Pfizer-BioNTech COVID-19 Vaccine

COVID-19 mRNA Vaccine (nucleoside modified)

Reference market: US

AfME markets using the same LPD: Saudi Arabia

SUMMARY OF PRODUCT CHARACTERISTICS

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See section 4.8 for how to report side effects.

1. NAME OF THE MEDICINAL PRODUCT

Pfizer-BioNTech COVID-19 Vaccine
COVID-19 mRNA Vaccine (nucleoside modified)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pfizer-BioNTech COVID-19 Vaccine is a sterile suspension for injection for intramuscular use. COVID-19 Vaccine is supplied in a multiple dose vial with an orange cap and a label with an orange border.

Pfizer-BioNTech COVID-19 Vaccine, Multiple Dose Vial with Orange Cap and Label with Orange Border

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
5 through 11 years (Vial labels state: Age 5y to <12y)	Dilute with 1.3 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	10	0.2 mL

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pfizer-BioNTech COVID-19 Vaccine is a suspension for injection.

After preparation, each dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with orange caps and labels with orange borders is 0.2 mL for individuals 5 through 11 years of age

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pfizer-BioNTech COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) 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.

4.2 Posology and method of administration

Posology

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a primary series of 2 doses (0.2 mL each) 3 weeks apart in individuals 5 through 11 years of age.

Paediatric population

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with orange caps and labels with orange borders for use in individuals 5 through 11 years of age is based on safety and effectiveness data in this age group and in adolescents and adults.

For adolescents 12 through 17 years of age, a different formulation and a different presentation of this formulation of the Pfizer-BioNTech COVID-19 Vaccine are authorized.

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine does not include use in individuals younger than 5 years of age.

Method of administration

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

Visually inspect each dose in the dosing syringe prior to administration. The 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 discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine with orange caps and labels with orange borders 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. 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 content.
- Do not pool excess vaccine from multiple vials.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine listed in section 6.1.

4.4 Special warnings and precautions for use

Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine.

Limitation of Effectiveness

The Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

4.5 Interaction with other medicinal products and other forms of interaction

There are no data to assess the concomitant administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

4.6 Fertility, pregnancy and lactation

Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of Pfizer-BioNTech COVID-19 Vaccine was administered to female rats by the intramuscular route on 4 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.

Breastfeeding

Risk Summary

Data are not available to assess the effects of Pfizer-BioNTech COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

Fertility

In a developmental toxicity study in rats with Pfizer-BioNTech COVID-19 Vaccine there were no

vaccine-related effects on female fertility.

4.7 Effects on ability to drive and use machines

Not available.

4.8 Undesirable effects

4.8.1: adverse reactions:

In a clinical study in children 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine containing 10 mcg of a nucleoside-modified messenger RNA encoding the viral spike (S) glycoprotein of SARS-CoV-2 (10 mcg modRNA), adverse reactions following administration of any primary series dose 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%), nausea (0.4%), rash (0.3%), malaise (0.1%), and decreased appetite (0.1%).

Post Authorization Experience in Individuals 12 Years of Age and Older

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

4.8.2 Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of the primary series Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 5 years of age and older in 3 clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America.

Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 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 43,448 participants [21,720 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 21,728 placebo] in Phase 2/3 are 16 years of age or older (including 138 and 145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2,260 adolescents are 12 through 15 years of age (1,131 and 1,129 in the vaccine and placebo groups, respectively). Study C4591007 (Study 3) is a Phase 1/2/3 multicenter, randomized, dose-finding, open-label (Phase 1) and multinational, saline placebo-controlled, observer-blind, immunogenicity and efficacy (Phase 2/3) study that has enrolled 4,695 participants 5 through 11 years of age, of whom 3109 participants received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 1538 participants received placebo in Phase 2/3.

