コミナティ筋注 5～11 歳用
に関する資料

ファイザー株式会社

1. 起源又は発見の経緯

1.1. 製品開発の根拠

当該内容については M2.5.1 項参照。

2. 開発の経緯図

開発の経緯図を Table 1 に示す。

Table 1.　開発の経緯図

試験項目		試験内容	2021 年（令和 3 年）			
			1-3月	4-6月	7-9月	10-12月
品質に関する試験	外国	製剤	[redacted]			
		その他				
臨床試験	外国	第I/II/III相 (C4591007)	3			継続中

1. 外国における承認申請状況

コミナティ筋注は，SARS-CoV-2 ウイルスによって引き起こされるコロナウイルス感染症 2019（COVID-19）の予防について，最初に英国で 2020 年 12 月 2 日に Temporary authorization under regulation 174 を取得した［2021 年 4 月 22 日に条件付き販売承認（Conditional marketing authorization approval）取得］。その後，2020 年 12 月 9 日にカナダで authorization under the Interim Order を，2020 年 12 月 11 日に米国で緊急使用許可（Emargency Use Approval：EUA）を，2020 年 12 月 21 日に欧州連合で条件付き販売承認（中央審査手続き）を，2021 年 1 月 24 日にオーストラリアで条件付き販売承認をそれぞれ取得した。当初，投与の対象は 16 歳以上であったが，2021 年 5 月以降，順次 12 歳以上に拡大されている。2021 年 9 月 30 日現在，コミナティ筋注は 90 以上の国または地域で使用可能となっている。

さらに米国では，2021 年 8 月 12 日，EUA が改訂され，臓器移植を受けた人または同等の免疫不全状態と考えられると診断された人への追加投与（3 回目の投与）が可能となった。また，16 歳以上における投与について 2021 年 8 月 23 日に biologics license application（BLA）の正式承認を取得した。

追加接種については，米国では 2021 年 8 月 25 日に段階的な BLA の一部変更申請（supplemental BLA）を開始したが，審査の結果，65 歳以上の者，ならびに 18 歳以上 64 歳以下で重症 COVID-19 のリスクが高い者および SARS-CoV-2 への頻繁な職業性曝露により重症 COVID-19 を含む COVID-19 の重篤な合併症のリスクが高い者を対象に，コミナティ筋注 2 回目接種から少なくとも 6 ヵ月経過後のコミナティ筋注の追加接種に関する EUA を 2021 年 9 月 22 日に取得した。また，欧州連合では 2021 年 10 月 5 日に，18 歳以上の者に対して COVID-19 ワクチンの 2 回目接種から少なくとも 6 ヵ月経過後に追加接種を可能とする条件付き販売承認の一部変更が承認された。

本剤（5～11 歳用製剤）については，2021 年 10 月 29 日に米国で EUA を，2021 年 11 月 26 日に欧州連合で条件付き販売承認の一部変更承認を取得した。

外国の添付文書として，米国添付文書および欧州製品概要（原文および和訳），ならびにコアデータシートを添付した。

（添付資料）

・米国添付文書（原文）

・米国添付文書（和訳）

・欧州製品概要（SmPC）（原文）

・欧州製品概要（SmPC）（和訳）

・コアデータシート

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

FOR 5 THROUGH 11 YEARS OF AGE
DILUTE BEFORE USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 5 years of age and older.

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with an orange cap and a label with an orange border which is authorized for use to provide a 2-dose primary series to individuals 5 through 11 years of age. The vial labels state: Age 5y to <12y. The carton labels state: For age 5 years to <12 years.

Pfizer-BioNTech COVID-19 Vaccine which is supplied in a multiple dose vial with an orange cap and a label with an orange border, should not be used in individuals 12 years of age and older.[1]

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine. See “MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION” for reporting requirements.

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

The Pfizer-BioNTech COVID-19 Vaccine, which is supplied in a multiple dose vial with an orange cap and a label with an orange border, is administered, after

[1] Notwithstanding the age limitations for use of the different formulations and presentations described above, individuals who will turn from 11 years to 12 years of age between their first and second dose in the primary regimen may receive, for either dose, either: (1) the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 5 through 11 years of age (each 0.2 mL dose containing 10 mcg modRNA) (supplied in multidose vials with orange caps); or (2) COMIRNATY (COVID-19 Vaccine, mRNA) or the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age and older (each 0.3 mL dose containing 30 mcg modRNA) (supplied in multidose vials with gray caps and multidose vials with purple caps).

dilution, as a primary series of 2 doses (0.2 mL each) 3 weeks apart in individuals 5 through 11 years of age.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine for active immunization against COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

The storage, preparation, and administration information in this Fact Sheet apply to the Pfizer-BioNTech COVID-19 Vaccine which is supplied in a multiple dose vial with an orange cap and a label with an orange border and **MUST BE DILUTED** before use.

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

Storage and Handling

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

Do not refreeze thawed vials.

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.

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 9 months from the date of manufacture printed on the vial and cartons. Expiry dates based on 9 months from the date of the manufacture are shown below.

Printed Manufacturing Date	**9-Month Expiry Date**
06/2021	28-Feb-2022
07/2021	31-Mar-2022
08/2021	30-Apr-2022
09/2021	31-May-2022
10/2021	30-Jun-2022
11/2021	31-Jul-2022
12/2021	31-Aug-2022
01/2022	30-Sep-2022
02/2022	31-Oct-2022

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 room temperature [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 2ºC 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 Fact Sheet 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).

Dosing and Schedule

The Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with orange caps and labels with orange borders is administered intramuscularly as a primary series of 2 doses (0.2 mL each) 3 weeks apart to individuals 5 through 11 years of age.

Pfizer-BioNTech COVID-19 Vaccine that is supplied in vials with purple or gray caps should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors.

Dose Preparation

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

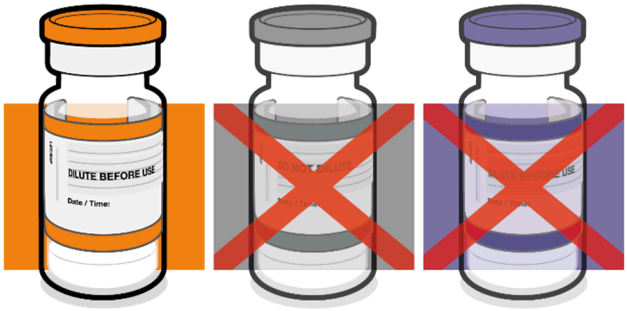
Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine.

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.

Dilution and Preparation Instructions

Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border –
VIAL VERIFICATION



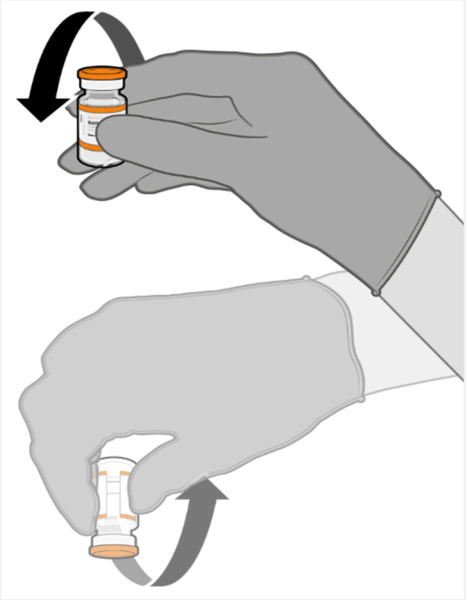
✓ **Orange plastic cap and label with orange border.**

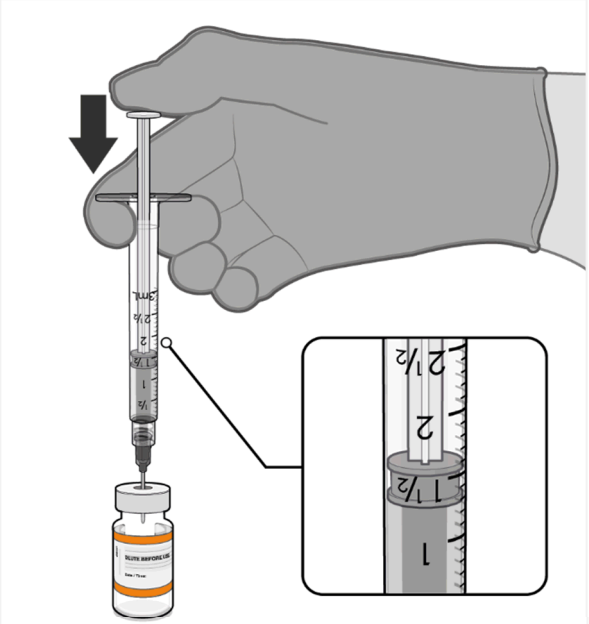
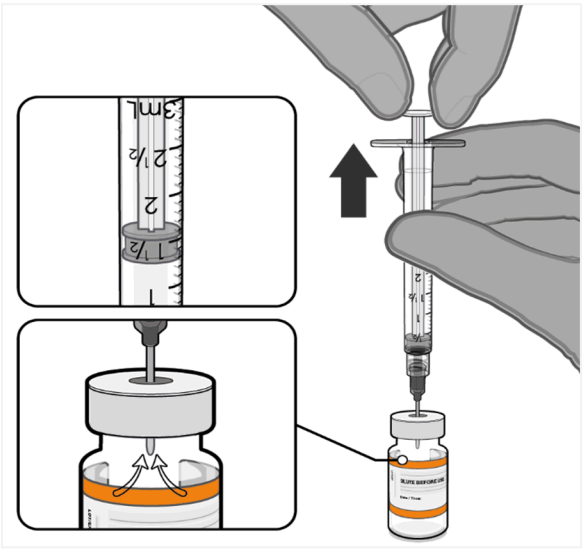
- Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has an orange plastic cap and a label with an orange border and states "Age 5y to < 12y."

