicity (see **16 NON-CLINICAL TOXICOLOGY**).

Hematologic

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

Immune

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine. In these individuals, a third dose may be considered as part of the primary series.

7.1 Special Populations

7.1.1 Pregnant Women

The safety and efficacy of COMIRNATY in pregnant women have not yet been established.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/ fetal development, parturition, or post-natal development (see **16 NON-CLINICAL TOXICOLOGY**).

7.1.2 Breast-feeding

It is unknown whether COMIRNATY is excreted in human milk. A risk to the newborns/infants cannot be excluded.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of COMIRNATY in children under 5 years of age have not yet been established.

7.1.4 Geriatrics

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 **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

The safety and immunogenicity of a booster dose of COMIRNATY in individuals 65 years of age and older is based on safety and immunogenicity data in adults 18 through 55 years of age (See **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety of 2 doses of COMIRNATY was evaluated in participants 5 years of age and older in three clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America.

Study BNT162-01 (Study 1) was a Phase 1/2, two-part dose-escalation trial that enrolled 60 participants 18 through 55 years of age and 36 participants 56 through 85 years of age.

Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2260 adolescents are 12 to 15 years of age (1131 and 1129 in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

Additionally, 306 existing Phase 3 participants 18 through 55 years of age received a booster dose of COMIRNATY approximately 6 months (range of 4.8 to 8.0 months) after completing the second dose. The overall safety profile for the booster dose was similar to that seen after 2 doses.

Study C4591007 (Study 3) is a Phase 1/2/3 study comprised of an open-label vaccine dose-finding portion (Phase 1) and a multicenter, multinational, randomized, saline placebo-controlled, observer-blind efficacy portion (Phase 2/3) that has enrolled approximately 4,600 participants 5 through less than 12 years of age. Of these, approximately 3,100 participants received COMIRNATY 10 mcg and approximately 1,500 participants received placebo in the Phase 2/3 part of the study.

The safety evaluation of participants in Study 2 and Study 3 is ongoing. In Study 2 and Study 3, all participants 5 through <12 years of age, 12 to 15 years of age and 16 years of age and older in the reactogenicity subset, and participants who received a booster dose in Study 2, were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination with an electronic diary during the 7 days following any dose of vaccination. Participants continue to be monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 to 1 month after Dose 2 (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination].

Participants 12 Years of Age and Older

At the time of the analysis of Study 2 (data accrued through March 13, 2021), a total of 25,651 (58.2%) participants (13,031 in vaccine group and 12,620 in placebo group) 16 years of age and older had been followed up for at least 4 months, with 3,082 (7.0%) participants (1,778 in vaccine group and 1,304 in placebo group) followed up for at least 6 months after the second dose during the blinded placebo-controlled follow-up period. A total of 12,006 (54.5%) participants originally randomized to the vaccine group in Study 2 had been followed up for at least 6 months after the second dose including the blinded and open-label periods.

In an analysis of Study 2, based on data up to the cut-off date of March 13, 2021, a total of 2260 adolescents (1131 COMIRNATY; 1129 placebo) were 12 to 15 years of age. Of these, 1308 (660 COMIRNATY and 648 placebo) adolescents have been followed for at least 2 months after the second dose of COMIRNATY.

In clinical studies with a data cut-off of March 13, 2021, and where 2 doses were administered 3 weeks apart, the most common adverse reactions in the reactogenicity subset (n=4924) of participants 16 years of age and older after any dose included injection site pain (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), and injection site redness (9.9%). Additional adverse events reported in the safety population (n=21,926) of participants 16 years of age and older from dose 1 to 1 month after dose 2 included nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination.

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

Adverse reactions after either the first or second dose in the reactogenicity subset (n=1131) of adolescents 12 to 15 years of age included injection site pain (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%).

In a clinical study of participants 18 through 55 years of age (N=306), 289 participants (94%) completed the e-diary recording adverse reactions. The most commonly reported adverse reactions (≥10%) following administration of a booster dose were pain at the injection site (83.0%), fatigue (63.7%), headache (48.4%), muscle pain (39.1%), chills (29.1%), and joint pain (25.3%).

Participants 5 Through Less Than 12 Years of Age

In an analysis of Study 3 Phase 2/3, based on data up to the cut-off date of October 8, 2021, 2,268 participants (initial enrolment group: 1,518 COMIRNATY 10 mcg and 750 placebo) were 5 through less than 12 years of age. Of these, 2,171 (95.7%) (1,456 COMIRNATY 10 mcg and 715 placebo) participants have been followed for at least 3 months after Dose 2. An analysis of Study 3 Phase 2/3 adverse event data also included another 2,379 participants (safety expansion group: 1,591 COMIRNATY 10 mcg and 788 placebo), of whom 71.2% had a follow-up period for at least 2 weeks after Dose 2. The safety evaluation in Study 3 is ongoing.

Adverse reactions following administration of any dose in the initial enrolment safety population (n = 1,518) of children 5 to less than 12 years of age included pain at the injection site (84.3%), fatigue (51.7%), headache (38.2%), injection site redness (26.4%), injection site swelling (20.4%), muscle pain (17.5%), chills (12.4%), fever (8.3%), joint pain (7.6%), lymphadenopathy (0.9%), rash (0.5%), nausea (0.4%), malaise (0.1%), and decreased appetite (0.1%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Participants 16 Years of Age and Older – Primary Series (Two Doses)

Solicited Adverse Reactions

Tables 3 through 6 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 years of age and older (n=9839) in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3: Study 2 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Participants 16-55 Years of Age (Reactogenicity Subset of the Safety Population*)

Local Reaction	Dose 1		Dose 2	
	COMIRNATY N[a]=2899 n[b] (%)	Placebo N[a]=2908 n[b] (%)	COMIRNATY N[a]=2682 n[b] (%)	Placebo N[a]=2684 n[b] (%)
Redness				
Any[c]	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Severe[d]	7 (0.2)	3 (0.1)	11 (0.4)	0 (0.0)
Swelling				
Any[c]	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Severe[d]	6 (0.2)	2 (0.1)	7 (0.3)	0 (0.0)
Pain at the injection site				
Any[c]	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Severe[e]	39 (1.3)	3 (0.1)	39 (1.5)	0 (0.0)
Any local reaction[c]	2444 (84.3)	432 (14.9)	2108 (78.6)	325 (12.1)

*Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. No Grade 4 solicited local reactions were reported in participants 16-55 years of age.
b. n = Number of participants with the specified reaction.
c. Any local reaction: any redness >2.0 cm, any swelling >2.0 cm, or any pain at the injection site.
d. Severe: >10.0 cm.
e. Severe: prevents daily activity.

