PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PFIZER-BIONTECH COVID-19 VACCINE

COVID-19 mRNA Vaccine, Suspension for Intramuscular Injection

Multiple Dose Vial
(after dilution each vial contains 5 doses of 0.3 mL)

Active Immunizing Agent

HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS COVID-19 Vaccine UNDER AN INTERIM ORDER
PFIZER-BIONTECH COVID-19 VACCINE 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 16 years of age and older. The use of PFIZER-BIONTECH COVID-19 VACCINE is permitted under an interim authorization delivered in accordance with section 5 of the COVID-19 Interim order (IO)*. Patients should be advised of the nature of the authorization. The interim authorization is associated with Terms and Conditions that need to be met by the Market Authorization Holder to ascertain the continued quality, safety and efficacy of the product. For further information on authorization under this pathway, please refer to Health Canada's IO Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19. * https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/interim-order-import-sale-advertising-drugs.html#a2.8

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Date of Initial Authorization:
December 9, 2020

Imported and distributed by:
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Submission Control Number: 244906

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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

Pfizer-BioNTech COVID-19 Vaccine (COVID-19 mRNA Vaccine) 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 16 years of age and older.

1.1 Pediatrics

The safety and efficacy of Pfizer-BioNTech COVID-19 Vaccine in children under 16 years of age have not yet been established (see **ADVERSE REACTIONS** and **CLINICAL TRIALS** sections).

1.2 Geriatrics

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see **ADVERSE REACTIONS** and **CLINICAL TRIALS** sections).

2 CONTRAINDICATIONS

Pfizer-BioNTech COVID-19 Vaccine is contraindicated in individuals who are hypersensitive to the active substance or to any ingredient in the formulation. For a complete listing, see **DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** section**.**

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

4.1 Dosing Considerations

Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection which must be diluted prior to administration. After preparation, a single dose is 0.3 mL.

4.2 Recommended Dose and Dosage Adjustment

Vaccination Schedule for Individuals 16 Years of Age and Older

Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly after dilution as a series of two doses (0.3 mL each) 21 days apart (see **Trial Design and Study Demographics** section).

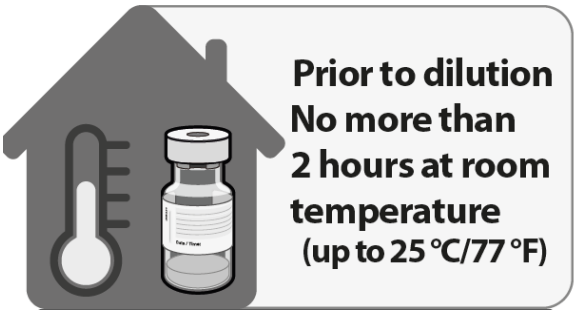
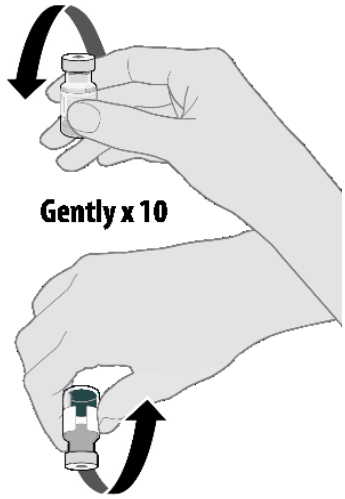
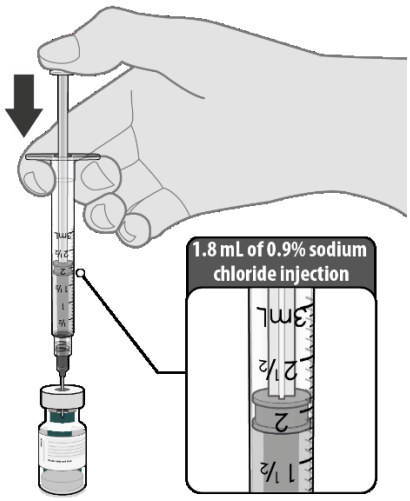
There are no data available on the interchangeability of Pfizer-BioNTech COVID-19 Vaccine