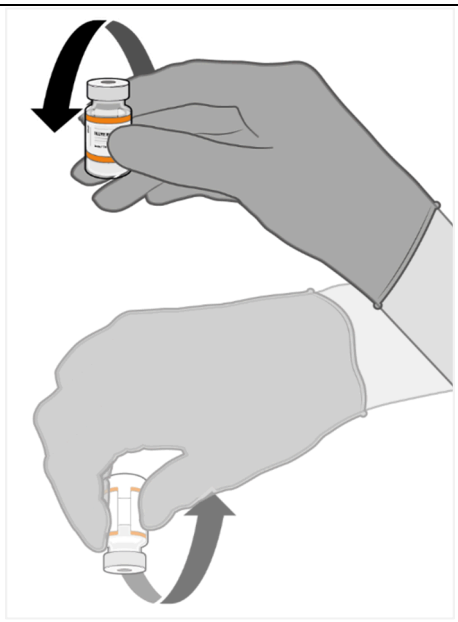
Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border –
THAWING PRIOR TO DILUTION

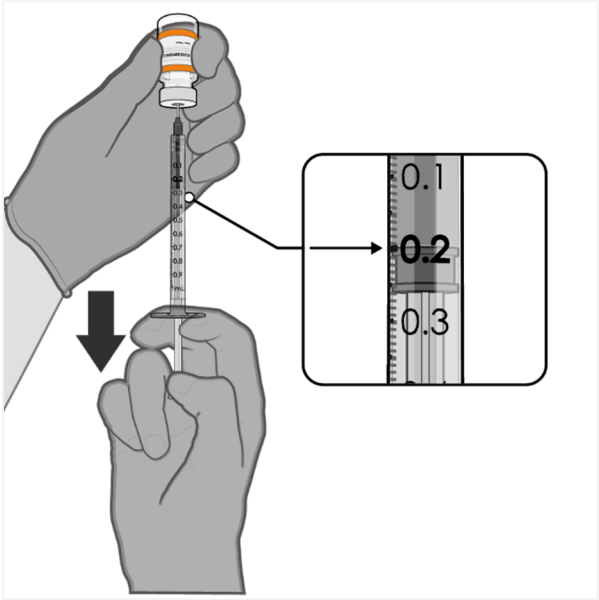
Store in the refrigerator for up to 10 weeks prior to use.

- Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
  - 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.
  - Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
  - Vials may be stored at room temperature [up to 25ºC (77ºF)] for up to 12 hours prior to use.

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 sterile 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.

Administration

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.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

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.

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 *(see Full EUA Prescribing Information)*.

Warnings

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

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

Adverse Reactions

Adverse Reactions in Clinical Trials
Adverse reactions in children 5 through 11 years following administration of the primary series included pain at the injection site, fatigue, headache, injection site redness, injection site swelling, muscle pain, chills, fever, joint pain, lymphadenopathy, nausea, malaise, decreased appetite, and rash *(see Full EUA Prescribing Information)*.

Adverse Reactions in Individuals 12 years of Age and Older in Post Authorization Experience
Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), diarrhea, vomiting, pain in extremity (arm), and syncope 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.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Pfizer-BioNTech COVID-19 Vaccine.

Use with Other Vaccines

There is no information on the co-administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Vaccine Information Fact Sheet) prior to the individual receiving each dose of Pfizer-BioNTech COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse Pfizer-BioNTech COVID-19 Vaccine.
- The significant known and potential risks and benefits of Pfizer-BioNTech COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Pfizer-BioNTech COVID-19 Vaccine.

Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION[2]

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of Pfizer-BioNTech COVID-19 Vaccine, the following items are required. Use of unapproved Pfizer-BioNTech COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. Pfizer-BioNTech COVID-19 Vaccine is authorized for use in individuals 5 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Pfizer-BioNTech COVID-19 Vaccine or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" prior to the individual receiving Pfizer-BioNTech COVID-19 Vaccine.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):
    - vaccine administration errors whether or not associated with an adverse event,
    - serious adverse events* (irrespective of attribution to vaccination),
    - cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
    - cases of COVID-19 that result in hospitalization or death.

[2] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of MIS in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine to recipients.

* Serious adverse events are defined as:
- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND PFIZER INC.

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

ADDITIONAL INFORMATION

For general questions, visit the website or call the telephone number provided below.

To access the most recent Pfizer-BioNTech COVID-19 Vaccine Fact Sheets, please scan the QR code provided below.

Global website	Telephone number
www.cvdvaccine.com 	1-877-829-2619 (1-877-VAX-CO19)

AVAILABLE ALTERNATIVES

There may be clinical trials or availability under EUA of other COVID-19 vaccines.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, Health Resources & Services Administration [HRSA] COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or https://TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. In response, FDA has issued an EUA for the unapproved product, Pfizer-BioNTech COVID-19 Vaccine for active immunization against COVID-19. Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with an orange cap and a label with an orange border is authorized for use to provide a 2-dose primary series in individuals 5 through 11 years of age.

FDA issued this EUA, based on Pfizer-BioNTech's request and submitted data.

For the authorized uses, although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Pfizer-BioNTech COVID-19 Vaccine will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

The Countermeasures Injury Compensation Program

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the Pfizer-BioNTech COVID-19 Vaccine used to prevent COVID-19, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Manufactured by
Pfizer Inc., New York, NY 10017

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

LAB-1502-2.0

Revised: 16 December 2021

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

PFIZER-BIONTECH COVID-19 VACCINE

FULL EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full emergency use authorization prescribing information are not listed.

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

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.

This EUA Prescribing Information pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with an orange cap and a label with an orange border, which is authorized for use in individuals 5 through 11 years of age. The vial labels state: Age 5y to <12y. The carton labels state: For age 5 years to <12 years.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

The storage, preparation, and administration information in this Prescribing Information apply to the Pfizer-BioNTech COVID-19 Vaccine, which 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 a Label with an 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

2.1 Preparation for Administration

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

Prior to Dilution

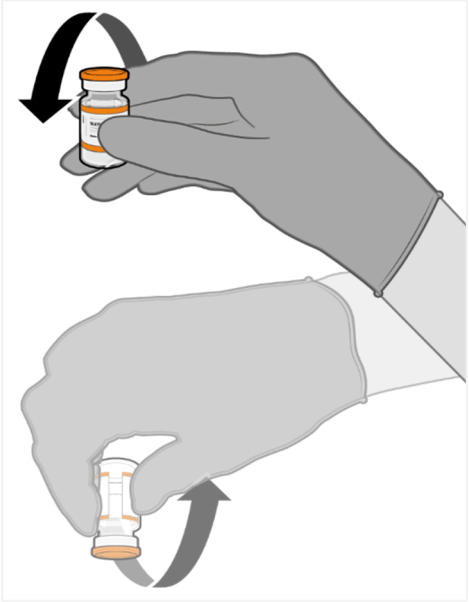
- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with an orange cap and a label with an orange border contains a volume of 1.3 mL, and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
  - Vials may be thawed in the refrigerator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

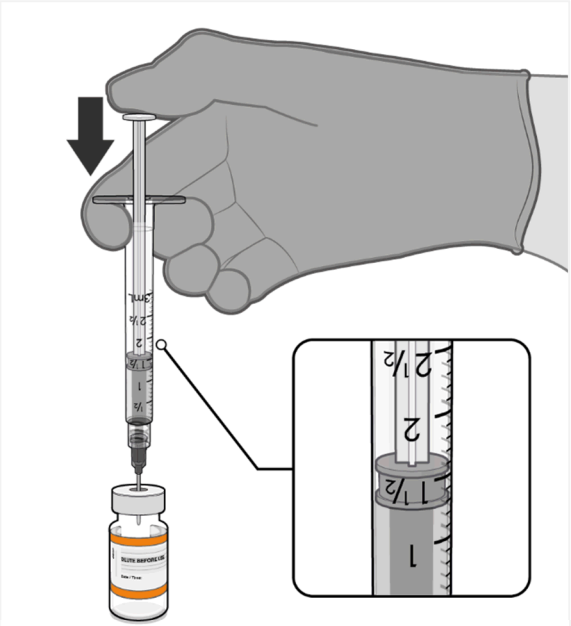
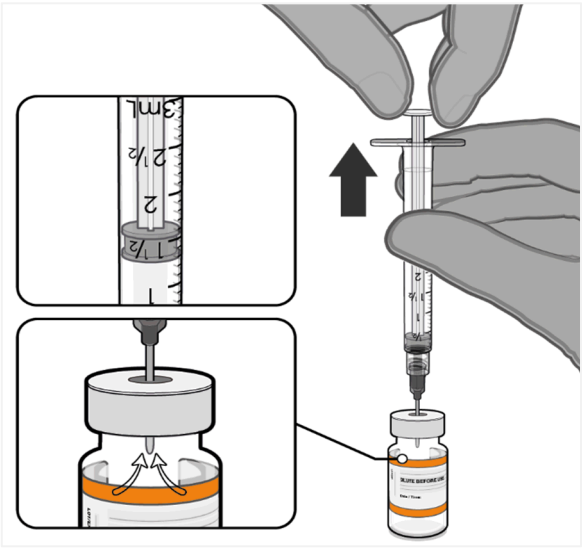
Dilution

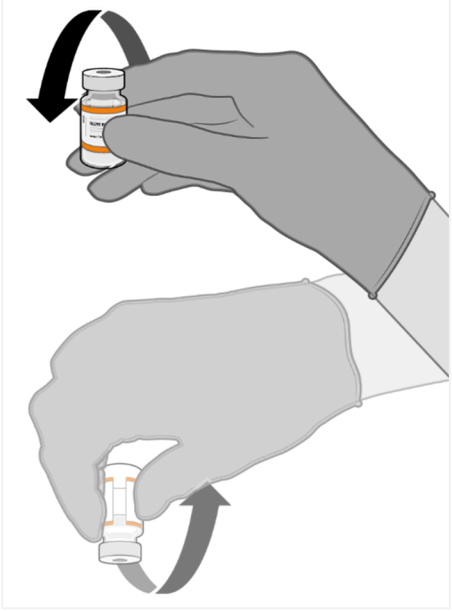
- Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not 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.

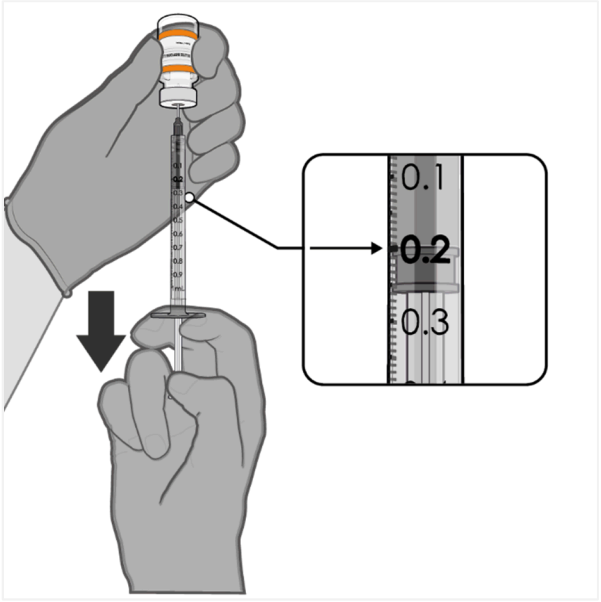
<table>
<tr><th colspan="2">Dilution and Preparation Instructions</th></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Orange Cap and Label with Orange Border – VIAL VERIFICATION</td></tr>
<tr><td> 

✓ 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 sterile 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. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be a white to off-white suspension. Do not use if vaccine is 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.

2.2 Administration Information

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.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

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.

2.3 Vaccination Schedule

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.

3 DOSAGE FORMS AND STRENGTHS

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 *[see Dosage and Administration (2.1)]*.

4 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 *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 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).

5.2 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).

5.3 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.

5.4 Altered Immunocompetence

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

5.5 Limitation of Effectiveness

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

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and hospitalized or fatal cases of COVID-19 following vaccination with the Pfizer-BioNTech COVID-19 Vaccine.[3] To the extent feasible, provide a copy of the VAERS form to Pfizer Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and Pfizer Inc.