Table 4: Study 2 – Frequency of Solicited Systemic Reactions Within 7 Days After Each Dose – Participants 16-55 Years of Age (Reactogenicity Subset of the Safety Population*)

Systemic Reaction	Dose 1		Dose 2	
	COMIRNATY N[a]=2899 n[b] (%)	Placebo N[a]=2908 n[b] (%)	COMIRNATY N[a]=2682 n[b] (%)	Placebo N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
>38.9°C	8 (0.3)	4 (0.1)	40 (1.5)	2 (0.1)
Fatigue				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Severe[d]	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Severe[d]	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Severe[d]	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Severe[e]	0 (0.0)	1 (0.0)	4 (0.1)	0 (0.0)
Diarrhea				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Severe[f]	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Severe[d]	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Severe[d]	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Any systemic reaction[c]	1979 (68.3)	1559 (53.6)	2034 (75.8)	1026 (38.2)
Use of antipyretic or pain medication	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

*Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N =Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. No Grade 4 solicited systemic reactions were reported in participants 16-55 years of age.
b. n = Number of participants with the specified reaction.
c. Any systemic reaction: any fever ≥38.0°C, any fatigue, any vomiting, any chills, any diarrhea, any headache, any new or worsened muscle pain, or any new or worsened joint pain.
d. Severe: prevents daily activity.
e. Severe: requires intravenous hydration.
f. Severe: 6 or more loose stools in 24 hours.

Table 5: Study 2 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Participants 56 Years of Age and Older (Reactogenicity Subset of the Safety Population*)

Local Reaction	Dose 1		Dose 2	
	COMIRNATY N[a]=2008 n[b] (%)	Placebo N[a]=1989 n[b] (%)	COMIRNATY N[a]=1860 n[b] (%)	Placebo N[a]=1833 n[b] (%)
Redness				
Any[c]	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Severe[d]	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling				
Any[c]	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Severe[d]	2 (0.1)	0 (0.0)	4 (0.2)	1 (0.1)
Pain at the injection site				
Any[c]	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Severe[e]	4 (0.2)	0 (0.0)	10 (0.5)	0 (0.0)
Any local reaction[c]	1433 (71.4)	207 (10.4)	1243 (66.8)	158 (8.6)

*Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. No Grade 4 solicited local reactions were reported in participants 56 years of age and older.
b. n = Number of participants with the specified reaction.
c. Any local reaction: any redness >2.0 cm, any swelling >2.0 cm, or any pain at the injection site.
d. Severe: >10.0 cm.
e. Severe: prevents daily activity.

Table 6: Study 2 – Frequency of Solicited Systemic Reactions Within 7 Days After Each Dose – Participants 56 Years of Age and Older (Reactogenicity Subset of the Safety Population*)

Systemic Reaction	Dose 1		Dose 2	
	COMIRNATY N[a]=2008 n[b] (%)	Placebo N[a]=1989 n[b] (%)	COMIRNATY N[a]=1860 n[b] (%)	Placebo N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
>38.9°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
Fatigue				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Severe[d]	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4[g]	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Headache				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Severe[d]	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Severe[d]	0 (0.0)	1 (0.1)	21 (1.1)	0 (0.0)
Vomiting				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Severe[e]	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
Diarrhea				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Severe[f]	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Severe[d]	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Severe[d]	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Any systemic reaction[c]	984 (49.0)	749 (37.7)	1203 (64.7)	516 (28.2)
Use of antipyretic or pain medication	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

*Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.
b. n = Number of participants with the specified reaction.
c. Any systemic reaction: any fever ≥38.0°C, any fatigue, any vomiting, any chills, any diarrhea, any headache, any new or worsened muscle pain, or any new or worsened joint pain.
d. Severe: prevents daily activity.
e. Severe: requires intravenous hydration.
f. Severe: 6 or more loose stools in 24 hours.
g. Grade 4: emergency room visit or hospitalization.

Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. The safety profile of the participants with stable HIV infection receiving COMIRNATY (n = 100) was similar to that seen in the general population.

Unsolicited Adverse Events

The participants were unblinded to offer placebo participants COMIRNATY when they became locally eligible under regulatory approval in December 2020. A total of 25,651 (58.2%) participants (13,031 in vaccine group and 12,620 in placebo group) 16 years of age and older had been followed up for at least 4 months, with 3,082 (7.0%) participants (1,778 in vaccine group and 1,304 in placebo group) followed up for at least 6 months after the second dose during the blinded placebo-controlled follow-up period in Study 2. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

No deaths related to the vaccine were reported in the study.

Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group.

Lymphadenopathy was reported in 87 (0.4%) participants in the vaccine group compared to 8 (<0.1%) participants in the placebo group, which is plausibly related to vaccination. Bell's palsy (facial paralysis and facial paresis) was reported by four participants in the vaccine group and two in the placebo group. In the four vaccinated participants, events began from 3 to 48 days after their last dose, were mild to moderate in severity, and duration ranged from 3 to 68 days. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. Cumulative safety follow-up to at least 6 months after Dose 2 for approximately 12,000 participants who received COMIRNATY showed no other safety signals arising from longer-term follow-up of the study.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

Pericarditis was reported for one participant in the vaccine group, and no case was reported in the placebo group. Appendicitis was reported as a serious adverse event for 27 participants, 15 vaccine participants and 12 placebo participants. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, thrombotic events, myocarditis or anaphylactic reaction to the vaccine) reported during the blinded placebo-controlled follow-up period of the study.