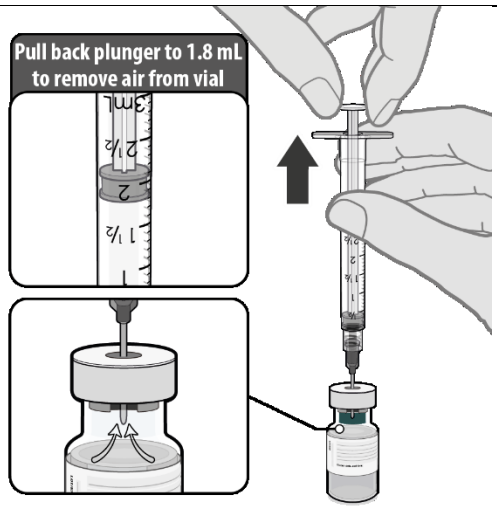
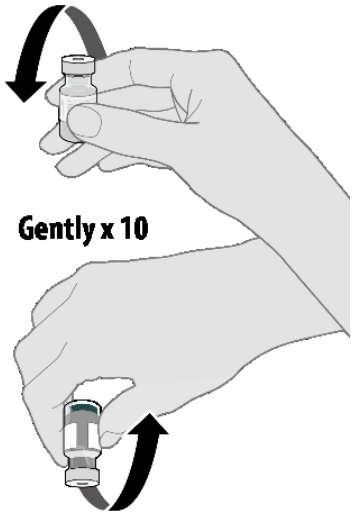
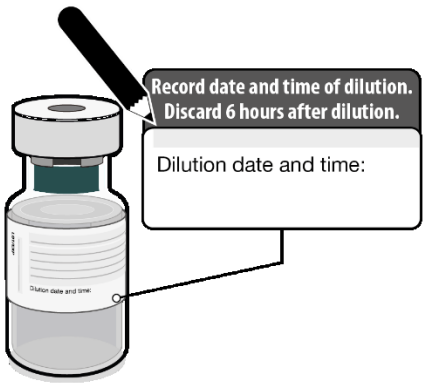
with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine to complete the vaccination series.

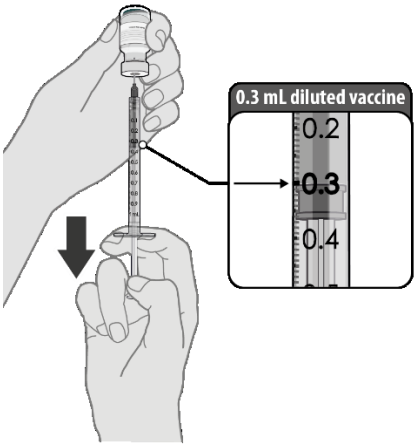
4.3 Reconstitution

Preparation for Administration

- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial contains a frozen suspension that does not contain preservative and must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator (2^0C to 8^OC)or at room temperature (up to 25°C [77°F]) (see **STORAGE, STABILITY AND DISPOSAL** section).
- Prior to dilution, the thawed suspension may contain white to off-white opaque amorphous particles.
- The contents of the vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form the Pfizer-BioNTech COVID-19 Vaccine.
- 0.9% Sodium Chloride Injection, USP 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, the vial contains 5 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.

DILUTE BEFORE USE	
	• Remove a thawed vial of Pfizer-BioNTech COVID-19 Vaccine from the refrigerator and allow it to come to room temperature. • If using a frozen vial of Pfizer-BioNTech COVID-19 Vaccine, thaw for 30 minutes at room temperature. Vials at room temperature must be diluted within 2 hours.
	• Before dilution, invert **gently** 10 times to mix. • <u>Do not shake.</u>
	• Obtain sterile 0.9% Sodium Chloride Injection, USP. • Cleanse the vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the Pfizer-BioNTech COVID-19 Vaccine vial using a needle 21-gauge or narrower.

	• 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 the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • <u>Do not shake</u>.
	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine 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 PFIZER-BIONTECH COVID-19 VACCINE	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine. • Administer immediately, and no later than 6 hours after dilution.

4.4 Administration

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, and
- confirm there are no particulates and that no discolouration is observed.