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.

6.1 Clinical Trials 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,

[3] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

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

	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] (%)
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.
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

	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] (%)
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)
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.

6.2 Post Authorization 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

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS[4]

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following Pfizer-BioNTech COVID-19 Vaccine to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome (MIS) in children and adults
- Cases of COVID-19 that result in hospitalization or death

[4] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

*Serious adverse events are defined as:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using 1 of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of the Pfizer-BioNTech COVID-19 Vaccine
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Pfizer-BioNTech COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within 1 month prior.
2. In Box 18, description of the event:
    a. Write “Pfizer-BioNTech COVID-19 Vaccine EUA” as the first line.
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.

c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

10 DRUG INTERACTIONS

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

11 USE IN SPECIFIC POPULATIONS

11.1 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.

11.2 Lactation

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.

11.3 Pediatric Use

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.

13 DESCRIPTION

The Pfizer-BioNTech COVID-19 Vaccine in multiple dose vials with orange caps and labels with orange borders is supplied as a frozen suspension; each vial must be diluted with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. 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 contains 10 mcg of modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2.

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.

14 CLINICAL PHARMACOLOGY

14.1 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.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Primary Series 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.

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

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)
- 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 $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

g. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

18.2 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 (Na=1305) nb (%)	**Placebo (Na=663) nb (%)**
Sex		
Male	679 (52.0)	343 (51.7)
Female	626 (48.0)	320 (48.3)

	Pfizer-BioNTech COVID-19 Vaccine* 10 mcg/Dose (N[a]=1305) n[b] (%)	Placebo (N[a]=663) n[b] (%)
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.

18.3 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.

19 HOW SUPPLIED/STORAGE AND HANDLING

The information in this section applies to 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.

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

Do not refreeze thawed vials.

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.

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 9 months from the date of manufacture printed on the vial and cartons. Expiry dates based on 9 months from the date of the manufacture are shown below.

Printed Manufacturing Date	9-Month Expiry Date
06/2021	28-Feb-2022
07/2021	31-Mar-2022
08/2021	30-Apr-2022
09/2021	31-May-2022
10/2021	30-Jun-2022
11/2021	31-Jul-2022
12/2021	31-Aug-2022
01/2022	30-Sep-2022
02/2022	31-Oct-2022

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 room temperature [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).

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Vaccine Information Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.cvdvaccine.com.

Manufactured by
Pfizer Inc., New York, NY 10017

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

LAB-1503-2.0

Revised: 16 December 2021

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Comirnaty 30 micrograms/dose concentrate for dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

One vial (0.45 mL) contains 6 doses of 0.3 mL after dilution, see sections 4.2 and 6.6.

One dose (0.3 mL) contains 30 micrograms of tozinameran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for dispersion for injection (sterile concentrate).
The vaccine is a white to off-white frozen dispersion (pH: 6.9 - 7.9).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Comirnaty 30 micrograms/dose concentrate for dispersion for injection is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 12 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 12 years of age and older
Comirnaty is administered intramuscularly after dilution as a primary course of 2 doses (0.3 mL each). It is recommended to administer the second dose 3 weeks after the first dose (see sections 4.4 and 5.1).

A booster dose (third dose) of Comirnaty may be administered intramuscularly at least 6 months after the second dose in individuals 18 years of age and older. The decision when and for whom to implement a third dose of Comirnaty should be made based on available vaccine effectiveness data, taking into account limited safety data (see sections 4.4 and 5.1).

The interchangeability of Comirnaty with COVID-19 vaccines from other manufacturers to complete the primary vaccination course or the booster dose (third dose) has not been established. Individuals who have received 1 dose of Comirnaty should receive a second dose of Comirnaty to complete the primary vaccination course and for any additional doses. Doses of Comirnaty 30 micrograms/dose concentrate for dispersion for injection after dilution and Comirnaty 30 micrograms/dose dispersion for injection are considered interchangeable.

Severely immunocompromised aged 12 years and older
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised (see section 4.4).

Paediatric population
There is a paediatric formulation available for children 5 to 11 years of age (i.e. 5 to less than 12 years of age). For details, please refer to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.

Elderly population
No dosage adjustment is required in elderly individuals ≥ 65 years of age. The safety and immunogenicity of a booster dose (third dose) of Comirnaty in individuals 65 years of age and older is based on safety and immunogenicity data in adults 18 to 55 years of age.

Method of administration

Comirnaty 30 micrograms/dose concentrate for dispersion for injection should be administered intramuscularly after dilution (see section 6.6).

After dilution, vials of Comirnaty contain 6 doses of 0.3 mL of vaccine. In order to extract 6 doses from a single vial, low dead-volume syringes and/or needles should be used. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle:

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

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

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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

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

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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

General recommendations

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

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Comirnaty.

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

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees (including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

The risk of myocarditis after a third dose of Comirnaty has not yet been characterised.

Anxiety-related reactions
Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, tingling sensations and sweating) may occur in association with the vaccination process itself. Stress-related reactions are temporary and resolve on their own. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation. It is important that precautions are in place to avoid injury from fainting.

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

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

Immunocompromised individuals
The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty may be lower in immunocompromised individuals.

The recommendation to consider a third dose in severely immunocompromised individuals is based on limited serological evidence from a case-series in the literature from the clinical management of patients with iatrogenic immunocompromisation after solid organ transplantation (see section 4.2).

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

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

Excipients

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

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of Comirnaty in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of Comirnaty in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether Comirnaty is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of safety profile

The safety of Comirnaty was evaluated in participants 12 years of age and older in 2 clinical studies that included 23,205 participants (comprised of 22,074 participants 16 years of age and older and 1,131 adolescents 12 to 15 years of age) that have received at least one dose of Comirnaty.

The overall safety profile of Comirnaty in adolescents 12 to 15 years of age was similar to that seen in participants 16 years of age and older.

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

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

At the time of the analysis of Study 2 with a data cut-off of 13 March 2021 for the placebo-controlled blinded follow-up period up to the participants' unblinding dates, a total of 25,651 (58.2%) participants (13,031 Comirnaty and 12,620 placebo) 16 years of age and older were followed up for ≥ 4 months after the second dose. This included a total of 15,111 (7,704 Comirnaty and 7,407 placebo) participants 16 to 55 years of age and a total of 10,540 (5,327 Comirnaty and 5,213 placebo) participants 56 years of age and older.

The most frequent adverse reactions in participants 16 years of age and older that received 2 doses were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia (> 40%), chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

The safety profile in 545 participants 16 years of age and older receiving Comirnaty, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Adolescents 12 to 15 years of age – after 2 doses
In an analysis of Study 2, based on data up to the cut-off date of 13 March 2021, 2,260 adolescents (1,131 Comirnaty and 1,129 placebo) were 12 to 15 years of age. Of these, 1,308 adolescents (660 Comirnaty and 648 placebo) have been followed for at least 2 months after the second dose of Comirnaty. The safety evaluation in Study 2 is ongoing.

The most frequent adverse reactions in adolescents 12 to 15 years of age that received 2 doses were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).

Participants 18 years of age and older – after booster dose (third dose)
A subset from Study 2 Phase 2/3 participants of 306 adults 18 to 55 years of age who completed the original Comirnaty 2-dose course, received a booster dose (third dose) of Comirnaty approximately 6 months (range of 4.8 to 8.0 months) after receiving Dose 2.

The most frequent adverse reactions in participants 18 to 55 years of age were injection site pain (> 80%), fatigue (> 60%), headache (> 40%), myalgia (> 30%), chills and arthralgia (> 20%).

Tabulated list of adverse reactions from clinical studies and post-authorisation experience in individuals 12 years of age and older

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

Very common (≥ 1/10),
Common (≥ 1/100 to < 1/10),
Uncommon (≥ 1/1,000 to < 1/100),
Rare (≥ 1/10,000 to < 1/1,000),
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data).

Table 1: Adverse reactions from Comirnaty clinical trials and post-authorisation experience in individuals 12 years of age and older

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy[a]		
Immune system disorders			Hypersensitivity reactions (e.g. rash, pruritus, urticaria,[b] angioedema[b])		Anaphylaxis
Metabolism and nutrition disorders			Decreased appetite		
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache		Lethargy	Acute peripheral facial paralysis[c]	
Cardiac disorders					Myocarditis;[d] Pericarditis[d]
Gastrointestinal disorders	Diarrhoea[d]	Nausea; Vomiting[d]			
Skin and subcutaneous tissue disorder			Hyperhidrosis; Night sweats		
Musculoskeletal and connective tissue disorders	Arthralgia; Myalgia		Pain in extremity[e]		

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

a. A higher frequency of lymphadenopathy (5.2% vs 0.4%) was observed in participants receiving a booster dose (third dose) compared to participants receiving 2 doses.
b. The frequency category for urticaria and angioedema was Rare.
c. Through the clinical trial safety follow-up period to 14 November 2020, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group.
d. Adverse reaction determined post-authorisation.
e. Refers to vaccinated arm.
f. A higher frequency of pyrexia was observed after the second dose compare to the first dose.
g. Facial swelling in vaccine recipients with a history of injection of dermatological fillers has been reported in the post-marketing phase.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

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

Efficacy

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

Efficacy in participants 16 years of age and older – after 2 doses
In the Phase 2/3 portion of Study 2, based on data accrued through 14 November 2020, approximately 44,000 participants were randomised equally and were to receive 2 doses of COVID-19 mRNA Vaccine or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a minimum interval of 14 days before and after administration of an influenza vaccine in order to receive either placebo or COVID-19 mRNA Vaccine. In the clinical study, participants were required to observe a minimum interval of 60 days before or after receipt of blood/plasma products or immunoglobulins within through conclusion of the study in order to receive either placebo or COVID-19 mRNA Vaccine.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COVID-19 mRNA 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. In addition, 134 participants were between the ages of 16 to 17 years of age (66 in the COVID-19 mRNA Vaccine group and 68 in the placebo group) and 1,616 participants 75 years of age and older (804 in the COVID-19 mRNA Vaccine group and 812 in the placebo group).

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for in total 2,214 person-years for the COVID-19 mRNA Vaccine and in total 2,222 person-years in the placebo group.

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

The vaccine efficacy information is presented in Table 2.

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

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

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time. CI not adjusted for multiplicity.

Efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 94.6% (95% confidence interval of 89.6% to 97.6%) in participants 16 years of age and older with or without evidence of prior infection with SARS-CoV-2.

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

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

The updated vaccine efficacy information is presented in Table 3.

Table 3: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of prior SARS-CoV-2 infection* prior to 7 days after Dose 2 – evaluable efficacy (7 days) population during the placebo-controlled follow-up period

Subgroup	COVID-19 mRNA Vaccine N[a]=20,998 Cases n1[b] Surveillance time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance time[c] (n2[d])	Vaccine efficacy % (95% CI[e])
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 to 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 to 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided 95% confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 to 15 years of age: 0 in the COVID-19 mRNA Vaccine group; 16 in the placebo group.