Participants 18 to 55 Years of Age – After Booster Dose

A subset, from Study 2 Phase 2/3 participants, of 306 adults 18 through 55 years of age who completed the original COMIRNATY 2-dose series, received a booster dose of COMIRNATY approximately 6 months (range of 4.8 to 8.0 months) after receiving Dose 2.

Solicited Local and Systemic Adverse Reactions

Overall, among participants who received a booster dose, the median age was 42 years (range 19 through 55 years of age), 45.8% were male and 54.2% were female, 81.4% were White, 27.8% were Hispanic/Latino, 9.2% were Black or African American, 5.2% were Asian, and 0.7% were American Indian/Alaska Native.

Table 7: Study 2 – Frequency and Percentages of Participants With Solicited Local Reactions, By Maximum Severity, Within 7 Days After the Booster Dose of COMIRNATY – Booster Dose Safety Population*

Solicited Local Reaction	COMIRNATY Booster Dose N[a] = 289 n[b] (%)
Redness[c]	
Any (>2 cm)	17 (5.9)
Severe	0
Swelling[c]	
Any (>2 cm)	23 (8.0)
Severe	1 (0.3)
Pain at the injection site[d]	
Any	240 (83.0)
Severe	1 (0.3)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after the booster dose.
Note: No Grade 4 solicited local reactions were reported.
*Participants in the safety analysis population who received the booster dose of COMIRNATY.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to 5.0 cm; Moderate: >5.0 to 10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

In participants who received a booster dose the mean duration of pain at the injection site after the booster dose was 2.6 days (range 1 to 8 days), for redness 2.2 days (range 1 to 15 days), and for swelling 2.2 days (range 1 to 8 days).

Table 8: Study 2 – Frequency and Percentages of Participants With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After the Booster Dose of COMIRNATY – Booster Dose Safety Population*

Solicited Systemic Reaction	COMIRNATY Booster Dose N[a] = 289 n[b] (%)
Fever	
≥38.0°C	25 (8.7)
≥38.0°C to 38.4°C	12 (4.2)
>38.4°C to 38.9°C	12 (4.2)
>38.9°C to 40.0°C	1 (0.3)
>40.0°C	0
Fatigue[c]	
Any	184 (63.7)
Severe	13 (4.5)
Headache[c]	
Any	140 (48.4)
Severe	3 (1.0)
Chills[c]	
Any	84 (29.1)
Severe	3 (1.0)
Vomiting[d]	
Any	5 (1.7)
Severe	0
Diarrhea[e]	
Any	25 (8.7)
Severe	0
New or worsened muscle pain[c]	
Any	113 (39.1)
Severe	4 (1.4)
New or worsened joint pain[c]	
Any	73 (25.3)
Severe	1 (0.3)
Use of antipyretic or pain medication[f]	135 (46.7)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after the booster dose.

Note: No Grade 4 solicited systemic reactions were reported.

*Randomized participants in the safety analysis population who received the booster dose of COMIRNATY.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Overall, the 306 participants who received a booster dose had a median follow-up time of 2.6 months (range: 1.1 to 2.8 months) after the booster dose to the cut-off date (17 Jun 2021).

In an analysis of all unsolicited adverse events reported following the booster dose, through 1 month after the booster dose, in participants 18 through 55 years of age (N = 289), those assessed as adverse reactions not already captured by solicited local and systemic reactions were lymphadenopathy (16, 5.2%), nausea (2, 0.7%), decreased appetite (1, 0.3%), rash (1, 0.3%), and pain in extremity (1, 0.3%).

Serious Adverse Events

Of the 306 participants who received a booster dose of COMIRNATY, there were no serious adverse events reported from the booster dose through 30 days after the booster dose.

Adolescents 12 to 15 Years of Age – Primary Series (Two Doses)

Solicited Adverse Reactions

Table 9 and Table 10 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in adolescents 12 to 15 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 9: Study 2 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Adolescents 12 to 15 Years of Age – Safety Population*

Local Reaction	COMIRNATY Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	COMIRNATY Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Redness				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Severe[c]	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Severe[c]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain at the injection site				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Severe[d]	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)
Any local reaction[e]	976 (86.6)	271 (24.0)	872 (79.5)	198 (18.4)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Severe: >10.0 cm.
d. Severe: prevents daily activity.
e. Any local reaction: any redness >2.0 cm, any swelling >2.0 cm, or any pain at the injection site
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

Table 10: Study 2 – Frequency of Solicited Systemic Reactions Within 7 Days After Each Dose – Adolescents 12 to 15 Years of Age – Safety Population*

Systemic Reaction	COMIRNATY Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	COMIRNATY Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Fever				
≥38.0°C	114 (10.1)	12 (1.1)	215 (19.6)	7 (0.6)
>38.9°C	11 (1.0)	2 (0.2)	25 (2.3)	1 (0.1)
Fatigue				
Any	677 (60.1)	457 (40.6)	726 (66.2)	264 (24.5)
Severe[c]	15 (1.3)	8 (0.7)	26 (2.4)	4 (0.4)
Headache				
Any	623 (55.3)	396 (35.1)	708 (64.5)	263 (24.4)
Severe[c]	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills				
Any	311 (27.6)	109 (9.7)	455 (41.5)	73 (6.8)
Severe[c]	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Severe[d]	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea				
Any	90 (8.0)	82 (7.3)	65 (5.9)	43 (4.0)
Severe[e]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Severe[c]	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)
New or worsened joint pain				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Severe[c]	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Any systemic reactions[f]	877 (77.8)	636 (56.4)	904 (82.4)	439 (40.7)
Use of antipyretic or pain medication	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Severe: prevents daily activity.
d. Severe: requires intravenous hydration.
e. Severe: 6 or more loose stools in 24 hours.
f. Any systemic reaction: any fever ≥38.0°C, any fatigue, any vomiting, any chills, any diarrhea, any headache, any new or worsened muscle pain, or any new or worsened joint pain

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

Unsolicited Adverse Events

In the analysis of Study 2 among adolescents 12 to 15 years of age, 98.3% of study participants had at least 30 days of follow-up after Dose 2 (1131 adolescents received COMIRNATY and 1129 adolescents received placebo).