If the visual inspection fails, do not administer the vaccine.

Administer Pfizer-BioNTech COVID-19 Vaccine intramuscularly in the deltoid muscle.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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

Pfizer-BioNTech COVID-19 Vaccine 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.

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension (to be diluted) Multiple dose vial (after dilution, each vial contains 5 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

Pfizer-BioNTech COVID-19 Vaccine is a white to off-white, sterile, preservative-free, frozen suspension for intramuscular injection. Pfizer-BioNTech COVID-19 Vaccine contains a nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2 and the non-medicinal ingredients listed in Table 1 above.

Pfizer-BioNTech COVID-19 Vaccine is packaged in a clear glass 2 mL vial with a rubber stopper (not made with natural rubber latex), aluminum overseal, and flip-off cap.

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.

7 WARNINGS AND PRECAUTIONS

General

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of this vaccine.

The administration of Pfizer-BioNTech COVID-19 Vaccine should be postponed in individuals suffering from acute severe febrile illness.

As with any vaccine, vaccination with Pfizer-BioNTech COVID-19 Vaccine may not protect all recipients.

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

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.

7.1 Special Populations

7.1.1 Pregnant Women

The safety and efficacy of Pfizer-BioNTech COVID-19 Vaccine in pregnant women have not yet been established.

7.1.2 Breast-feeding

It is unknown whether Pfizer-BioNTech COVID-19 Vaccine 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 Pfizer-BioNTech COVID-19 Vaccine in children under 16 years of age have not yet been established.

7.1.4 Geriatrics

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (See **ADVERSE REACTIONS** and **CLINICAL TRIALS** sections).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety of Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 16 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America. Study BNT162-01 (Study 1) enrolled 60 participants, 18 through 55 years of age. Study C4591001 (Study 2) enrolled approximately 44,000 participants, 12 years of age or older.

In Study 2, a total of 21,720 participants 16 years of age or older received at least one dose of Pfizer-BioNTech COVID-19 Vaccine and a total of 21,728 participants 16 years of age or older received placebo.

At the time of the analysis of Study 2, a total of 19,067 (9,531 Pfizer-BioNTech COVID-19 Vaccine and 9,536 placebo) participants 16 years of age or older were evaluated for safety 2 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine.

The safety evaluation of participants in Study 2 is still ongoing. Participants were monitored for solicited local and systemic events, and use of antipyretic medication after each vaccination. Participants continue to be monitored for unsolicited adverse events, including serious adverse events up to six months after the last vaccine dose (see **CLINICAL TRIALS** section).

The most frequent adverse reactions in a subset (n=8183) of participants 18 years of age and older, who received the vaccine and comprised a subset of the safety population monitored for reactogenicity with an electronic diary were:, injection site pain (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%),joint pain (23.6%) and fever (14.2%) and were usually mild or moderate in intensity and resolved within a few days after vaccination.

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.

Tables 2 through 5 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID-19 Vaccine and placebo in the subset of participants 18 years of age and older (n=8183) in the safety population who were monitored for reactogenicity with an electronic diary.

Table 2: Study 2 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Participants 18-55 Years of Age (Reactogenicity subset Safety Population*#)

Local Reaction	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=2291 %	Placebo N[a]=2298 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=2098 %	Placebo N[a]=2103 %
Redness				
Any[b]	4.5	1.1	5.9	0.7
Severe[c]	0.3	0.2	0.5	0
Swelling				
Any[b]	5.8	0.5	6.3	0.2
Severe[c]	0.2	0.1	0.3	0
Pain at the Injection Site				
Any[b]	83.1	14.0	77.8	11.7
Severe[d]	1.0	0.1	1.2	0
Any local reaction[b]	83.6	14.7	78.1	12.2

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. Any local reaction: any redness >2.0 cm, any swelling >2.0 cm, or any pain at the injection site
c. Severe: >10.0 cm
d. Severe: prevents daily activity
* Randomized participants who received at least 1 dose of the study intervention
# Five participants were between 16 and 17 years of age

Table 3: Study 2 – Frequency of Solicited Systemic Events Within 7 Days After Each Dose – Participants 18-55 Years of Age (Reactogenicity subset Safety Population*#)