In the updated efficacy analysis, efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 91.1% (95% CI of 88.8% to 93.0%) in participants in the evaluable efficacy population with or without evidence of prior infection with SARS-CoV-2.

Additionally, the updated efficacy analyses by subgroup showed similar efficacy point estimates across sexes, ethnic groups, geography and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy against severe COVID-19
Updated efficacy analyses of secondary efficacy endpoints supported benefit of the COVID-19 mRNA Vaccine in preventing severe COVID-19.

As of 13 March 2021, vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 4) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COVID-19 mRNA Vaccine and placebo groups.

Table 4: Vaccine efficacy – First severe COVID-19 occurrence in participants with or without prior SARS-CoV-2 infection based on the Food and Drug Administration (FDA)* after Dose 1 or from 7 days after Dose 2 in the placebo-controlled follow-up

	COVID-19 mRNA Vaccine Cases n1[a] Surveillance time (n2[b])	Placebo Cases n1[a] Surveillance time (n2[b])	Vaccine efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

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

* Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 beats per minute, saturation of oxygen ≤ 93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen < 300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomised participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1,000 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 Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomised participants who receive all dose(s) of study intervention as randomised within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1,000 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.

Efficacy and immunogenicity in adolescents 12 to 15 years of age – after 2 doses

In an analysis of Study 2 in adolescents 12 to 15 years of age without evidence of prior infection, there were no cases in 1,005 participants who received the vaccine and 16 cases out of 978 who received placebo. The point estimate for efficacy is 100% (95% confidence interval 75.3, 100.0). In participants with or without evidence of prior infection there were 0 cases in the 1,119 who received vaccine and 18 cases in 1,110 participants who received placebo. This also indicates the point estimate for efficacy is 100% (95% confidence interval 78.1, 100.0).

In Study 2, an analysis of SARS-CoV-2 neutralising titres 1 month after Dose 2 was conducted in a randomly selected subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2, comparing the response in adolescents 12 to 15 years of age (n = 190) to participants 16 to 25 years of age (n = 170).

The ratio of the geometric mean titres (GMT) in the 12 to 15 years of age group to the 16 to 25 years of age group was 1.76, with a 2-sided 95% CI of 1.47 to 2.10. Therefore, the 1.5-fold noninferiority criterion was met as the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] was > 0.67.

Immunogenicity in participants 18 years of age and older – after booster dose (third dose)
Effectiveness of a booster dose of Comirnaty was based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). In Study 2, analyses of NT50 1 month after the booster dose compared to 1 month after the primary series in individuals 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination demonstrated noninferiority for both geometric mean ratio (GMR) and difference in seroresponse rates. Seroresponse for a participant was defined as achieving a ≥ 4-fold rise in NT50 from baseline (before primary series). These analyses are summarized in Table 5.

Table 5: SARS-CoV-2 neutralization assay - NT50 (titer)† (SARS-CoV-2 USA_WA1/2020) – GMT and seroresponse rate comparison of 1 month after booster dose to 1 month after primary series – participants 18 through 55 years of age without evidence of infection up to 1 month after booster dose* – booster dose evaluable immunogenicity population±

	N	1 month after booster dose (95% CI)	1 month after primary series (95% CI)	1 month after booster dose/- 1 month after primary series (97.5% CI)	Met noninferiority objective (Y/N)
Geometric mean 50% neutralizing titer (GMT[b])	212[a]	2466.0[b] (2202.6, 2760.8)	750.6[b] (656.2, 858.6)	3.29[c] (2.77, 3.90)	Y[d]
Seroresponse rate (%) for 50% neutralizing titer†	200[e]	199[f] 99.5% (97.2%, 100.0%)	196[f] 98.0% (95.0%, 99.5%)	1.5%[g] (-0.7%, 3.7%[h])	Y[i]

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

† SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

* Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of Comirnaty) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.

± All eligible participants who had received 2 doses of Comirnaty as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Comirnaty, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.

a. n = Number of participants with valid and determinate assay results at both sampling time points within specified window.

b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

c. GMRs and 2-sided 97.5% CIs were calculated by exponentiating the mean differences in the logarithms of the assay and the corresponding CIs (based on the Student t distribution).

d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is > 0.67 and the point estimate of the GMR is ≥ 0.80.

e. n = Number of participants with valid and determinate assay results for the specified assay at baseline, 1 month after Dose 2 and 1 month after the booster dose within specified window. These values are the denominators for the percentage calculations.
f. Number of participants with seroresponse for the given assay at the given dose/sampling time point. Exact 2-sided CI based on the Clopper and Pearson method.
g. Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).
h. Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.
i. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is > -10%.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Comirnaty in the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

General toxicity

Rats intramuscularly administered Comirnaty (receiving 3 full human doses once weekly, generating relatively higher levels in rats due to body weight differences) demonstrated some injection site oedema and erythema and increases in white blood cells (including basophils and eosinophils) consistent with an inflammatory response as well as vacuolation of portal hepatocytes without evidence of liver injury. All effects were reversible.

Genotoxicity/Carcinogenicity

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

Reproductive toxicity

Reproductive and developmental toxicity were investigated in rats in a combined fertility and developmental toxicity study where female rats were intramuscularly administered Comirnaty prior to mating and during gestation (receiving 4 full human doses that generate relatively higher levels in rat due to body weight differences, spanning between pre-mating day 21 and gestational day 20). SARS-CoV-2 neutralizing antibody responses were present in maternal animals from prior to mating to the end of the study on postnatal day 21 as well as in foetuses and offspring. There were no vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development. No Comirnaty data are available on vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
Cholesterol
Potassium chloride
Potassium dihydrogen phosphate
Sodium chloride
Disodium phosphate dihydrate
Sucrose
Water for injections
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

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

Unopened vial

Frozen vial
9 months when stored at -90 °C to -60 °C.
Within the 9-month shelf life unopened vials may be stored and transported at -25 °C to -15 °C for a single period of up to 2 weeks and can be returned to -90 °C to -60 °C.

When stored frozen at -90 °C to -60 °C, 195-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 3 hours or individual vials can be thawed at room temperature (up to 30 °C) for 30 minutes.

Thawed vial
1 month at 2 °C to 8 °C within the 9-month shelf life.
Within the 1-month shelf life at 2 °C to 8 °C, up to 12 hours may be used for transportation.
Prior to use, the unopened vial can be stored for up to 2 hours at temperatures up to 30 °C.
Thawed vials can be handled in room light conditions.

Once thawed, the vaccine should not be re-frozen.

Handling of temperature excursions once removed from the freezer
Stability data indicate that the unopened vial is stable for up to:
- 24 hours when stored at temperatures from -3 °C to 2 °C
- a total of 4 hours when stored at temperatures from 8 °C to 30 °C; this includes the 2 hours at up to 30 °C detailed above

This information is intended to guide healthcare professionals only in case of temporary temperature excursion.

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

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

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

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

Diluted medicinal product

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

6.4 Special precautions for storage

Store in a freezer at -90 °C to -60 °C.
Store in the original package in order to protect from light.
During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

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

6.5 Nature and contents of container

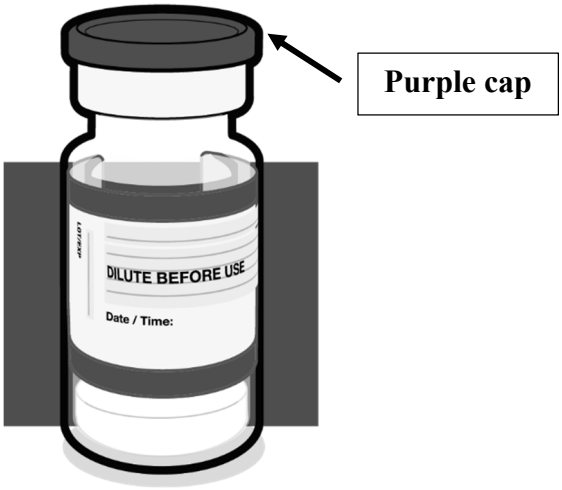
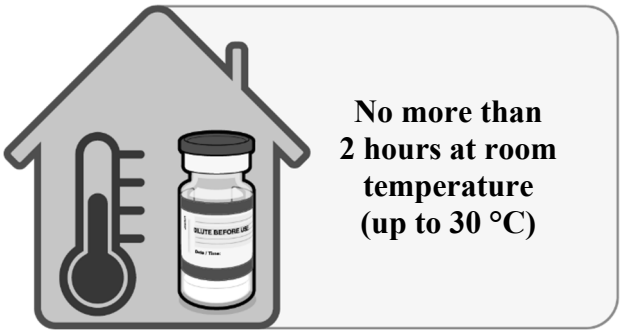
0.45 mL concentrate in a 2 mL clear multidose vial (type I glass) with a stopper (synthetic bromobutyl rubber) and a purple flip-off plastic cap with aluminium seal. Each vial contains 6 doses, see section 6.6.

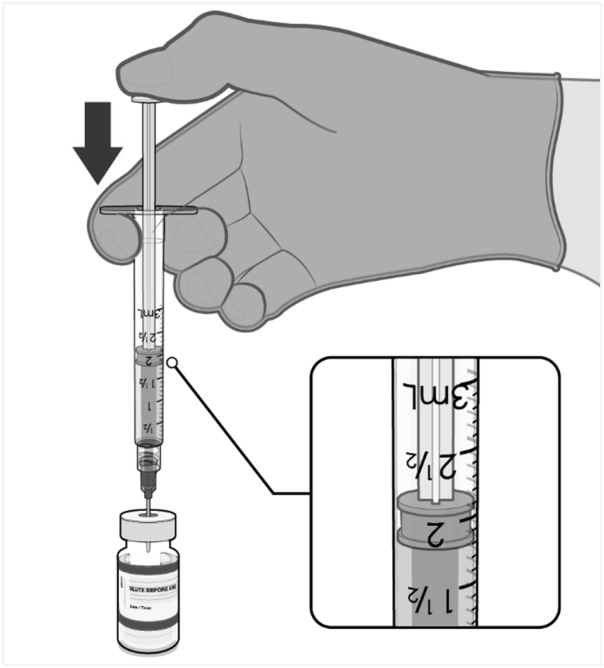
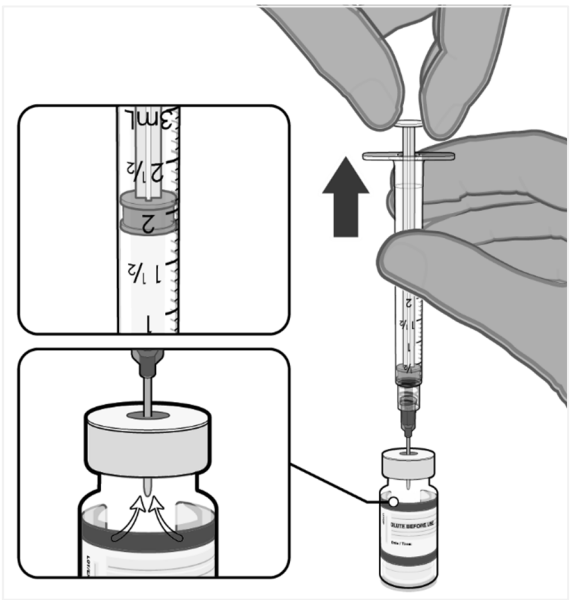
Pack size: 195 vials