Unsolicited adverse events (both serious and non-serious) were reported by 6.4% of COMIRNATY recipients and by 6.3% of placebo recipients. Lymphadenopathy was reported in 9 participants (0.8%) in the vaccine group compared to 2 participants (0.2%) in the placebo group. Serious adverse events were reported by 0.4% of COMIRNATY recipients and by 0.2% of placebo recipients.

Children 5 Through Less Than 12 Years of Age – Primary Series (Two Doses)

Solicited Adverse Reactions

Table 11 and Table 12 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in children 5 through less than 12 years of age included in the initial enrolment safety population who were monitored for reactogenicity with an electronic diary.

Table 11: Study 3 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Children 5 Through Less Than 12 Years of Age – Safety Population*

	COMIRNATY Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	COMIRNATY Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)
Redness[d]				
Any (≥0.5 cm)	222 (14.7)	43 (5.7)	278 (18.5)	40 (5.4)
Severe	0 (0.0)	0 (0.0)	3 (0.2)	0 (0.0)
Swelling[d]				
Any (≥0.5 cm)	158 (10.5)	20 (2.7)	229 (15.3)	20 (2.7)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Pain at the injection site[e]				
Any	1119 (74.1)	234 (31.3)	1065 (71.0)	218 (29.5)
Severe	4 (0.3)	0 (0.0)	5 (0.3)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. The denominators (N) used in the percentage calculations for redness and swelling were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.
c. n = Number of participants with the specified reaction.
d. Severe: >7.0 cm.
e. Severe: prevents daily activity.

* Randomized participants who received at least 1 dose of the study intervention.

Table 12: Study 3 – Frequency of Solicited Systemic Reactions Within 7 Days After Each Dose – Children 5 Through Less Than 12 Years of Age – Safety Population*

	COMIRNATY Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	COMIRNATY Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)
Fever				
≥38.0°C	38 (2.5)	10 (1.3)	98 (6.5)	9 (1.2)
>38.9°C	3 (0.2)	1 (0.1)	9 (0.6)	1 (0.1)
Fatigue[d]				
Any	508 (33.6)	234 (31.3)	592 (39.4)	180 (24.3)
Severe	4 (0.3)	1 (0.1)	11 (0.7)	1 (0.1)
Headache[d]				
Any	339 (22.4)	180 (24.1)	420 (28.0)	138 (18.6)
Severe	2 (0.1)	4 (0.5)	3 (0.2)	0 (0.0)
Chills[d]				
Any	70 (4.6)	35 (4.7)	147 (9.8)	32 (4.3)
Severe	0 (0.0)	0 (0.0)	2 (0.1)	1 (0.1)
Vomiting[e]				
Any	33 (2.2)	11 (1.5)	28 (1.9)	6 (0.8)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea[f]				
Any	89 (5.9)	31 (4.1)	79 (5.3)	35 (4.7)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain[d]				
Any	137 (9.1)	51 (6.8)	175 (11.7)	55 (7.4)
Severe	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
New or worsened joint pain[d]				
Any	50 (3.3)	41 (5.5)	78 (5.2)	27 (3.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Use of antipyretic or pain medication[g]	217 (14.4)	62 (8.3)	296 (19.7)	60 (8.1)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. The denominators (N) used in the percentage calculations for fever and use of antipyretic or pain medication were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.
c. n = Number of participants with the specified reaction.
d. Severe: prevents daily activity.
e. Severe: requires intravenous hydration.
f. Severe: 6 or more loose stools in 24 hours.
g. Severity was not collected for use of antipyretic or pain medication.

* Randomized participants who received at least 1 dose of the study intervention.

Unsolicited Adverse Events

In the analyses of Study 3 in children 5 through less than 12 years of age (initial enrolment group: 1,518 COMIRNATY 10 mcg and 750 placebo), 99.5% of participants had at least 30 days and 95.7% of participants had at least 3 months follow-up after Dose 2.

Serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up in the initial enrolment group were reported by 1 participant (0.1%) in each group after receiving the vaccine or placebo through the data cut-off date. No serious adverse events were reported that were considered related to vaccination.

Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up in the initial enrolment group were reported by 10.9% of COMIRNATY 10 mcg recipients and by 9.1% of placebo recipients. Lymphadenopathy was reported in 13 (0.9%) participants in the COMIRNATY 10 mcg group vs. 1 (0.1%) in the placebo group. All cases were considered to be mild, with a median onset of 3 days after Dose 1, and 2 days after Dose 2 in the vaccine group. The median duration was 3.5 days (ranged from 1 to 14 days) in the vaccine group. Skin and subcutaneous tissue disorders (including skin rash, dermatitis, eczema and urticaria) were reported in 17 (1.1%) participants in the vaccine group and 5 (0.7%) participants in the placebo group. Most of the events began from 3-11 days after the second dose and were characterized as mild and self-limited. There were no other notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY. There were no reports of myocarditis/pericarditis or anaphylaxis by the study cut-off date.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been identified during post authorization use of COMIRNATY.

Cardiac Disorders: myocarditis and/or pericarditis (see **WARNING AND PRECAUTIONS** section)

Immune System Disorders: severe allergic reactions, including anaphylaxis

Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

Nervous System Disorders: Facial paralysis / Bell's Palsy

Skin and subcutaneous tissue disorders and other hypersensitivity reactions: skin rash, pruritus, urticaria, angioedema

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. They are included because: a) they represent reactions that are known to occur following immunizations generally; b) they are potentially serious; or c) on the basis of their frequency of reporting.

9 DRUG INTERACTIONS

No interaction studies have been performed. There is no information on the co-administration of COMIRNATY with other vaccines.

Do not mix COMIRNATY with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The nucleoside-modified messenger RNA in COMIRNATY is formulated in lipid nanoparticles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19 disease.