In Study 2 and Study 3, all participants 5 through 11 years of age, 12 through 15 years of age, and 16 years of age and older in the reactogenicity subset, were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination]. Tables 1 and 2 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID

19 Vaccine (10 mcg modRNA) and placebo in children 5 through 11 years of age.

Children 5 Through 11 Years of Age

In an analysis of Study 3 Phase 2/3, based on data up to the cutoff date of September 06, 2021, 2,268 participants [1,518 Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA); 750 placebo] were 5 through 11 years of age. Of these, 2,158 (95.1%) [1,444 Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 714 placebo] participants have been followed for at least 2 months after the second dose. An analysis of Study 3 Phase 2/3 adverse event data also included another 2,379 participants [1,591 Pfizer BioNTech COVID-19 Vaccine (10 mcg modRNA) and 788 placebo], of whom 71.2% had a follow-up period for at least 2 weeks after Dose 2 up to the cutoff date of October 8, 2021. The safety evaluation in Study 3 is ongoing.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and those who received placebo. Among the 4,647 participants 5 through 11 years of age who received at least 1 dose of the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA), 51.8% were male and 48.2% were female, 77.3% were White, 5.8% were Black or African American, 16.9% were Hispanic/Latino, 8.3% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions
The mean duration of pain at the injection site after Dose 2 was 2.3 days (range 1 to 11 days), for redness 2.2 days (range 1 to 10 days), and for swelling 2.2 days (range 1 to 10 days) for children in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group up to the cutoff date of September 06, 2021.

Table 1: Study 3 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Children 5 Through 11 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	**Placebo Dose 1 N[a,b]=748 n[c] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± 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)
Mild	143 (9.5)	37 (4.9)	143 (9.5)	31 (4.2)
Moderate	79 (5.2)	6 (0.8)	132 (8.8)	9 (1.2)
Severe	0	0	3 (0.2)	0
Swelling[d]				
Any (≥0.5 cm)	158 (10.5)	20 (2.7)	229 (15.3)	20 (2.7)
Mild	85 (5.6)	13 (1.7)	117 (7.8)	15 (2.0)
Moderate	72 (4.8)	7 (0.9)	112 (7.5)	5 (0.7)
Severe	1 (0.1)	0	0	0
Pain at the injection site[e]				
Any	1119 (74.1)	234 (31.3)	1065 (71.0)	218 (29.5)
Mild	890 (58.9)	204 (27.3)	793 (52.8)	192 (25.9)
Moderate	225 (14.9)	30 (4.0)	267 (17.8)	26 (3.5)
Severe	4 (0.3)	0	5 (0.3)	0

Note: Reactions were collected in an 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.

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)

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. Mild: ≥0.5 to ≤2.0 cm; Moderate: >2.0 to ≤7.0 cm; Severe: >7.0 cm.
e. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

Table 2: Study 3 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Children 5 Through 11 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	Pfizer-BioNTech COVID-19 Vaccine± 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)
≥38.0°C to 38.4°C	23 (1.5)	4 (0.5)	51 (3.4)	5 (0.7)
>38.4°C to 38.9°C	12 (0.8)	5 (0.7)	38 (2.5)	3 (0.4)
>38.9°C to 40.0°C	3 (0.2)	1 (0.1)	8 (0.5)	1 (0.1)
>40.0°C	0	0	1 (0.1)	0
Fatigue[d]				
Any	508 (33.6)	234 (31.3)	592 (39.4)	180 (24.3)
Mild	333 (22.0)	150 (20.1)	321 (21.4)	96 (13.0)
Moderate	171 (11.3)	83 (11.1)	260 (17.3)	83 (11.2)
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)
Mild	249 (16.5)	131 (17.5)	281 (18.7)	93 (12.6)
Moderate	88 (5.8)	45 (6.0)	136 (9.1)	45 (6.1)
Severe	2 (0.1)	4 (0.5)	3 (0.2)	0
Chills[d]				
Any	70 (4.6)	35 (4.7)	147 (9.8)	32 (4.3)
Mild	54 (3.6)	30 (4.0)	105 (7.0)	24 (3.2)
Moderate	16 (1.1)	5 (0.7)	40 (2.7)	7 (0.9)
Severe	0	0	2 (0.1)	1 (0.1)
Vomiting[e]				
Any	33 (2.2)	11 (1.5)	28 (1.9)	6 (0.8)
Mild	26 (1.7)	11 (1.5)	27 (1.8)	6 (0.8)
Moderate	7 (0.5)	0	1 (0.1)	0
Severe	0	0	0	0
Diarrhea[f]				
Any	89 (5.9)	31 (4.1)	79 (5.3)	35 (4.7)
Mild	79 (5.2)	31 (4.1)	72 (4.8)	32 (4.3)
Moderate	10 (0.7)	0	7 (0.5)	3 (0.4)