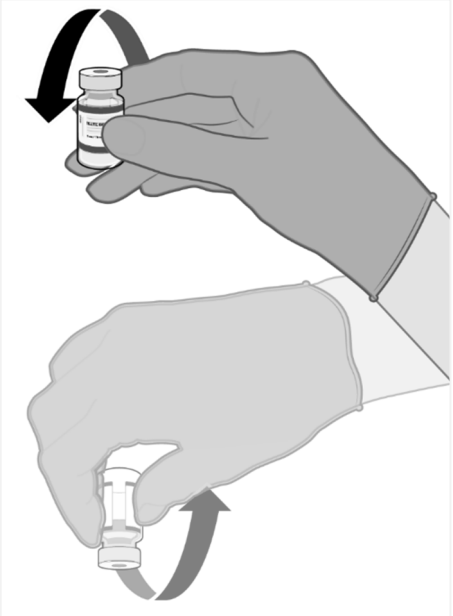
6.6 Special precautions for disposal and other handling

Handling instructions

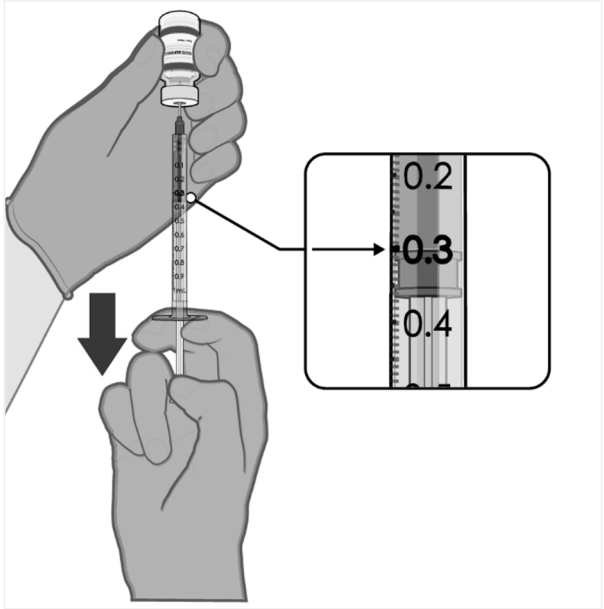
Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

DOSE VERIFICATION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)	
	• Verify that the vial has a purple plastic cap. • If the vial has a grey plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose dispersion for injection. • If the vial has an orange plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.
THAWING PRIOR TO DILUTION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)	
	• The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use. • The unopened vial can be stored for up to 1 month at 2 °C to 8 °C within the 9-month shelf life. Within the 1-month shelf life at 2 °C to 8 °C, up to 12 hours may be used for transportation. • Allow the thawed vial to come to room temperature. Prior to use, the unopened vial can be stored for up to 2 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions. • Gently invert the vial 10 times prior to dilution. Do not shake. • Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.

DILUTION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)	
 **1.8 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.
 **Pull back plunger to 1.8 mL to remove air from vial.**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

 **Gently × 10**	• Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as an off-white dispersion with no particulates visible. Do not use the diluted vaccine if particulates or discolouration are present.
 **Record appropriate date and time.** **Use within 6 hours after dilution.**	• The diluted vials should be marked with the appropriate date and time. • After dilution, store at 2 ºC to 30 ºC and use within 6 hours, including any transportation time. • Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)



0.3 mL diluted vaccine

- After dilution, the vial contains 2.25 mL from which 6 doses of 0.3 mL can be extracted.
- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab.
- Withdraw 0.3 mL of Comirnaty.

  Low dead-volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres.

  If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Discard any unused vaccine within 6 hours after dilution.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1528/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 December 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Comirnaty 30 micrograms/dose dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial. Do not dilute prior to use.

One vial (2.25 mL) contains 6 doses of 0.3 mL, see sections 4.2 and 6.6.

One dose (0.3 mL) contains 30 micrograms of tozinameran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection.
The vaccine is a white to off-white frozen dispersion (pH: 6.9 - 7.9).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Comirnaty 30 micrograms/dose dispersion for injection is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 12 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 12 years of age and older
Comirnaty is administered intramuscularly as a primary course of 2 doses (0.3 mL each). It is recommended to administer the second dose 3 weeks after the first dose (see sections 4.4 and 5.1).

A booster dose (third dose) of Comirnaty may be administered intramuscularly at least 6 months after the second dose in individuals 18 years of age and older. The decision when and for whom to implement a third dose of Comirnaty should be made based on available vaccine effectiveness data, taking into account limited safety data (see sections 4.4 and 5.1).

The interchangeability of Comirnaty with COVID-19 vaccines from other manufacturers to complete the primary vaccination course or the booster dose (third dose) has not been established. Individuals

who have received 1 dose of Comirnaty should receive a second dose of Comirnaty to complete the primary vaccination course and for any additional doses. Doses of Comirnaty 30 micrograms/dose concentrate for dispersion for injection after dilution and Comirnaty 30 micrograms/dose dispersion for injection are considered interchangeable.

Severely immunocompromised aged 12 years and older
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised (see section 4.4).

Paediatric population
There is a paediatric formulation available for children 5 to 11 years of age (i.e. 5 to less than 12 years of age). For details, please refer to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.

Elderly population
No dosage adjustment is required in elderly individuals ≥ 65 years of age. The safety and immunogenicity of a booster dose (third dose) of Comirnaty in individuals 65 years of age and older is based on safety and immunogenicity data in adults 18 to 55 years of age.

Method of administration

Comirnaty 30 micrograms/dose dispersion for injection should be administered intramuscularly (see section 6.6). Do not dilute prior to use.

Vials of Comirnaty contain 6 doses of 0.3 mL of vaccine. In order to extract 6 doses from a single vial, low dead-volume syringes and/or needles should be used. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle:

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

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

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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

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

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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

General recommendations

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

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Comirnaty.

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

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees (including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

The risk of myocarditis after a third dose of Comirnaty has not yet been characterised.

Anxiety-related reactions
Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, tingling sensations and sweating) may occur in association with the vaccination process itself. Stress-related reactions are temporary and resolve on their own. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation. It is important that precautions are in place to avoid injury from fainting.

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

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

Immunocompromised individuals
The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty may be lower in immunocompromised individuals.

The recommendation to consider a third dose in severely immunocompromised individuals is based on limited serological evidence from a case-series in the literature from the clinical management of patients with iatrogenic immunocompromisation after solid organ transplantation (see section 4.2).

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

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of Comirnaty in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of Comirnaty in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether Comirnaty is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of safety profile

The safety of Comirnaty was evaluated in participants 12 years of age and older in 2 clinical studies that included 23,205 participants (comprised of 22,074 participants 16 years of age and older and 1,131 adolescents 12 to 15 years of age) that have received at least one dose of Comirnaty.

The overall safety profile of Comirnaty in adolescents 12 to 15 years of age was similar to that seen in participants 16 years of age and older.

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

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

At the time of the analysis of Study 2 with a data cut-off of 13 March 2021 for the placebo-controlled blinded follow-up period up to the participants' unblinding dates, a total of 25,651 (58.2%) participants (13,031 Comirnaty and 12,620 placebo) 16 years of age and older were followed up for ≥ 4 months after the second dose. This included a total of 15,111 (7,704 Comirnaty and 7,407 placebo) participants 16 to 55 years of age and a total of 10,540 (5,327 Comirnaty and 5,213 placebo) participants 56 years of age and older.

The most frequent adverse reactions in participants 16 years of age and older that received 2 doses were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia (> 40%), chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

The safety profile in 545 participants 16 years of age and older receiving Comirnaty, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Adolescents 12 to 15 years of age – after 2 doses
In an analysis of Study 2, based on data up to the cut-off date of 13 March 2021, 2,260 adolescents (1,131 Comirnaty and 1,129 placebo) were 12 to 15 years of age. Of these, 1,308 adolescents (660 Comirnaty and 648 placebo) have been followed for at least 2 months after the second dose of Comirnaty. The safety evaluation in Study 2 is ongoing.

The most frequent adverse reactions in adolescents 12 to 15 years of age that received 2 doses were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).

Participants 18 years of age and older – after booster dose (third dose)
A subset from Study 2 Phase 2/3 participants of 306 adults 18 to 55 years of age who completed the original Comirnaty 2-dose course, received a booster dose (third dose) of Comirnaty approximately 6 months (range of 4.8 to 8.0 months) after receiving Dose 2.

The most frequent adverse reactions in participants 18 to 55 years of age were injection site pain (> 80%), fatigue (> 60%), headache (> 40%), myalgia (> 30%), chills and arthralgia (> 20%).

Tabulated list of adverse reactions from clinical studies and post-authorisation experience in individuals 12 years of age and older

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

Very common (≥ 1/10),
Common (≥ 1/100 to < 1/10),
Uncommon (≥ 1/1,000 to < 1/100),
Rare (≥ 1/10,000 to < 1/1,000),
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data).

Table 1: Adverse reactions from Comirnaty clinical trials and post-authorisation experience in individuals 12 years of age and older

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy[a]		
Immune system disorders			Hypersensitivity reactions (e.g. rash, pruritus, urticaria,[b] angioedema[b])		Anaphylaxis
Metabolism and nutrition disorders			Decreased appetite		
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache		Lethargy	Acute peripheral facial paralysis[c]	
Cardiac disorders					Myocarditis;[d] Pericarditis[d]
Gastrointestinal disorders	Diarrhoea[d]	Nausea; Vomiting[d]			
Skin and subcutaneous tissue disorder			Hyperhidrosis; Night sweats		
Musculoskeletal and connective tissue disorders	Arthralgia; Myalgia		Pain in extremity[e]		
General disorders and administration site conditions	Injection site pain; Fatigue; Chills; Pyrexia;[f] Injection site swelling	Injection site redness	Asthenia; Malaise; Injection site pruritus		Extensive swelling of vaccinated limb;[d] Facial swelling[g]

a. A higher frequency of lymphadenopathy (5.2% vs 0.4%) was observed in participants receiving a booster dose (third dose) compared to participants receiving 2 doses.
b. The frequency category for urticaria and angioedema was Rare.
c. Through the clinical trial safety follow-up period to 14 November 2020, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group.
d. Adverse reaction determined post-authorisation.
e. Refers to vaccinated arm.
f. A higher frequency of pyrexia was observed after the second dose compare to the first dose.
g. Facial swelling in vaccine recipients with a history of injection of dermatological fillers has been reported in the post-marketing phase.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

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

Efficacy

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

Efficacy in participants 16 years of age and older – after 2 doses
In the Phase 2/3 portion of Study 2, based on data accrued through 14 November 2020, approximately 44,000 participants were randomised equally and were to receive 2 doses of COVID-19 mRNA Vaccine or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a minimum interval of 14 days before and after administration of an influenza vaccine in order to receive either placebo or COVID-19 mRNA Vaccine. In the clinical study, participants were required to observe a minimum interval of 60 days before or after receipt of blood/plasma products or immunoglobulins within through conclusion of the study in order to receive either placebo or COVID-19 mRNA Vaccine.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COVID-19 mRNA 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.