11 STORAGE, STABILITY AND DISPOSAL

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

Do not refreeze thawed vials.

For 12 Years and Older (Vials with Purple Caps)

Frozen Vials Prior to Use

Cartons of COMIRNATY multiple dose vials arrive in thermal containers with dry ice. To ensure all appropriate safeguards are in place, refer to the Dry Ice Safety Data Sheet and the COMIRNATY Storage and Handling Reference Guide provided (also available at COMIRNATY.ca). Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90°C to -60°C (-130°F to -76°F) until the expiry date printed on the label. Vials may also be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F).

Thawed Vials Prior to Dilution

Thawed Under Refrigeration: Thaw and then store undiluted vials in the refrigerator (2°C to 8°C [35°F to 46°F]) for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature: For immediate use, thaw undiluted vials at room temperature (up to 25°C (77°F)] for 30 minutes.

Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours. Any hours used for transport at 2°C to 8°C (35°F to 46°F) count against the 1-month limit for storage at 2°C to 8°C (35°F to 46°F).

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. Any vaccine remaining in vials must be discarded after 6 hours. After dilution, the vaccine vials can be handled in room light conditions. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Do not freeze. If the vaccine is frozen, it must be discarded.

For Age 5 Years to <12 Years (Vials with Orange Caps and Orange Label Border)

Vial Storage Prior to Use

Cartons of COMIRNATY (for age 5 years to <12 years) may arrive frozen at ultra-cold conditions in thermal containers with dry ice or at -25°C to -15°C (-13°F to 5°F).

Once received, frozen vials may be immediately transferred to the refrigerator [2°C to 8°C (35°F to 46°F)], thawed and stored for up to 10 weeks. The 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. A carton of 10 vials may take up to 4 hours to thaw at this temperature.

Alternatively, frozen vials may be stored in an ultra-low temperature freezer at -90°C to -60°C (-130°F to -76°F). Do not store vials at -25°C to -15°C (-13°F to 5°F). Once vials are thawed they should not be refrozen.

Cartons of COMIRNATY (for age 5 years to <12 years) may also arrive at 2°C to 8°C (35°F to 46°F). If vials are received at 2°C to 8°C, they should be stored at 2°C to 8°C. Check that the carton has been updated to reflect the 10-week refrigerated expiry date.

Regardless of storage condition, vaccines should not be used after 6 months from the date of manufacture printed on the vial and cartons.

Vial Storage During Use

If not previously thawed at 2°C to 8°C (35°F to 46°F), allow vials to thaw at room temperature [up to 25°C (77°F)] for 30 minutes.

Vials of COMIRNATY (for age 5 years to <12 years) may be stored at temperatures up to 25°C (77°F) for a total of 12 hours prior to dilution.

After dilution the vials should be stored at 2°C to 25°C (35°F to 77°F). Vials should be discarded 12 hours after dilution (i.e., the first puncture). Vial labels and cartons may state that a vial should be

discarded 6 hours after dilution. The information in this Product Monograph supersedes the number of hours printed on vial labels and cartons.

Thawed vials can be handled in room light conditions.

Transportation of Vials

If local redistribution is needed, full cartons containing undiluted vials may be transported at -90°C to -60°C (-130°F to -76°F); full cartons or individual undiluted vials may also be transported at 2°C to 8°C (35°F to 46°F).

12 SPECIAL HANDLING INSTRUCTIONS

The COMIRNATY multiple dose vial contains a frozen suspension that does not contain preservative and must be thawed and diluted prior to administration.

For important information on handling and preparation for administration, please refer to **11 STORAGE, STABILITY AND DISPOSAL** and **4.3 Reconstitution**.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance:

Proper name: COVID-19 Vaccine, mRNA

International nonproprietary name: Tozinameran

Product Characteristics:

COMIRNATY (COVID-19 Vaccine, mRNA) is highly purified 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 SARS-CoV-2.

This vaccine is a white to off-white frozen suspension provided as a multiple dose vial and must be diluted before use.

For 12 Years and Older (Vials with Purple Caps)
One vial (0.45 mL) contains 6[†] doses of 0.3 mL after dilution. One dose (0.3 mL) contains 30 micrograms of COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

For Age 5 Years to <12 Years (Vials with Orange Caps and Orange Label Border)
One vial (1.3 mL) contains 10* doses of 0.2 mL after dilution. One dose (0.2 mL) contains 10 micrograms of COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The safety and efficacy of COMIRNATY were evaluated in Study 2, a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study in participants 12 years of age and older. Randomization 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 hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 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, for assessments of safety and efficacy against COVID-19.

[†] Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a 6th dose from a single vial.

* Low dead-volume syringes and/or needles can be used to extract 10 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.

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. Table 13 presents the specific demographic characteristics in the studied population.

To assess boostability, a subset of study participants were enrolled in selected sites, and 306 participants aged 18 to 55 years were re-randomized to receive a booster dose approximately 6 months after completion of the two-dose regimen (median interval between dose 2 and booster dose – 6.8 months; range 4.8 to 8.0 months). The median age at the time of booster vaccination was 42.0 years, and 46.3% of participants were male.

Table 13: Demographics (Population for the Primary Efficacy Endpoint)[a] (Data Accrued Through November 14, 2020)

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
12 to 15 years	46 (0.3)	42 (0.2)
16 to 64 years	14,216 (77.9)	14,299 (77.8)
65 to 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.
b. Includes multiracial and not reported.
c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease.
   - Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
   - Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
   - Obesity (body mass index ≥30 kg/m^2)
   - Diabetes (Type 1, Type 2, or gestational)
   - Liver disease
   - Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Study 3 is a Phase 1/2/3 study comprised of an open-label vaccine dose finding portion (Phase 1) and a multicentre, multinational, randomized, saline placebo-controlled, observer-blind efficacy portion (Phase 2/3) that has enrolled participants 5 to <12 years of age.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 5 through less than 12 years of age who received COMIRNATY 10 mcg and those who received placebo. Among the 1,518 participants (initial enrolment group) 5 through less than 12 years of age who received at least 1 dose of COMIRNATY 10 mcg, 52.6% were male and 47.4% were female, 79.3% were White, 5.9% were Black or African American, 21.0% were Hispanic/Latino, 5.9% were Asian, and 0.8% were American Indian/Alaska Native.