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 Na=1511 nc (%)	Placebo Dose 1 Na,b=748 nc (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 Na=1501 nc (%)	Placebo Dose 2 Na,b=740 nc (%)
Severe	0	0	0	0
New or worsened muscle pain[d]				
Any	137 (9.1)	51 (6.8)	175 (11.7)	55 (7.4)
Mild	96 (6.4)	35 (4.7)	116 (7.7)	38 (5.1)
Moderate	40 (2.6)	16 (2.1)	58 (3.9)	17 (2.3)
Severe	1 (0.1)	0	1 (0.1)	0
New or worsened joint pain[d]				
Any	50 (3.3)	41 (5.5)	78 (5.2)	27 (3.6)
Mild	34 (2.3)	31 (4.1)	57 (3.8)	20 (2.7)
Moderate	16 (1.1)	10 (1.3)	21 (1.4)	7 (0.9)
Severe	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 an 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. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

e. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

f. 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.

g. Severity was not collected for use of antipyretic or pain medication.

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

± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

Unsolicited Adverse Events

In the following analyses of Study 3 in children 5 through 11 years of age (1,518 of whom received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 750 of whom received placebo), 99.5% of participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events

In 1 group of participants (initial enrollment cohort) with a median of 2.3 months follow-up post Dose 2, no serious adverse events were reported that were considered related to vaccination. In a second group of participants (expansion cohort) with a median of 2.4 weeks follow-up post Dose 2, no serious adverse events were reported that were considered related to vaccination.

Non-Serious Adverse Events

In 1 group of participants (initial enrollment cohort), non-serious adverse events from Dose 1 through up to 30 days after Dose 2 up to the cutoff date of September 06, 2021, in ongoing follow-up were reported by 10.9% of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) recipients and by 9.1% of placebo recipients. In this group of participants, >99% had follow-up 30 days post Dose 2. In a second group of participants (expansion cohort) for which the median follow-up was 2.4 weeks

(range 0 – 3.7 weeks), non-serious adverse events from Dose 1 through the cutoff date of October 8, 2021, were reported by 7.1% of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) recipients and by 6.3% of placebo recipients.

In the initial enrollment cohort, from Dose 1 through 30 days after Dose 2, lymphadenopathy was reported in 13 (0.9%) participants in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group vs. 1 (0.1%) in the placebo group. In the expansion cohort from Dose 1 through the cut-off date, lymphadenopathy was reported in 6 (0.4%) participants in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group vs. 3 (0.4%) in the placebo group. There were no other notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Adolescents 12 Through 15 Years of Age

In an analysis of Study 2, based on data up to the cutoff date of March 13, 2021, 2,260 adolescents [1,131 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 1,129 placebo] were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) adolescents have been followed for at least 2 months after the second dose. The safety evaluation in Study 2 is ongoing.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among adolescents who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the adolescents who received the Pfizer-BioNTech COVID-19 Vaccine, 50.1% were male and 49.9% were female, 85.9% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Unsolicited Adverse Events

In the following analyses of Study 2 in adolescents 12 through 15 years of age (1,131 of whom received Pfizer-BioNTech COVID-19 Vaccine and 1,129 of whom received placebo), 98.3% of study participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events
Serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.1% of placebo recipients. There were no notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events
Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 5.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 5.8% of placebo recipients. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy plausibly related to the study intervention were imbalanced, with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (7) vs. the placebo group (1). There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 16 Years of Age and Older