In addition, 134 participants were between the ages of 16 to 17 years of age (66 in the COVID-19 mRNA Vaccine group and 68 in the placebo group) and 1,616 participants 75 years of age and older (804 in the COVID-19 mRNA Vaccine group and 812 in the placebo group).

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for in total 2,214 person-years for the COVID-19 mRNA Vaccine and in total 2,222 person-years in the placebo group.

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

The vaccine efficacy information is presented in Table 2.

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

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

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time. CI not adjusted for multiplicity.

Efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 94.6% (95% confidence interval of 89.6% to 97.6%) in participants 16 years of age and older with or without evidence of prior infection with SARS-CoV-2.

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

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

The updated vaccine efficacy information is presented in Table 3.

Table 3: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of prior SARS-CoV-2 infection* prior to 7 days after Dose 2 – evaluable efficacy (7 days) population during the placebo-controlled follow-up period

Subgroup	COVID-19 mRNA Vaccine N[a]=20,998 Cases n1[b] Surveillance time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance time[c] (n2[d])	Vaccine efficacy % (95% CI[e])
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 to 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 to 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided 95% confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 to 15 years of age: 0 in the COVID-19 mRNA Vaccine group; 16 in the placebo group.

In the updated efficacy analysis, efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 91.1% (95% CI of 88.8% to 93.0%) in participants in the evaluable efficacy population with or without evidence of prior infection with SARS-CoV-2.

Additionally, the updated efficacy analyses by subgroup showed similar efficacy point estimates across sexes, ethnic groups, geography and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy against severe COVID-19
Updated efficacy analyses of secondary efficacy endpoints supported benefit of the COVID-19 mRNA Vaccine in preventing severe COVID-19.

As of 13 March 2021, vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 4) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COVID-19 mRNA Vaccine and placebo groups.

Table 4: Vaccine efficacy – First severe COVID-19 occurrence in participants with or without prior SARS-CoV-2 infection based on the Food and Drug Administration (FDA)* after Dose 1 or from 7 days after Dose 2 in the placebo-controlled follow-up

	COVID-19 mRNA Vaccine Cases n1[a] Surveillance time (n2[b])	**Placebo Cases n1[a] Surveillance time (n2[b])**	**Vaccine efficacy % (95% CI[c])**
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

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

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 beats per minute, saturation of oxygen ≤ 93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen < 300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomised participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1,000 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 Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomised participants who receive all dose(s) of study intervention as randomised within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1,000 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.

Efficacy and immunogenicity in adolescents 12 to 15 years of age – after 2 doses
In an analysis of Study 2 in adolescents 12 to 15 years of age without evidence of prior infection, there were no cases in 1,005 participants who received the vaccine and 16 cases out of 978 who received placebo. The point estimate for efficacy is 100% (95% confidence interval 75.3, 100.0). In participants

with or without evidence of prior infection there were 0 cases in the 1,119 who received vaccine and 18 cases in 1,110 participants who received placebo. This also indicates the point estimate for efficacy is 100% (95% confidence interval 78.1, 100.0).

In Study 2, an analysis of SARS-CoV-2 neutralising titres 1 month after Dose 2 was conducted in a randomly selected subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2, comparing the response in adolescents 12 to 15 years of age (n = 190) to participants 16 to 25 years of age (n = 170).

The ratio of the geometric mean titres (GMT) in the 12 to 15 years of age group to the 16 to 25 years of age group was 1.76, with a 2-sided 95% CI of 1.47 to 2.10. Therefore, the 1.5-fold noninferiority criterion was met as the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] was > 0.67.

Immunogenicity in participants 18 years of age and older – after booster dose (third dose)
Effectiveness of a booster dose of Comirnaty was based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). In Study 2, analyses of NT50 1 month after the booster dose compared to 1 month after the primary series in individuals 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination demonstrated noninferiority for both geometric mean ratio (GMR) and difference in seroresponse rates. Seroresponse for a participant was defined as achieving a ≥ 4-fold rise in NT50 from baseline (before primary series). These analyses are summarized in Table 5.

Table 5: SARS-CoV-2 neutralization assay - NT50 (titer)† (SARS-CoV-2 USA_WA1/2020) – GMT and seroresponse rate comparison of 1 month after booster dose to 1 month after primary series – participants 18 through 55 years of age without evidence of infection up to 1 month after booster dose* – booster dose evaluable immunogenicity population±

	n	1 month after booster dose (95% CI)	1 month after primary series (95% CI)	1 month after booster dose/- 1 month after primary series (97.5% CI)	Met noninferiority objective (Y/N)
Geometric mean 50% neutralizing titer (GMT[b])	212[a]	2466.0[b] (2202.6, 2760.8)	750.6[b] (656.2, 858.6)	3.29[c] (2.77, 3.90)	Y[d]
Seroresponse rate (%) for 50% neutralizing titer†	200[e]	199[f] 99.5% (97.2%, 100.0%)	196[f] 98.0% (95.0%, 99.5%)	1.5%[g] (-0.7%, 3.7%[h])	Y[i]

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

† SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

* Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of Comirnaty) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.

± All eligible participants who had received 2 doses of Comirnaty as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Comirnaty, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.

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

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Comirnaty in the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

General toxicity

Rats intramuscularly administered Comirnaty (receiving 3 full human doses once weekly, generating relatively higher levels in rats due to body weight differences) demonstrated some injection site oedema and erythema and increases in white blood cells (including basophils and eosinophils) consistent with an inflammatory response as well as vacuolation of portal hepatocytes without evidence of liver injury. All effects were reversible.

Genotoxicity/Carcinogenicity

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

Reproductive toxicity

Reproductive and developmental toxicity were investigated in rats in a combined fertility and developmental toxicity study where female rats were intramuscularly administered Comirnaty prior to mating and during gestation (receiving 4 full human doses that generate relatively higher levels in rat due to body weight differences, spanning between pre-mating day 21 and gestational day 20). SARS-CoV-2 neutralizing antibody responses were present in maternal animals from prior to mating

to the end of the study on postnatal day 21 as well as in foetuses and offspring. There were no vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development. No Comirnaty data are available on vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
Cholesterol
Trometamol
Trometamol hydrochloride
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened vial

Frozen vial
6 months when stored at -90 °C to -60 °C.

The vaccine may be received frozen at -90 °C to -60 °C or at -25 °C to -15 °C. Frozen vaccine can be stored either at -90 °C to -60 °C or 2 °C to 8 °C upon receipt.

When stored frozen at -90 °C to -60 °C, 10-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 6 hours or individual vials can be stored at room temperature (up to 30 °C) for 30 minutes.

Thawed vial
10 weeks storage and transportation at 2 °C to 8 °C within the 6-month shelf life.

- Upon moving the product to 2 °C to 8 °C storage, the updated expiry date must be written on the outer carton and the vaccine should be used or discarded by the updated expiry date. The original expiry date should be crossed out.
- If the vaccine is received at 2 °C to 8 °C it should be stored at 2 °C to 8 °C. Check that the expiry date on the outer carton has been updated to reflect the refrigerated expiry date and that the original expiry date has been crossed out.

Prior to use, the unopened vials can be stored for up to 12 hours at temperatures between 8 °C and 30 °C.

Thawed vials can be handled in room light conditions.

Once thawed, the vaccine should not be re-frozen.

Handling of temperature excursions during refrigerated storage
- Stability data indicate that the unopened vial is stable for up to 10 weeks when stored at temperatures from -2 °C to 2 °C, within the 10-week storage period between 2 °C and 8 °C.
- Stability data indicate the vial can be stored for up to 24 hours at temperatures of 8 °C to 30 °C, including up to 12 hours following first puncture.

This information is intended to guide healthcare professionals only in case of temporary temperature excursion.

Opened vial

Chemical and physical in-use stability has been demonstrated for12 hours at 2 ºC to 30 ºC. From a microbiological point of view, unless the method of opening precludes the risks of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a freezer at -90 °C to -60 °C.
Store in the original package in order to protect from light.
During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

For storage conditions after thawing and first opening, see section 6.3.

6.5 Nature and contents of container

2.25 mL solution in a 2 mL clear multidose vial (type I glass) with a stopper (synthetic bromobutyl rubber) and a grey flip-off plastic cap with aluminium seal. Each vial contains 6 doses, see section 6.6.

Pack sizes: 195 vials or 10 vials

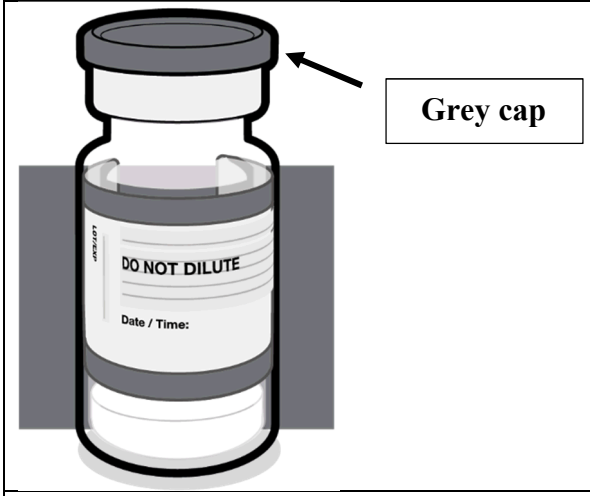
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions

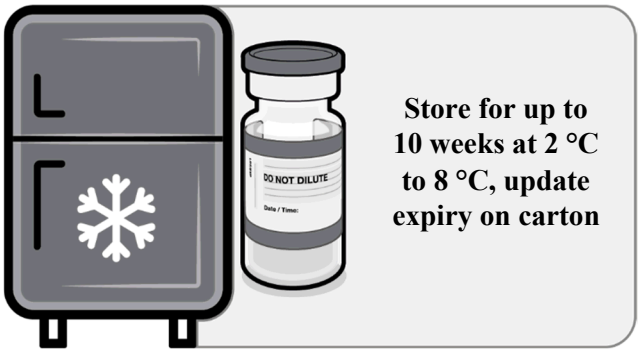
Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

DOSE VERIFICATION OF COMIRNATY 30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER)

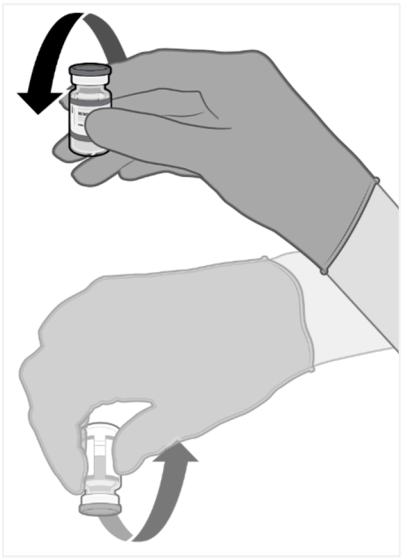


- Verify that the vial has a grey plastic cap.
- If the vial has a purple plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose concentrate for dispersion for injection.
- If the vial has an orange plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.