14.2 Study Results

14.2.1 Efficacy in Participants 16 Years of Age and Older After Two Doses

Primary Vaccine Efficacy Analysis (Based on Cut-off Date of November 14, 2020)

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for at least 2214 person-years in the COMIRNATY group and at least 2222 person-years in 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]. The primary endpoint was defined as any symptomatic COVID-19 case[2] confirmed by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). The population for the analysis of the primary efficacy endpoint included participants who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose (first primary efficacy endpoint), as well as participants with and without evidence of prior infections with SARS-CoV-2 through 7 days after the second dose (second primary efficacy endpoint). The pre-specified success criterion for vaccine efficacy was met. The vaccine efficacy information is presented in Table 14.

[2] Case definition defined by Study 2 protocol: (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, diarrhea or vomiting.

Table 14: 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 (Data Accrued Through November 14, 2020)

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)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 through 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases (n1[b]) Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases (n1[b]) Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 through 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]

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; diarrhea; vomiting).

Abbreviations: NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

* 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. No confirmed cases were identified in adolescents 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy (VE) was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated Vaccine Efficacy (Based on Cut-off Date of March 13, 2021)

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population. There were 77 confirmed COVID-19 cases identified in the COMIRNATY and 850 in the placebo groups, respectively. In this analysis, compared to placebo, the vaccine efficacy of COMIRNATY in participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 was 91.3% (95% confidence interval of 89.0% to 93.2%); in participants 65 years of age and older without evidence of prior infection vaccine efficacy was 94.5% (two-sided 95% confidence interval 88.3% to 97.8%). The vaccine efficacy of COMIRNATY in participants with or without evidence of prior infection was 91.1% (95% confidence interval: 88.8% to 93.0%) with 81 COVID-19 cases in the COMIRNATY group compared to 873 cases in the placebo group.

Efficacy Against Severe COVID-19 (Based on Cut-off Date of March 13, 2021)

Secondary efficacy analyses in Study 2 supported benefit of COMIRNATY in preventing severe COVID-19. During blinded placebo-controlled follow-up through March 13, 2021, the vaccine efficacy against severe COVID 19 (as defined by the study protocol) in participants **with or without evidence** of SARS-CoV-2 infection prior to 7 days after Dose 2 was 95.3% (95% CI: 70.9%, 99.9%) with 1 and 21 cases in the vaccine and placebo groups, respectively. The COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

14.2.2 Immunogenicity in Participants 18 to 55 Years of Age – After Booster Dose

Noninferiority of immune responses 1 month after a COMIRNATY booster dose compared to 1 month after completion of the primary 2-dose series was assessed, in a subset of participants enrolled at selected sites in the US, by evaluating SARS-CoV-2 50% neutralizing titers (NT50) against the reference strain. Immunogenicity was evaluated in subjects who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination. The analysis demonstrated noninferior immune responses 1 month after a booster dose compared to 1 month after Dose 2 in individuals 18 through 55 years of age (Table 15).

Table 15: SARS-CoV-2 neutralization assay - NT50 (titer)[†] – GMT and seroresponse rate comparison of 1 month after booster dose to 1 month after primary series – participants without evidence of infection up to 1 month after booster dose* – booster dose evaluable immunogenicity population[±]

Assay	n	COMIRNATY Sampling Time Point		1 month after booster dose/ - 1 month after primary series	Met noninferiority objective
		1 month after booster dose	1 month after Dose 2		
		(95% CI)	(95% CI)	(97.5% CI)	(Y/N)
Geometric mean 50% neutralizing titer (GMT[b])	210[a]	2476.4[b] (2210.1, 2774.9)	753.7[b] (658.2, 863.1)	3.29[c] (2.76, 3.91)	Y[d]
Seroresponse rate (%) for 50% neutralizing titer	198[e]	197[f] 99.5% (97.2%, 100.0%)	194[f] 98.0% (94.4%, 99.4%)	1.5%[g] (-0.7%, 3.7%[h])	Y[i]

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.

†SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.
*Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of COMIRNATY) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.

a. n = Number of participants with valid and determinate assay results at both sampling time points within specified window.
b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
c. GMRs and 2-sided 97.5% CIs were calculated by exponentiating the mean differences in the logarithms of the assay and the corresponding CIs (based on the Student t distribution).
d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.80.
e. n = Number of participants with valid and determinate assay results for the specified assay at baseline, 1 month after Dose 2 and 1 month after the booster dose within specified window. These values are the denominators for the percentage calculations.
f. Number of participants with seroresponse for the given assay at the given dose/sampling time point. Exact 2-sided CI based on the Clopper and Pearson method. Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
g. Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).
h. Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.
i. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is >-10%.

14.2.3 Efficacy and Immunogenicity in Adolescents 12 to 15 Years of Age (Based on Cut-off Date of March 13, 2021)

Efficacy

The vaccine efficacy in participants 12 to 15 years of age was evaluated on a subgroup analysis of Study 2 based on a cut-off date of March 13, 2021 (Table 16).

Table 16: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period (Data Accrued Through March 13, 2021), 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 of Age	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 of Age	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 (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; diarrhea; 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. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

Immunogenicity – After Two Doses

In Study 2 an analysis of SARS-CoV-2 neutralizing titers 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 noninferior to the immune response in participants 16 to 25 years of age (n=170), based on results for SARS-CoV-2 neutralizing titers at 1 month after Dose 2. The geometric mean titers (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 noninferiority criterion (the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] >0.67).

14.2.4 Immunogenicity and Efficacy in Children 5 Through Less Than 12 Years of Age (Based on Cut-off Date of October 8, 2021)

Immunogenicity

In Study 3, an analysis of SARS-CoV-2 50% neutralizing titers (NT50) 1 month after Dose 2 in a randomly selected subset of participants demonstrated effectiveness by immunobridging of immune responses. Children 5 through less than 12 years of age in the Phase 2/3 part of Study 3 were compared to participants 16 through 25 years of age in the Phase 2/3 part of Study 2 who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2. The study met the prespecified immunobridging criteria for both the geometric mean ratio (GMR) and the seroresponse difference with seroresponse defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from baseline (before Dose 1).