At the time of the analysis of Study 2 for the EUA, 37,586 [18,801 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) and 18,785 placebo] participants 16 years of age or older had been followed for a median of 2 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants 16 years and

older enrolled by October 9, 2020, and includes safety data accrued through November 14, 2020.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the total participants who received either the Pfizer-BioNTech COVID-19 Vaccine or placebo, 50.6% were male and 49.4% were female, 83.1% were White, 9.1% were Black or African American, 28.0% were Hispanic/Latino, 4.3% were Asian, and 0.5% were American Indian/Alaska Native.

Unsolicited Adverse Events

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 (Pfizer-BioNTech COVID-19 Vaccine = 10,841; placebo = 10,851), serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.3% of placebo recipients. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 7,960, placebo = 7,934), serious adverse events were reported by 0.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.6% of placebo recipients who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

Appendicitis was reported as a serious adverse event for 12 participants, and numerically higher in the vaccine group, 8 vaccine participants and 4 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, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events
In Study 2 in which 10,841 participants 16 through 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 10,851 participants received placebo, non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up 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 a similar analysis in which 7,960 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. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following vaccination that are consistent with adverse reactions solicited among participants in the reactogenicity subset. 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. Throughout the safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the Pfizer-BioNTech COVID-19 Vaccine group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of Bell's palsy were reported in the placebo group. 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 Pfizer-BioNTech COVID-19 Vaccine.

4.8.3 Postmarketing Experience

The following adverse reactions have been identified during post authorization use of Pfizer-BioNTech COVID-19 Vaccine. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)
Nervous System Disorders: syncope

To report any side effect(s):

Saudi Arabia:

The National Pharmacovigilance Centre (NPC):
- SFDA Call Center: 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: https://ade.sfda.gov.sa/

Other GCC States:

- Please contact the relevant competent authority.

4.9 Overdose

Not available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

The modRNA in the Pfizer-BioNTech COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Clinical efficacy and safety

Efficacy in Participants 16 Years of Age and Older

Study 2 is 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 preexisting 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 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) or placebo separated by 21 days. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the Pfizer-BioNTech COVID-19 Vaccine 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 3 presents the specific demographic characteristics in the studied population.

Table 3: Demographics (population for the primary efficacy endpoint)[a]

	Pfizer-BioNTech COVID-19 Vaccine* (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 through 15 years[b]	46 (0.3)	42 (0.2)
≥16 through 17 years	66 (0.4)	68 (0.4)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 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[c]	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[d]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

* Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

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. 100 participants 12 through 15 years of age with limited follow-up in the randomized population received at least 1 dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the efficacy evaluation depending on the population analyzed. They contributed to exposure information but with no confirmed COVID-19 cases, and did not affect efficacy conclusions.

c. Includes multiracial and not reported.

d. 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)

	Pfizer-BioNTech COVID-19 Vaccine* (N=18,242) n (%)	Placebo (N=18,379) n (%)

- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 4.

Table 4: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine± Na=18,198 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=18,325 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All subjects[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	**Pfizer-BioNTech COVID-19 Vaccine± Na=19,965 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,172 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All subjects[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).

* 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.

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

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 through 15 years of age.
f. Credible interval for vaccine efficacy (VE) was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=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. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Efficacy of Primary Series in Children 5 Through 11 Years of Age

A descriptive efficacy analysis of Study 3 has been performed in 1,968 children 5 through 11 years of age without evidence of infection prior to 7 days after Dose 2. This analysis evaluated confirmed symptomatic COVID-19 cases accrued up to a data cutoff date of October 8, 2021.

Table 5 presents the specific demographic characteristics in participants who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose.