Systemic Event	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=2291 %	Placebo N[a]=2298 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=2098 %	Placebo N[a]=2103 %
Fever				
≥38.0°C	3.7	0.9	15.8	0.5
>38.9°C	0.3	0.2	1.2	0.1
Fatigue				
Any	47.4	33.4	59.4	22.8
Severe[c]	1.4	0.5	4.6	0.7
Headache				
Any	41.9	33.7	51.7	24.1
Severe[c]	1.0	0.8	3.2	0.7
Chills				

Systemic Event	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=2291 %	Placebo N[a]=2298 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=2098 %	Placebo N[a]=2103 %
Any	14.0	6.4	35.1	3.8
Severe[c]	0.4	0.1	2.1	0
Vomiting				
Any	1.2	1.2	1.9	1.2
Severe[d]	0	0	0.2	0
Diarrhea				
Any	11.1	11.7	10.4	8.4
Severe[d]	0.1	0.0	0.2	0.0
New or worsened muscle pain				
Any	21.3	10.8	37.3	8.2
Severe[c]	0.6	0.1	2.2	0.1
New or worsened joint pain				
Any	11.0	6.0	21.9	5.2
Severe[c]	0.2	0	1.0	0.2
Any systemic event[b]	67.1	54.1	74.2	38.2
Use of antipyretic or pain medication	27.8	14.4	45.0	12.6

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. Any systemic event: 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
c. Severe: prevents daily activity
d. Severe: requires intravenous hydration
*All randomized participants who received at least 1 dose of the study intervention
[#] Five participants were between 16 and 17 years of age

Table 4: Study 2 – Frequency of Solicited Local Reactions Within 7 Days After Each Dose – Participants 56 Years of Age and Older (Reactogenicity subset Safety Population*)

Local Reaction	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=1802 %	Placebo N[a]=1792 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=1660 %	Placebo N[a]=1646 %
Redness				
Any[b]	4.7	1.1	7.2	0.7

Local Reaction	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=1802 %	Placebo N[a]=1792 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=1660 %	Placebo N[a]=1646 %
Severe[c]	0.2	0.1	0.5	0.1
Swelling				
Any[b]	6.5	1.2	7.5	0.7
Severe[c]	0.1	0	0.2	0.1
Pain at the Injection Site				
Any[b]	71.1	9.3	66.1	7.7
Severe[d]	0.2	0	0.5	0
Any local reaction[b]	72.1	10.4	66.9	8.5

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

Table 5: Study 2 – Frequency of Solicited Systemic Events Within 7 Days After Each Dose – Participants 56 Years of Age and Older (Reactogenicity subset Safety Population*)

Systemic Event	Dose 1		Dose 2	
	Pfizer-BioNTech COVID-19 Vaccine N[a]=1802 %	Placebo N[a]=1792 %	Pfizer-BioNTech COVID-19 Vaccine N[a]=1660 %	Placebo N[a]=1646 %
Fever				
≥38.0°C	1.4	0.4	10.9	0.2
>38.9°C	0.1	0.1	0.3	0.1
Fatigue				
Any	34.1	22.6	50.5	16.8
Severe[c]	0.1	0.2	2.8	0.1
Headache				
Any	25.2	18.1	39.0	13.9
Severe[c]	0.1	0.2	0.5	0.2
Chills				
Any	6.3	3.2	22.7	2.8
Severe[c]	0	0.1	1.0	0
Vomiting				
Any	0.5	0.5	0.7	0.3
Severe[d]	0	0	0.1	0
Diarrhea				
Any	8.2	6.6	8.3	6.0
Severe[d]	0.2	0.1	0.1	0.2
New or worsened muscle pain				
Any	13.9	8.3	28.7	5.3
Severe[c]	0.1	0.2	1.0	0.1
New or worsened joint pain				
Any	8.6	6.1	18.9	3.7
Severe[c]	0.1	0.1	0.4	0.1
Any systemic event[b]	49.0	37.9	64.5	28.2
Use of antipyretic or pain medication	19.9	11.9	37.7	9.8