The ratio of the SARS-CoV-2 NT50 in children 5 through <12 years of age to that of young adults 16 to 25 years of age was 1.04 (2-sided 95% CI: 0.93, 1.18), meeting the 1.5-fold noninferiority criterion (the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] >0.67). Results are presented in Table 17.

Table 17: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of Children 5 Through Less Than 12 Years of Age (Study 3) to Participants 16 Through 25 Years of Age (Study 2) – Participants Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

		COMIRNATY			
		10 mcg/Dose 5 Through <12 Years n[a]=264	30 mcg/Dose 16 Through 25 Years n[a]=253	5 Through <12 Years/ 16 Through 25 Years	
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	Met Immunobridging Objective[e] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1 month after Dose 2	1197.6 (1106.1, 1296.6)	1146.5 (1045.5, 1257.2)	1.04 (0.93, 1.18)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic-acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence (up to 1 month post-Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 blood collection) and had no medical history of COVID-19 were included in the analysis.

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.
b. Protocol-specified timing for blood sample collection.
c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1[5 through <12 years of age] - Group 2 [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).
e. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the point estimate of the GMR is ≥0.8.
f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2, 99.2% of children 5 through less than 12 years of age and 99.2% of participants 16 through 25 years of age had a seroresponse from before vaccination to 1 month after Dose 2. The difference in proportions of participants who had seroresponse between the 2 age groups (children – young adult) was 0.0% (2-sided 95% CI: -2.0%, 2.2%), meeting the -10% noninferiority criterion (the lower bound of the 2-sided 95% CI for the difference in seroresponse rate>-10%). Results are presented in Table 18.

Table 18: Difference in Percentages of Participants With Seroresponse – Participants Without Evidence of Infection up to 1 Month After Dose 2 – Immunobridging Subset – Phase 2/3 – Comparison of 5 Through <12 Years of Age to Study 2 Phase 2/3 16 Through 25 Years of Age – Evaluable Immunogenicity Population

		COMIRNATY			
		Study 3 10 mcg/Dose 5 Through <12 Years N[a]=264	Study 2 30 mcg/Dose 16 Through 25 Years N[a]=253	5 Through <12 Years- 16 Through 25 Years	
Assay	Time Point[b]	n[c] (%) (95% CI[d])	n[c] (%) (95% CI[d])	Difference %[e] (95% CI[f])	Met Immunobridging Objective[g] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[h]	1 month after Dose 2	262 (99.2) (97.3, 99.9)	251 (99.2) (97.2, 99.9)	0.0 (-2.0, 2.2)	Y

Abbreviations: LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; NT50 = 50% neutralizing titer 50; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.

Note: Participants who had no serological or virological evidence (up to 1 month post-Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 blood collection) and had no medical history of COVID-19 were included in the analysis.

a. N = number of participants with valid and determinate assay results both before vaccination and at 1 month after Dose 2. These values are the denominators for the percentage calculations.
b. Protocol-specified timing for blood sample collection.
c. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.
d. Exact 2-sided CI based on the Clopper and Pearson method.
e. Difference in proportions, expressed as a percentage (Group 1 [5 through < 12 years of age] – Group 2 [16 through 25 years of age]).
f. 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.
g. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than -10.0%.
h. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Efficacy

An exploratory efficacy analysis (based on a cut-off date of October 8, 2021) in participants 5 to less than 12 years of age without evidence of SARS-CoV-2 infection prior to Dose 2 showed that the observed vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 90.7%

(95% CI: 67.7%, 98.3%), with 3 COVID-19 cases in the vaccine group compared to 16 in the placebo group (2:1 randomization in vaccine group to placebo group).

No severe COVID-19 or multisystem inflammatory syndrome in children (MIS-C) were reported in children 5 to less than 12 years of age, as of the data cut-off date (October 8, 2021).

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat dose toxicity.

General Toxicology:

In a repeat-dose toxicity study, rats were administered three once weekly doses of 30 mcg/animal (0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) and other ingredients included in a single human dose) of COMIRNATY by intramuscular injection. Vaccine administration resulted in transient erythema and edema at the site of injection, as well as increased cellularity in draining and inguinal lymph nodes, spleen, and bone marrow, along with transiently increased body temperature, increased white blood counts, and decreased reticulocyte counts coupled with decreased red blood cell mass. Clinical chemistry changes (e.g., increased acute phase protein levels) indicated an acute phase response. These changes are consistent with an expected immunostimulatory response following intramuscular administration of a vaccine. Transient periportal hepatocyte vacuolation was also observed without evidence of liver injury. Full or partial recovery from all findings was observed following a 3-week recovery period.

Carcinogenicity:

Carcinogenic potential was not assessed, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity:

Genotoxic potential was not assessed, as genotoxicity studies were not considered relevant to this vaccine.

Reproductive and Developmental Toxicology:

In a reproductive and developmental toxicity study, 30 mcg/animal (0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) and other ingredients included in a single human dose) of COMIRNATY was administered to female rats by the intramuscular route on four occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

COMIRNATY®

COVID-19 Vaccine, mRNA, Suspension for Intramuscular Injection

This leaflet is a summary and will not tell you everything about this vaccine. Talk to your/your child's healthcare professional about your/your child's medical condition and treatment and ask if there is any new information about **COMIRNATY**.

What is COMIRNATY used for?

COMIRNATY is a vaccine used to prevent COVID-19 disease caused by the SARS-CoV-2 virus.

COMIRNATY can be given to people from 5 years of age and older.

How does COMIRNATY work?

The vaccine causes our body to produce protection (such as antibodies) that prevent the COVID-19 virus from entering our cells to make us sick. The vaccine uses a new method (messenger RNA - mRNA, the genetic code for a piece of the virus) to help our bodies make protection against the virus. The vaccine is given by injection with a needle in the upper arm and will require two doses given 3 weeks apart.