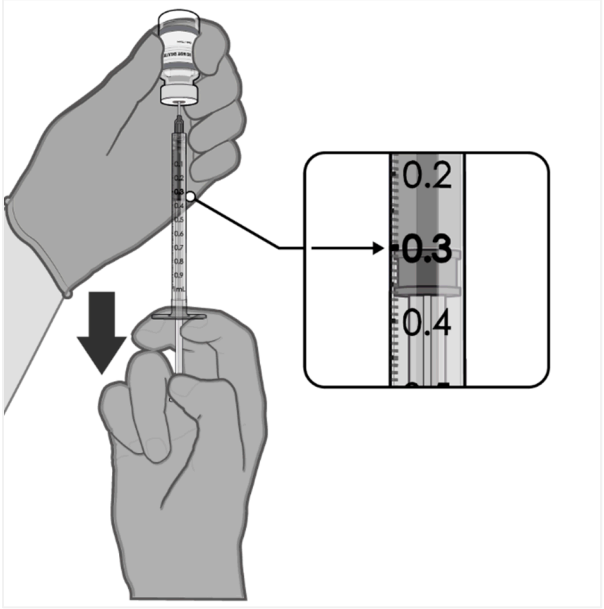
HANDLING PRIOR TO USE OF COMIRNATY 30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER))



- If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 10 vial pack may take 6 hours to thaw. Ensure vials are completely thawed prior to use.
- Upon moving vials to 2 °C to 8 °C storage, update the expiry date on the carton.
- Unopened vials can be stored for up to 10 weeks at 2 °C to 8 °C within the 6-month shelf life.
- Alternatively, individual frozen vials may be thawed for 30 minutes at temperatures up to 30 °C.
- Prior to use, the unopened vial can be stored for up to 12 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions.

<table>
<tr>
<td> 
Gently × 10</td>
<td>

Gently mix by inverting vials 10 times prior to use. Do not shake.
Prior to mixing, the thawed dispersion may contain white to off-white opaque amorphous particles.
After mixing, the vaccine should present as a white to off-white dispersion with no particulates visible. Do not use the vaccine if particulates or discolouration are present.

</td>
</tr>
<tr>
<td colspan="2">PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY
30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER)</td>
</tr>
<tr>
<td> 

0.3 mL vaccine</td>
<td>

Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab.
Withdraw 0.3 mL of Comirnaty.

Low dead-volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres.

If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial.
Each dose must contain 0.3 mL of vaccine.
If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
Discard any unused vaccine 12 hours after first puncture. Record the appropriate date/time on the vial.

</td>
</tr>
</table>

<u>Disposal</u>

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

7. MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1528/003
EU/1/20/1528/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 December 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Comirnaty 10 micrograms/dose concentrate for dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

One vial (1.3 mL) contains 10 doses of 0.2 mL after dilution, see sections 4.2 and 6.6.

One dose (0.2 mL) contains 10 micrograms of tozinameran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for dispersion for injection (sterile concentrate).
The vaccine is a white to off-white frozen dispersion (pH: 6.9 - 7.9).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Comirnaty 10 micrograms/dose concentrate for dispersion for injection is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in children aged 5 to 11 years.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Children 5 to 11 years of age (i.e. 5 to less than 12 years of age)
Comirnaty 10 micrograms/dose is administered intramuscularly after dilution as a course of 2 doses (0.2 mL each). It is recommended to administer the second dose 3 weeks after the first dose (see sections 4.4 and 5.1).

The interchangeability of Comirnaty with COVID-19 vaccines from other manufacturers to complete the vaccination course has not been established. Individuals who have received 1 dose of Comirnaty should receive a second dose of Comirnaty to complete the vaccination course.

Comirnaty 10 micrograms/dose should be used only for children 5 to 11 years of age.

Severely immunocompromised aged 5 years and older
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised (see section 4.4).

Paediatric population
The safety and efficacy of Comirnaty in paediatric children aged less than 5 years have not yet been established.

Method of administration

Comirnaty 10 micrograms/dose concentrate for dispersion for injection should be administered intramuscularly after dilution (see section 6.6).

After dilution, vials of Comirnaty contain 10 doses of 0.2 mL of vaccine. In order to extract 10 doses from a single vial, low dead-volume syringes and/or needles should be used. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial. Irrespective of the type of syringe and needle:

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

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

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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

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

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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

General recommendations

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

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Comirnaty.

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

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees (including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

The risk of myocarditis after a third dose of Comirnaty has not yet been characterised.

Anxiety-related reactions
Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, tingling sensations and sweating) may occur in association with the vaccination process itself. Stress-related reactions are temporary and resolve on their own. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation. It is important that precautions are in place to avoid injury from fainting.

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

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

Immunocompromised individuals
The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty may be lower in immunocompromised individuals.

The recommendation to consider a third dose in severely immunocompromised individuals is based on limited serological evidence from a case-series in the literature from the clinical management of adult patients with iatrogenic immunocompromisation after solid organ transplantation (see section 4.2).

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

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of Comirnaty in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of Comirnaty in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether Comirnaty is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of safety profile

The safety of Comirnaty was evaluated in participants 5 years of age and older in 3 clinical studies that included 24,675 participants (comprised of 22,026 participants 16 years of age and older, 1,131 adolescents 12 to 15 years of age, and 3,109 children 5 to 11 years of age) that have received at least 1 dose of Comirnaty.

The overall safety profile of Comirnaty in participants 5 to 15 years of age was similar to that seen in participants 16 years of age and older.

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

Children 5 to 11 years of age (i.e. 5 to less than 12 years of age) – after 2 doses
In Study 3, a total of 1,518 children 5 to 11 years of age received at least 1 dose of Comirnaty 10 mcg and a total of 750 children 5 to 11 years of age received placebo. At the time of the analysis of Study 3 Phase 2/3 with data up to the cut-off date of 6 September 2021, 2,158 (95.1%) (1,444 Comirnaty 10 mcg and 714 placebo) children have been followed for at least 2 months after the second dose of Comirnaty 10 mcg. An analysis of Study 3 Phase 2/3 adverse event data also included another 2,379 participants [1,591 Comirnaty 10 mcg and 788 placebo], of whom 71.2% had a follow-up period for at least 2 weeks after Dose 2 up to the cut-off date of 8 October 2021. The safety evaluation in Study 3 is ongoing.

The most frequent adverse reactions in children 5 to 11 years of age were injection site pain (>80%), fatigue (>50%), headache (>30%), injection site redness and swelling (>20%), myalgia and chills (>10%).

Participants 16 years of age and older – after 2 doses
In Study 2, a total of 22,026 participants 16 years of age or older received at least 1 dose of Comirnaty 30 mcg and a total of 22,021 participants 16 years of age or older received placebo (including 138 and

145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively). A total of 20,519 participants 16 years of age or older received 2 doses of Comirnaty.

At the time of the analysis of Study 2 with a data cut-off of 13 March 2021 for the placebo-controlled blinded follow-up period up to the participants' unblinding dates, a total of 25,651 (58.2%) participants (13,031 Comirnaty and 12,620 placebo) 16 years of age and older were followed up for ≥ 4 months after the second dose. This included a total of 15,111 (7,704 Comirnaty and 7,407 placebo) participants 16 to 55 years of age and a total of 10,540 (5,327 Comirnaty and 5,213 placebo) participants 56 years of age and older.

The most frequent adverse reactions in participants 16 years of age and older that received 2 doses were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia (> 40%), chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

The safety profile in 545 participants 16 years of age and older receiving Comirnaty, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Adolescents 12 to 15 years of age – after 2 doses
In an analysis of Study 2, based on data up to the cutoff date of 13 March 2021, 2,260 adolescents (1,131 Comirnaty 30 mcg and 1,129 placebo) were 12 to 15 years of age. Of these, 1,308 adolescents (660 Comirnaty and 648 placebo) have been followed for at least 2 months after the second dose of Comirnaty. The safety evaluation in Study 2 is ongoing.

The most frequent adverse reactions in adolescents 12 to 15 years of age that received 2 doses were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).

Participants 18 years of age and older – after booster dose (third dose)
A subset from Study 2 Phase 2/3 participants of 306 adults 18 to 55 years of age who completed the original Comirnaty 2-dose course, received a booster dose (third dose) of Comirnaty approximately 6 months (range of 4.8 to 8.0 months) after receiving Dose 2.

The most frequent adverse reactions in participants 18 to 55 years of age were injection site pain (> 80%), fatigue (> 60%), headache (> 40%), myalgia (> 30%), chills and arthralgia (> 20%).

<u>Tabulated list of adverse reactions from clinical studies and post-authorisation experience in individuals 5 years of age and older</u>

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

Very common (≥ 1/10),
Common (≥ 1/100 to < 1/10),
Uncommon (≥ 1/1,000 to < 1/100),
Rare (≥ 1/10,000 to < 1/1,000),
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data).

Table 1: Adverse reactions from Comirnaty clinical trials and post-authorisation experience in individuals 5 years of age and older

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy[a]		
Immune system disorders			Hypersensitivity reactions (e.g. rash, pruritus, urticaria,[b] angioedema[b])		Anaphylaxis
Metabolism and nutrition disorders			Decreased appetite		
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache		Lethargy	Acute peripheral facial paralysis[c]	
Cardiac disorders					Myocarditis;[d] Pericarditis[d]
Gastrointestinal disorders	Diarrhoea[d]	Nausea; Vomiting[d]			
Skin and subcutaneous tissue disorder			Hyperhidrosis; Night sweats		
Musculoskeletal and connective tissue disorders	Arthralgia; Myalgia		Pain in extremity[e]		
General disorders and administration site conditions	Injection site pain; Fatigue; Chills; Pyrexia;[f] Injection site swelling	Injection site redness[h]	Asthenia; Malaise; Injection site pruritus		Extensive swelling of vaccinated limb;[d] Facial swelling[g]

a. A higher frequency of lymphadenopathy (5.2% vs 0.4%) was observed in participants receiving a booster dose (third dose) compared to participants receiving 2 doses.
b. The frequency category for urticaria and angioedema was Rare.
c. Through the clinical trial safety follow-up period to 14 November 2020, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group.
d. Adverse reaction determined post-authorisation.
e. Refers to vaccinated arm.
f. A higher frequency of pyrexia was observed after the second dose compare to the first dose.
g. Facial swelling in vaccine recipients with a history of injection of dermatological fillers has been reported in the post-marketing phase.
h. Injection site redness occurred at a higher frequency (very common) in children 5 to 11 years of age.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

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

Efficacy

Study 2 is a multicentre, multinational, Phase 1/2/3 randomised, placebo-controlled, observer-blind dose-finding, vaccine candidate selection and efficacy study in participants 12 years of age and older. Randomisation was stratified by age: 12 to 15 years of age, 16 to 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥ 56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrolment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV).
Efficacy in participants 16 years of age and older – after 2 doses
In the Phase 2/3 portion of Study 2, based on data accrued through 14 November 2020, approximately 44,000 participants were randomised equally and were to receive 2 doses of COVID-19 mRNA Vaccine or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a minimum interval of 14 days before and after administration of an influenza vaccine in order to receive either placebo or COVID-19 mRNA Vaccine. In the clinical study, participants were required to observe a minimum interval of 60 days before or after receipt of blood/plasma products or immunoglobulins within through conclusion of the study in order to receive either placebo or COVID-19 mRNA Vaccine.