Table 5: Demographics Characteristics – Participants Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 – 5 Through 11 Years of Age – Evaluable Efficacy Population

	Pfizer-BioNTech COVID-19 Vaccine* 10 mcg/Dose (N[a]=1305) n[b] (%)	**Placebo (N[a]=663) n[b] (%)**
Sex		
Male	679 (52.0)	343 (51.7)
Female	626 (48.0)	320 (48.3)
Age at Vaccination		
Mean (SD)	8.2 (1.93)	8.1 (1.98)
Median	8.0	8.0
Min, max	(5, 11)	(5, 11)
Race		
White	1018 (78.0)	514 (77.5)
Black or African American	76 (5.8)	48 (7.2)
American Indian or Alaska Native	<1.0%	<1.0%
Asian	86 (6.6)	46 (6.9)
Native Hawaiian or other Pacific Islander	<1.0%	<1.0%
Other[c]	110 (8.4)	52 (7.8)
Ethnicity		
Hispanic or Latino	243 (18.6)	130 (19.6)
Not Hispanic or Latino	1059 (81.1)	533 (80.4)
Not reported	<1.0%	<1.0%
Comorbidities[d]		
Yes	262 (20.1)	133 (20.1)
No	1043 (79.9)	530 (79.9)

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).
a. N = number of participants in the specified group from the evaluable efficacy population with no evidence of SARS CoV-2 infection prior to 7 days after Dose 2. This value is the denominator for the percentage calculations. Evaluable efficacy population included all eligible randomized participants who received all vaccination(s) as randomized within the predefined window, had no other important protocol deviations as determined by the clinician.
b. n = Number of participants with the specified characteristic.
c. Includes multiracial and not reported.
d. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least 1 of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI ≥ 95th percentile).

The descriptive vaccine efficacy results in children 5 through 11 years of age without evidence of prior SARS-CoV-2 infection are presented in Table 6. None of the cases accrued met criteria for severe COVID-19 or multisystem inflammatory syndrome in children (MIS-C). No cases of COVID-19 were observed in either the vaccine group or the placebo group in participants with evidence of prior SARS-CoV-2 infection.

Table 6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 –Children 5 Through 11 Years of Age Evaluable Efficacy Population

First COVID-19 occurrence from 7 days after Dose 2 in children 5 through 11 years of age without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine± 10 mcg/dose N[a]=1305 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=663 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
Children 5 through 11 years of age	3 0.322 (1273)	16 0.159 (637)	90.7 (67.7, 98.3)

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.

± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

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.

Immunogenicity of Primary Series in Children 5 Through 11 Years of Age

SARS-CoV-2 50% neutralizing antibody titers (NT50) 1 month after the primary series were compared between randomly selected subsets of Phase 2/3 participants 5 through 11 years of age from study C4591007 and the efficacy study C4591001 Phase 2/3 participants 16 through 25 years of age, using a microneutralization assay against the reference strain (USA_WA1/2020). The primary immunobridging analyses compared the geometric mean titers (using a geometric mean ratio [GMR]) and the seroresponse (defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from before Dose 1) rates in the evaluable immunogenicity population of participants without evidence of prior SARS-CoV-2 infection up to 1 month after Dose 2 in each group. The prespecified immunobridging criteria were met for both the GMR and the seroresponse difference (Table 7 and Table 8).

Table 7: SARS-CoV-2 GMTs (NT50) at 1 Month After Primary Series – Immunobridging Subset - Participants 5 Through 11 Years of Age (Study 3) and Participants 16 Through 25 Years of Age (Study 2) – Without Evidence of SARS-CoV-2 Infection up to 1 Month After Dose 2 – Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine		GMT Ratio (95%CI) (5 Through 11 Years of Age/ 16 Through 25 Years of Age)[d,e]
		10 mcg/Dose* 5 Through 11 Years of Age n[a]=264	30 mcg/Dose± 16 Through 25 Years of Age n[a]=253	
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	
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)

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 pre-Dose 1 and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at pre-Dose 1 and pre-Dose 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.

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

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. GMT ratio and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1 [5 through 11 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 GMT ratio 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.