You cannot get COVID-19 from the vaccine.

As with any vaccine, COMIRNATY may not fully protect all those who receive it. Even after you/your child have had the vaccine, continue to follow the recommendations of local public health officials to prevent spread of COVID-19.

What are the ingredients in COMIRNATY?

Medicinal ingredient: mRNA

Non-medicinal ingredients: The non-medicinal ingredients differ depending on which version of the vaccine is given. If you are uncertain, check with your vaccination provider.

For 12 Years of Age or Older:

- ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)
- ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
- 1,2-distearoyl-sn-glycero-3-phosphocholine
- cholesterol
- dibasic sodium phosphate dihydrate
- monobasic potassium phosphate
- potassium chloride
- sodium chloride
- sucrose
- water for injection

For Age 5 Years to Less Than 12 Years:

- ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)
- ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
- 1,2-distearoyl-sn-glycero-3-phosphocholine
- cholesterol
- sodium chloride
- sucrose
- tromethamine
- tromethamine hydrochloride
- water for injection

COMIRNATY comes in the following dosage forms:

For 12 Years of Age and Older:
White to off-white suspension (to be diluted) provided in a multiple dose vial of 6 doses.

After dilution, the vial contains 6 doses of 0.3 mL, with 30 micrograms mRNA each.

For Age 5 Years to Less Than 12 Years:
White to off-white suspension (to be diluted) provided in a multiple dose vial of 10 doses.

After dilution, the vial contains 10 doses of 0.2 mL, with 10 micrograms mRNA each.

You/your child should not receive COMIRNATY if:

- you/your child are allergic to any of the ingredients in this vaccine (see **What are the ingredients in COMIRNATY?**)
- you/your child had a severe allergic reaction after a previous dose of this vaccine
- you/your child have any symptoms that could be due to COVID-19. Talk with your/your child's healthcare professional about your/your child's symptoms and getting a COVID-19 test. Your/your child's healthcare professional will advise you when you/your child are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your/your child's healthcare professional before you/your child receive COMIRNATY. Talk about any health conditions or problems you/your child may have, including if you/your child:

- have had any problems following a previous dose of COMIRNATY such as an allergic reaction or breathing problems
- have any allergies
- have a weakened immune system due to a medical condition or are on a medicine that affects the immune system
- have previously had episodes of myocarditis and/or pericarditis
- are feeling nervous about the vaccination process or have ever fainted in association with an injection
- have a bleeding problem, bruise easily or use a blood thinning medication
- are pregnant, think you may be pregnant or plan to become pregnant
- are breast-feeding

Other warnings you should know about:

It may take until 7 days after the second dose of COMIRNATY to develop protection against COVID-19. As with any vaccine, COMIRNATY may not fully protect all those who receive it.

Some of the effects of vaccination mentioned under "***What are possible side effects from using COMIRNATY?"*** may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

Tell your/your child's healthcare professional about all the medicines you/your child take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There is no information on the use of COMIRNATY with other vaccines.

Tell your healthcare professional if you/your child have recently received any other vaccine.

How COMIRNATY is given:

Usual dose:

For 12 Years of Age and Older:
COMIRNATY is given after dilution as an injection of 0.3 mL, preferably into a muscle of the upper arm.

You/your child will receive 2 injections, given 3 weeks apart. It is very important to return for the second injection, or the vaccine may not work as well.

A booster dose of COMIRNATY may be given at least 6 months after completion of the primary series in individuals 18 years of age and older.

For Age 5 Years to Less Than 12 Years:
COMIRNATY is given after dilution as an injection of 0.2 mL, preferably into a muscle of the upper arm.

Your child will receive 2 injections, given 3 weeks apart. It is very important that they return for the second injection, or the vaccine may not work as well.

If you have any further questions on the use of COMIRNATY, ask your healthcare professional.

Overdose:

In the event of suspected overdose with COMIRNATY, contact your regional poison control centre.

Missed Dose:

If you forget to go back to your healthcare professional at the scheduled time for your/your child's next dose, ask your/your child's healthcare professional for advice.

What are possible side effects from using COMIRNATY?

Like all vaccines, COMIRNATY can cause side effects, although not everybody gets them.

Side effects may occur at the following frequencies:

Very common: may affect more than 1 in 10 people

- injection site pain, swelling

- tiredness
- headache
- muscle pain
- chills
- joint pain
- fever
- diarrhea

Common: may affect more than 1 in 100 and up to 1 in 10 people

- injection site redness
- nausea
- vomiting

Uncommon: may affect more than 1 in 1000 and up to 1 in 100 people

- enlarged lymph nodes
- feeling unwell
- arm pain
- feeling weak or lack of energy/sleepy
- decreased appetite
- excessive sweating
- night sweats

Non-severe allergic reactions (such as rash, itching, hives or swelling of the face), severe allergic reactions and facial paralysis / Bell's palsy have been reported.

These are not all the possible side effects you/your child may have when taking COMIRNATY. If you/your child experience any side effects not listed here, tell your/your child's healthcare professional.

There is a remote chance that COMIRNATY could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of COMIRNATY. For this reason, the vaccination provider may ask you/your child to stay at the place where the vaccine was received for monitoring after vaccination. Should you/your child develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention right away. Symptoms of an allergic reaction include:

- hives (bumps on the skin that are often very itchy)
- swelling of the face, tongue or throat
- difficulty breathing
- a fast heartbeat
- dizziness and weakness

If you/your child experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Your/your child's health care provider should inform your local public health department of any serious side effects after vaccination.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Pfizer Canada ULC cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) and send it to your local Health Unit.

Storage:

COMIRNATY should be stored, supplied and administered by a healthcare professional.

Keep out of reach and sight of children.

If you want more information about COMIRNATY**:**

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website [www.pfizer.ca], or by calling 1-800-463-6001 (Pfizer Medical Information).

This leaflet was prepared by Pfizer Canada ULC.

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