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. Any systemic event: 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
c. Severe: prevents daily activity
d. Severe: requires intravenous hydration
*All randomized participants who received at least 1 dose of the study intervention

Unsolicited Adverse Events

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

Serious Adverse Events
In Study 2, in participants 16 to 55 years of age (Pfizer-BioNTech COVID-19 Vaccine = 10,841, placebo = 10,851), serious adverse events from Dose 1 through 30 days after Dose 2 were reported by 0.4% of participants and by 0.3% of participants who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In Study 2, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 7960, placebo = 7934), serious adverse events were reported by 0.8% of participants and by 0.6% of participants who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively.

Non-Serious Adverse Events
Overall in Study 2, in which 10,841 participants 16 to 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 10,851 participants received placebo, non-serious adverse events from Dose 1 through 30 days after Dose 2 were reported in 29.3% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 13.2% of participants in the placebo group, for participants who received at least 1 dose. Overall in Study 2, in which 7960 participants 56 years of age and older received Pfizer-BioNTech COVID-19 Vaccine, non-serious adverse events within 30 days were reported in 23.8% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 11.7% of participants in the placebo group, for participants who received at least 1 dose. It was reported in the study that lymphadenopathy had occurred. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy were imbalanced with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. 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 Pfizer-BioNTech COVID-19 Vaccine.

9 DRUG INTERACTIONS

No interaction studies have been performed.

Do not mix Pfizer-BioNTech COVID-19 Vaccine with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The nucleoside-modified messenger RNA in Pfizer-BioNTech COVID-19 Vaccine 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

Frozen Vials Prior to Use
Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials (after dilution each vial contains 5 doses of 0.3 mL) 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 Pfizer-BioNTech COVID-19 Vaccine Storage and Handling Reference Guide provided (also available at CVDvaccine.ca). Once received, remove the vial cartons immediately from the thermal container and store in the freezer between -80°C to -60°C (-112°F to -76°F). Vials must be kept frozen between -80°C to -60°C (-112°F to -76°F) and protected from light, in the original cartons, until ready to use.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine 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 within this temperature range is not considered an excursion from the recommended storage condition.

Thawed Vials Prior to Dilution
Prior to dilution, multiple dose vials of Pfizer-BioNTech COVID-19 Vaccine may be thawed and stored in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of 25 vials or 195 vials may take up to 2 or 3 hours to thaw in the refrigerator, respectively, whereas a fewer number of vials will thaw in less time. Vials may be stored in the refrigerator for up to 5 days (120 hours). Frozen vials may also be thawed at room temperature [up to 25°C (77°F)]. Prior to dilution, the multiple dose vial may be stored at room temperature for no more than 2 hours. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Thawed vials can be handled in room light conditions. Do not refreeze thawed vials (see **DOSAGE AND ADMINISTRATION** section).

Vials After Dilution
After dilution, multiple dose vials of Pfizer-BioNTech COVID-19 Vaccine must be stored between 2°C to 25°C (35°F to 77°F) and used within 6 hours from the time of dilution. Any vaccine remaining in vials must be discarded after 6 hours. During storage, minimize exposure

to room light, and avoid exposure to direct sunlight and ultraviolet light. After dilution, the vaccine vials can be handled in room light conditions. Do not freeze. If the vaccine is frozen, it must be discarded.

12 SPECIAL HANDLING INSTRUCTIONS

The Pfizer-BioNTech COVID-19 Vaccine 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 **STORAGE, STABILITY AND DISPOSAL** and **Reconstitution** sections.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance:

Proper name: COVID-19 mRNA Vaccine

Product Characteristics:

Pfizer-BioNTech COVID-19 Vaccine (COVID-19 mRNA Vaccine) 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. One vial contains 5 doses of 30 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 Pfizer-BioNTech COVID-19 Vaccine were evaluated in a Phase 2/3 randomized, placebo-controlled, multicentre study in participants 12 years of age and older. A total of 43,651 (21,823 in the Pfizer-BioNTech COVID-19 Vaccine group and 21,828 in the placebo group) participants were randomized equally to receive 2 doses of Pfizer-BioNTech COVID-19 Vaccine or placebo separated by 21 days (19-23 days, per protocol). 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. Note that subjects 12 through 15 years of age were not included in the analysis of efficacy.