Table 8: Percentages of Participants with Seroresponse at 1 Month After Primary Series – Immunobridging Subset –Participants 5 Through 11 Years of Age (Study 3) and Participants 16 Through 25 Years of Age (Study 2) Without Evidence of Infection up to 1 Month After Dose 2 – Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine		Difference in Seroresponse Rates %[e] (95% CI[f]) (5 Through 11 Years of Age minus 16 Through 25 Years of Age)[g]
		10 mcg/Dose* 5 Through 11 Years of Age N[a]=264	30 mcg/Dose± 16 Through 25 Years of Age N[a]=253	
Assay	Time Point[b]	n[c] (%) (95% CI[d])	n[c] (%) (95% CI[d])	
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)

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.

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).
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 11 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.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Pfizer-BioNTech COVID-19 Vaccine has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each 0.2 mL dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with orange caps and labels with orange borders also includes the following ingredients: lipids (0.14 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.02 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.03 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.06 mg cholesterol), 10.3 mg sucrose, 0.02 mg tromethamine, and 0.13 mg tromethamine hydrochloride. The diluent (sterile 0.9% Sodium Chloride Injection, USP) contributes 0.9 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine does not contain preservative.
The vial stoppers are not made with natural rubber latex.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Do not use this medicine after the expiry date which is stated on the carton and label after EXP.

Vial Storage Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with orange caps and labels with orange borders 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 [2ºC to 8ºC (35ºF to 46ºF)], 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 -90ºC to -60ºC (-130ºF to -76ºF). 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 Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with orange caps and labels with orange borders may also arrive at 2°C to 8°C. If 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 2ºC to 8ºC (35ºF to 46ºF), allow vials to thaw at room temperature [up to 25ºC (77ºF)] for 30 minutes.

Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with orange caps and labels with orange borders may be stored at 8°C to 25°C (46°F to 77°F) for a total of 12 hours prior to dilution. After dilution, the vial should be held between 2°C to 25°C (35°F to 77°F). Vials should be discarded 12 hours after dilution.

Vial labels and cartons may state that a vial should be discarded 6 hours after the first puncture. The information in this Full EUA Prescribing Information supersedes the number of hours printed on vial labels and cartons.

Transportation of Vials

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

6.4 Special precautions for storage

Store in a freezer at -90 °C to -60 °C.
Store in the original package in order to protect from light.

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

Do not refreeze thawed vials.

For storage conditions after thawing and dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

the Pfizer-BioNTech COVID-19 Vaccine that is supplied in multiple dose vials with orange caps and labels with orange borders. These multiple dose vials are supplied in a carton containing 10 multiple dose vials (NDC 59267-1055-4). After dilution, 1 vial contains 10 doses of 0.2 mL.

6.6 Special precautions for disposal and other handling

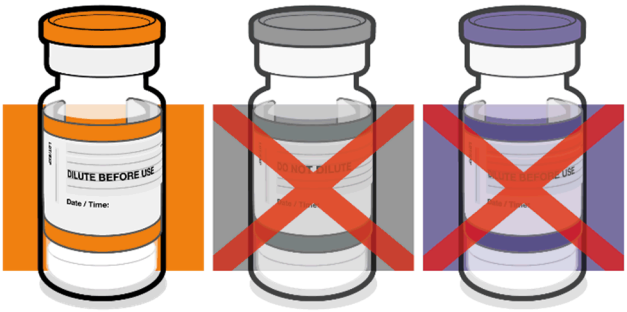
Each vial **MUST BE DILUTED** before administering the vaccine.