The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19 disease. 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 enrolment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV).

The primary endpoint was defined as any symptomatic* COVID-19 case 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). Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19 disease.

Table 6 presents the specific demographic characteristics in the studied population.

Table 6: Demographic Characteristics – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Pfizer-BioNTech COVID-19 Vaccine (N[a]=18,242) n (%)	Placebo (N[a]=18,379) n (%)	Total (N[a]=36,621) n (%)
Sex			
Male	9318 (51.1)	9225 (50.2)	18,543 (50.6)
Female	8924 (48.9)	9154 (49.8)	18,078 (49.4)
Age at Vaccination (years)			
Mean (SD)	50.6 (15.70)	50.4 (15.81)	50.5 (15.76)
Median	52.0	52.0	52.0
Min, max	(12, 89)	(12, 91)	(12, 91)
Age group			
12-15 years	46 (0.3)	42 (0.2)	88 (0.2)
16-55 years	10,428 (57.2)	10,507 (57.2)	20,935 (57.2)
>55 years	7768 (42.6)	7830 (42.6)	15,598 (42.6)
≥65 years	3980 (21.8)	4038 (22.0)	8018 (21.9)
Race			
White	15,110 (82.8)	15,301 (83.3)	30,411 (83.0)
Black or African American	1617 (8.9)	1617 (8.8)	3234 (8.8)
American Indian or Alaska native	118 (0.6)	106 (0.6)	224 (0.6)
Asian	815 (4.5)	810 (4.4)	1625 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)	77 (0.2)
Multiracial	448 (2.5)	402 (2.2)	850 (2.3)
Not reported	86 (0.5)	114 (0.6)	200 (0.5)
Ethnicity			
Hispanic or Latino	4886 (26.8)	4857 (26.4)	9743 (26.6)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)	26,665 (72.8)
Not reported	103 (0.6)	110 (0.6)	213 (0.6)
Country			
Argentina	2561 (14.0)	2539 (13.8)	5100 (13.9)
Brazil	1232 (6.8)	1223 (6.7)	2455 (6.7)
Germany	121 (0.7)	126 (0.7)	247 (0.7)
South Africa	287 (1.6)	279 (1.5)	566 (1.5)
USA	14,041 (77.0)	14,212 (77.3)	28,253 (77.1)
Comorbidities[1]			
Yes	8432 (46.2)	8450 (46.0)	16,882 (46.1)
No	9810 (53.8)	9929 (54.0)	19,739 (53.9)

a N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

1 Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: e.g. asthma, BMI ≥30 kg/m^2, chronic pulmonary disease, diabetes mellitus, hypertension.

14.2 **Study Results**

The analysis of the first primary efficacy endpoint (population **without evidence** of infection prior to 7 days after dose 2) included 36,523 participants 16 years of age and older (18,198 in the Pfizer-BioNTech COVID-19 Vaccine group and 18,325 in the placebo group). At the time of the final primary efficacy analysis, participants had been followed for symptomatic COVID-19 disease for a median of 2 months, corresponding to 2,214 person-years for the Pfizer-BioNTech COVID-19 Vaccine and 2,222 person-years in the placebo group.

There were 8 confirmed COVID-19 cases identified in the Pfizer-BioNTech COVID-19 Vaccine and 162 in placebo groups, respectively, for the first primary efficacy analysis. In this analysis, compared to placebo, efficacy of Pfizer-BioNTech COVID-19 Vaccine in participants with first COVID-19 occurrence from 7 days after Dose 2 (participants **without evidence** of prior infection with SARS-CoV-2) was 95.0% (95% credible interval of 90.3% to 97.6%). In participants 65 years of age and older **without evidence** of prior infections with SARS-CoV-2, efficacy of Pfizer-BioNTech COVID-19 Vaccine was 94.7% (two-sided 95% confidence interval of 66.7% to 99.9%). In the second primary efficacy analysis (participants 16 years of age and older **with or without evidence** of prior infection with SARS-CoV-2), compared to placebo, efficacy of Pfizer-BioNTech COVID-19 Vaccine in participants with first COVID-19 occurrence from 7 days after Dose 2 was 94.6% (95% credible interval of 89.9% to 97.3%).