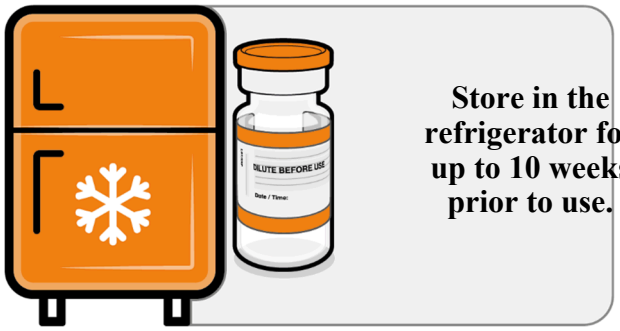
Prior to Dilution

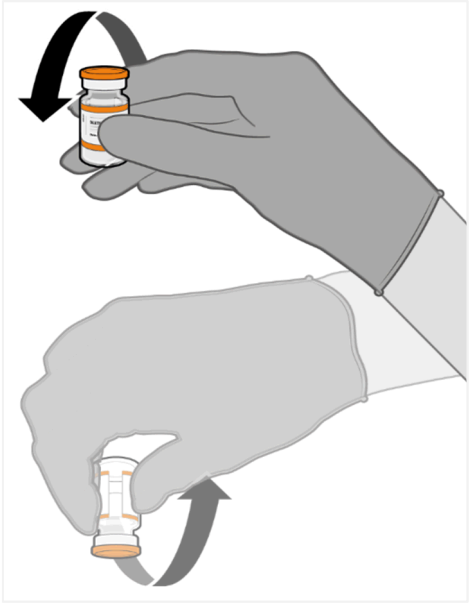
- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with an orange cap and a label with an orange border contains a volume of 1.3 mL and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
  - Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)].
  - Refer to thawing instructions in the panels below.

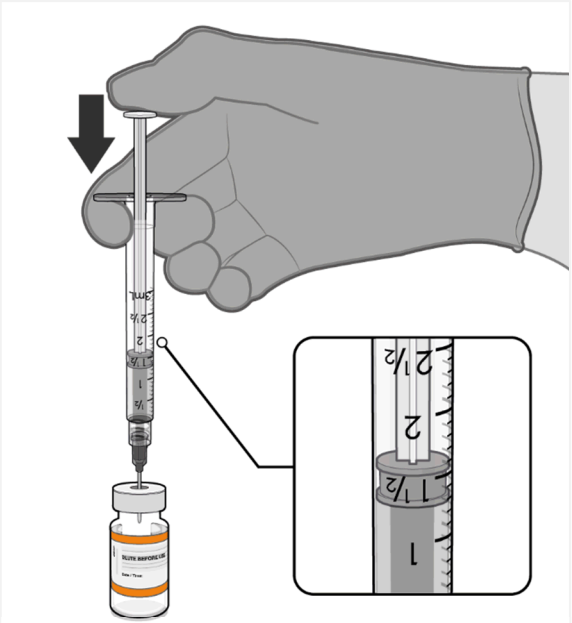
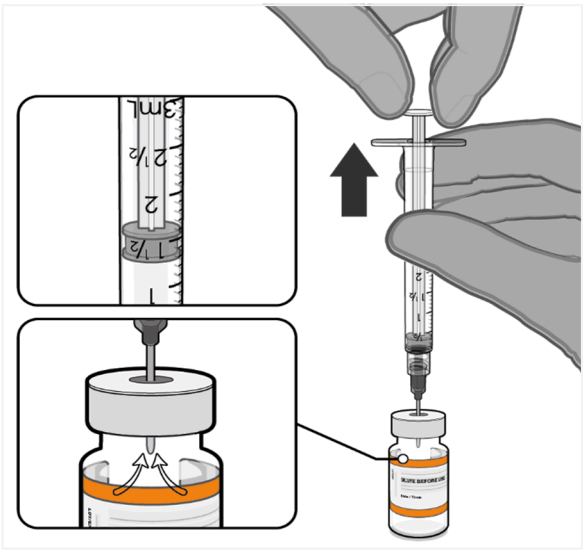
Dilution