*Case definition: (at least 1 of) fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhoea or vomiting.

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

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

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:

Reproduction and developmental toxicology studies in animals have not been completed.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PFIZER-BIONTECH COVID-19 VACCINE

COVID-19 mRNA Vaccine, Suspension for Intramuscular Injection

Health Canada has authorized the sale of this COVID-19 vaccine under an Interim Order.

This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Pfizer-BioNTech COVID-19 Vaccine**.

What is Pfizer-BioNTech COVID-19 Vaccine used for?

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

Pfizer-BioNTech COVID-19 Vaccine can be given to people from 16 years of age and older.

How does Pfizer-BioNTech COVID-19 Vaccine 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 21 days apart.

You cannot get COVID-19 from the vaccine.

As with any vaccine, Pfizer-BioNTech COVID-19 Vaccine may not fully protect all those who receive it. Even after you have had both doses of the vaccine, continue to follow the recommendations of local public health officials to prevent spread of COVID-19.

What are the ingredients in Pfizer-BioNTech COVID-19 Vaccine?

Medicinal ingredient: mRNA

Non-medicinal ingredients:

- 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

Pfizer-BioNTech COVID-19 Vaccine comes in the following dosage forms:

White to off-white suspension (to be diluted) provided in a multiple dose vial of 5 doses.

After dilution, the vial contains 5 doses of 0.3 mL, with 30 micrograms mRNA each.

You should not receive Pfizer-BioNTech COVID-19 Vaccine if:

- you are allergic to any of the ingredients in this vaccine (see **What are the ingredients in Pfizer-BioNTech COVID-19 Vaccine?**)
- have any symptoms that could be due to COVID-19. Talk with your healthcare professional about your symptoms and getting a COVID-19 test. Your healthcare professional will advise you when you are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you receive Pfizer-BioNTech COVID-19 Vaccine. Talk about any health conditions or problems you may have, including if you:

- have had any problems following previous administration of Pfizer-BioNTech COVID-19 Vaccine such as an allergic reaction or breathing problems.
- have a weakened immune system due to a medical condition or are on a medicine that affects your immune system.
- 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 Pfizer-BioNTech COVID-19 Vaccine to develop protection against COVID-19. As with any vaccine, Pfizer-BioNTech COVID-19 Vaccine may not fully protect all those who receive it.

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

There is no information on the use of Pfizer-BioNTech COVID-19 vaccine with other vaccines.

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

How Pfizer-BioNTech COVID-19 Vaccine is given:

Usual dose:

Pfizer-BioNTech COVID-19 Vaccine is given after dilution as an injection of 0.3 mL into a muscle of your upper arm.

You will receive 2 injections, given 21 days apart. It is very important that you return for the second injection, or the vaccine may not work as well.

If you have any further questions on the use of Pfizer-BioNTech COVID-19 Vaccine, ask your healthcare professional.

Overdose:

In the event of suspected overdose with Pfizer-BioNTech COVID-19 Vaccine, contact your regional poison control centre.

Missed Dose:

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

What are possible side effects from using Pfizer-BioNTech COVID-19 Vaccine?

Like all vaccines, Pfizer-BioNTech COVID-19 Vaccine can cause side effects.

Side effects may occur at the following frequencies:

Very common: may affect more than 1 in 10 people

- pain at injection site
- tiredness
- headache
- muscle pain
- chills
- joint pain
- fever

Uncommon: may affect up to 1 in 100 people

- enlarged lymph nodes

These are not all the possible side effects you may have when taking Pfizer-BioNTech COVID-19 Vaccine. If you experience any side effects not listed here, tell your healthcare professional.

Should you 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

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

Your 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:

Pfizer-BioNTech COVID-19 Vaccine should be stored, supplied and administered by a healthcare professional.

Keep out of reach and sight of children.

If you want more information about Pfizer-BioNTech COVID-19 Vaccine:

- 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.

Last Revised December 9, 2020