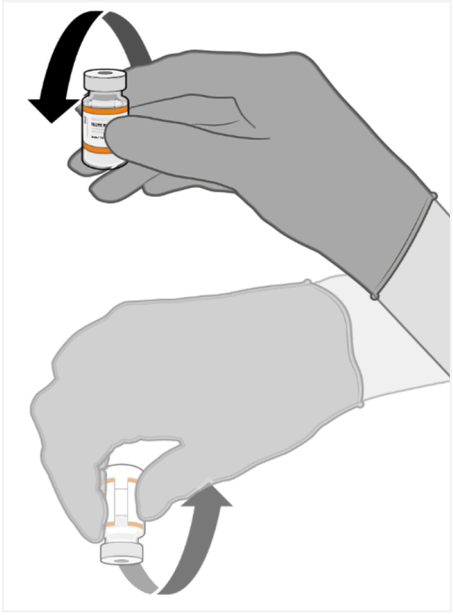
- Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent. Do not add more than 1.3 mL of diluent.
- After dilution, 1 vial contains 10 doses of 0.2 mL.

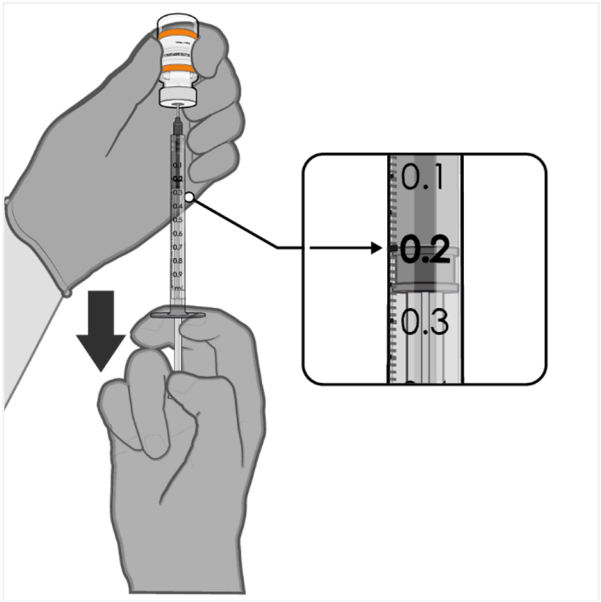
<table>
<tr><td colspan="2">Dilution and Preparation Instructions</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and a Label with Orange Border – VIAL VERIFICATION</td></tr>
<tr><td> 

✓ Orange plastic cap and label with orange border.</td><td>• Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has an orange plastic cap and a label with an orange border and states “Age 5y to < 12y.”.</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border – THAWING PRIOR TO DILUTION</td></tr>
<tr><td> 
</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. 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.
o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
o Vials may be stored at room temperature [up to 25ºC (77ºF)] for 12 hours prior to use.</td></tr>
</table>

Dilution and Preparation Instructions	
 **Gently × 10**	• Before dilution, mix by inverting vaccine vial gently 10 times. • <u>Do not shake</u>. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.

Dilution and Preparation Instructions	
Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border - DILUTION	
 **Add 1.3 mL of sterile 0.9% sodium chloride injection, USP.**	• 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 (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.
 **Pull back plunger to 1.3 mL to remove air from vial.**	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.3 mL air into the empty diluent syringe.

Dilution and Preparation Instructions	
 **Gently × 10**	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be a white to off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
 Use within 12 hours after dilution.	• Record the date and time of first vial puncture on the vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 12 hours after dilution.

Dilution and Preparation Instructions	
Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border - WITHRAWAL OF INDIVIDUAL 0.2 mL DOSES	
 **Withdraw 0.2 mL dose of vaccine**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.2 mL of the Pfizer-BioNTech COVID-19 Vaccine 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.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

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8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 10 December 2020

9. DATE OF REVISION OF THE TEXT

October 2021

Document Approval Record

Document Name:	Saudi Arabia 5-11 years-Emergency Use_Pfizer-BioNTECH COVID-19 vaccine_LPD
Document Title:	October 2021

Signed By:	Date(GMT)	Signing Capacity
Jundi, Reda	23-Nov-2021 08:19:27	Regulatory Affairs Approval
Elgouhary, Ahmed Tarek Fouad	24-Nov-2021 09:40:29	Manager Approval