The population for the analysis of the primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COVID-19 mRNA 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. In addition, 134 participants were between the ages of 16 to 17 years of age (66 in the COVID-19

mRNA Vaccine group and 68 in the placebo group) and 1,616 participants 75 years of age and older (804 in the COVID-19 mRNA Vaccine group and 812 in the placebo group).

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for in total 2,214 person-years for the COVID-19 mRNA Vaccine and in total 2,222 person-years in the placebo group.

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

The vaccine efficacy information is presented in Table 2.

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

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

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time. CI not adjusted for multiplicity.

Efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 94.6% (95% confidence interval of 89.6% to 97.6%) in participants 16 years of age and older with or without evidence of prior infection with SARS-CoV-2.

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

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

The updated vaccine efficacy information is presented in Table 3.

Table 3: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of prior SARS-CoV-2 infection* prior to 7 days after Dose 2 – evaluable efficacy (7 days) population during the placebo-controlled follow-up period

Subgroup	COVID-19 mRNA Vaccine N[a]=20,998 Cases n1[b] Surveillance time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance time[c] (n2[d])	Vaccine efficacy % (95% CI[e])
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 to 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 to 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided 95% confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 to 15 years of age: 0 in the COVID-19 mRNA Vaccine group; 16 in the placebo group.

In the updated efficacy analysis, efficacy of COVID-19 mRNA Vaccine in preventing first COVID-19 occurrence from 7 days after Dose 2 compared to placebo was 91.1% (95% CI of 88.8% to 93.0%) in participants in the evaluable efficacy population with or without evidence of prior infection with SARS-CoV-2.

Additionally, the updated efficacy analyses by subgroup showed similar efficacy point estimates across sexes, ethnic groups, geography and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy against severe COVID-19
Updated efficacy analyses of secondary efficacy endpoints supported benefit of the COVID-19 mRNA Vaccine in preventing severe COVID-19.

As of 13 March 2021, vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 4) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COVID-19 mRNA Vaccine and placebo groups.

Table 4: Vaccine efficacy – First severe COVID-19 occurrence in participants with or without prior SARS-CoV-2 infection based on the Food and Drug Administration (FDA)* after Dose 1 or from 7 days after Dose 2 in the placebo-controlled follow-up

	COVID-19 mRNA Vaccine Cases n1[a] Surveillance time (n2[b])	**Placebo Cases n1[a] Surveillance time (n2[b])**	**Vaccine efficacy % (95% CI[c])**
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

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

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 beats per minute, saturation of oxygen ≤ 93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen < 300 mm Hg);
- Respiratory failure [defined as needing highflow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomised participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1,000 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 Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomised participants who receive all dose(s) of study intervention as randomised within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1,000 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.

Efficacy and immunogenicity in adolescents 12 to 15 years of age – after 2 doses
In an analysis of Study 2 in adolescents 12 to 15 years of age without evidence of prior infection, there were no cases in 1005 participants who received the vaccine and 16 cases out of 978 who received placebo. The point estimate for efficacy is 100% (95% confidence interval 75.3, 100.0). In participants with or without evidence of prior infection there were 0 cases in the 1119 who received vaccine and

18 cases in 1110 participants who received placebo. This also indicates the point estimate for efficacy is 100% (95% confidence interval 78.1, 100.0).

In Study 2, an analysis of SARS-CoV-2 neutralising titres 1 month after Dose 2 was conducted in a randomly selected subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2, comparing the response in adolescents 12 to 15 years of age (n = 190) to participants 16 to 25 years of age (n = 170).

The ratio of the geometric mean titres (GMT) in the 12 to 15 years of age group to the 16 to 25 years of age group was 1.76, with a 2-sided 95% CI of 1.47 to 2.10. Therefore, the 1.5-fold noninferiority criterion was met as the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] was > 0.67.

Efficacy and immunogenicity in children 5 to 11 years of age (i.e. 5 to less than 12 years of age) – after 2 doses
Study 3 is a Phase 1/2/3 study comprised of an open-label vaccine dose-finding portion (Phase 1) and a multicentre, multinational, randomised, saline placebo-controlled, observer-blind efficacy portion (Phase 2/3) that has enrolled participants 5 to 11 years of age. The majority (94.4%) of randomised vaccine recipients received the second dose 19 days to 23 days after Dose 1.

The descriptive vaccine efficacy results in children 5 to 11 years of age without evidence of prior SARS-CoV-2 infection are presented in Table 5. 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 5: 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 to 11 years of age evaluable efficacy population

First COVID-19 occurrence from 7 days after Dose 2 in children 5 to 11 years of age without evidence of prior SARS-CoV-2 infection*			
	COVID-19 mRNA 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 to 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.

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.

In Study 3, an analysis of SARS-CoV-2 50% neutralising titres (NT50) 1 month after Dose 2 in a randomly selected subset of participants demonstrated effectiveness by immunobridging of immune responses comparing children 5 to 11 years of age (i.e. 5 to less than 12 years of age) in the Phase 2/3 part of Study 3 to participants 16 to 25 years of age in the Phase 2/3 part of Study 2 who had no

serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2, meeting the prespecified immunobridging criteria for both the geometric mean ratio (GMR) and the seroresponse difference with seroresponse defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from baseline (before Dose 1).

The GMR of the SARS-CoV-2 NT50 1 month after Dose 2 in children 5 to 11 years of age (i.e. 5 to less than 12 years of age) to that of young adults 16 to 25 years of age was 1.04 (2-sided 95% CI: 0.93, 1.18). Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2, 99.2% of children 5 to 11 years of age and 99.2% of participants 16 to 25 years of age had a seroresponse at 1 month after Dose 2. The difference in proportions of participants who had seroresponse between the 2 age groups (children – young adult) was 0.0% (2-sided 95% CI: -2.0%, 2.2%). This information is presented in Table 6.

Table 6: Summary of geometric mean ratio for 50% neutralising titre and difference in percentages of participants with seroresponse – comparison of children 5 to 11 years of age (Study 3) to participants 16 to 25 years of age (Study 2) – participants without evidence of infection up to 1 month after Dose 2 – immunobridging subset – Phase 2/3 – evaluable immunogenicity population

		COVID-19 mRNA Vaccine			
		10 mcg/dose 5 to 11 years N[a]=264	30 mcg/dose 16 to 25 years N[a]=253	5 to 11 years/ 16 to 25 years	
	Time point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	Met immunobridging objective[e] (Y/N)
Geometric mean 50% neutralizing titer[f] (GMT[c])	1 month after Dose 2	1197.6 (1106.1, 1296.6)	1146.5 (1045.5, 1257.2)	1.04 (0.93, 1.18)	Y
	Time point[b]	**n[g] (%) (95% CI[h])**	**n[g] (%) (95% CI[h])**	**Difference %[i] (95% CI[j])**	**Met immunobridging objective[k] (Y/N)**
Seroresponse rate (%) for 50% neutralizing titer[f]	1 month after Dose 2	262 (99.2) (97.3, 99.9)	251 (99.2) (97.2, 99.9)	0.0 (-2.0, 2.2)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titre; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; NT50 = 50% neutralising titre; 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 Dose 1 visit and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at Dose 1 and Dose 2 visits, 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.

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.

a. N = Number of participants with valid and determinate assay results before vaccination and at 1 month after Dose 2. These values are also the denominators used in the percentage calculations for seroresponse rates.
b. Protocol-specified timing for blood sample collection.
c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titres (5 to 11 years of age minus 16 to 25 years of age) and the corresponding CI (based on the Student t distribution).

e. Immunobridging based on GMT is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the point estimate of the GMR is ≥0.8.
f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralisation is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralised.
g. n = Number of participants with seroresponse based on NT50 1 month after Dose 2.
h. Exact 2-sided CI based on the Clopper and Pearson method.
i. Difference in proportions, expressed as a percentage (5 to 11 years of age minus16 to 25 years of age).
j. 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.
k. Immunobridging based on seroresponse rate is declared if the lower bound of the 2-sided 95% CI for the seroresponse difference is greater than -10.0%.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Comirnaty in the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

General toxicity

Rats intramuscularly administered Comirnaty (receiving 3 full human doses once weekly, generating relatively higher levels in rats due to body weight differences) demonstrated some injection site oedema and erythema and increases in white blood cells (including basophils and eosinophils) consistent with an inflammatory response as well as vacuolation of portal hepatocytes without evidence of liver injury. All effects were reversible.

Genotoxicity/Carcinogenicity

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

Reproductive toxicity

Reproductive and developmental toxicity were investigated in rats in a combined fertility and developmental toxicity study where female rats were intramuscularly administered Comirnaty prior to mating and during gestation (receiving 4 full human doses that generate relatively higher levels in rat due to body weight differences, spanning between pre-mating day 21 and gestational day 20). SARS-CoV-2 neutralizing antibody responses were present in maternal animals from prior to mating to the end of the study on postnatal day 21 as well as in foetuses and offspring. There were no vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development. No Comirnaty data are available on vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
Cholesterol
Trometamol
Trometamol hydrochloride
Sucrose
Water for injections

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

Unopened vial

Frozen vial
6 months when stored at -90 °C to -60 °C.

The vaccine will be received frozen at -90 °C to -60 °C. Frozen vaccine can be stored either at -90 °C to -60 °C or 2 °C to 8 °C upon receipt.

When stored frozen at -90 °C to -60 °C, 10-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 4 hours or individual vials can be thawed at room temperature (up to 30 °C) for 30 minutes.

Thawed vial
10 weeks storage and transportation at 2 °C to 8 °C within the 6-month shelf life.

- Upon moving the vaccine to 2 °C to 8 °C storage, the updated expiry date must be written on the outer carton and the vaccine should be used or discarded by the updated expiry date. The original expiry date should be crossed out.
- If the vaccine is received at 2 °C to 8 °C it should be stored at 2 °C to 8 °C. The expiry date on the outer carton should have been updated to reflect the refrigerated expiry date and the original expiry date should have been crossed out.

Prior to use, the unopened vials can be stored for up to 12 hours at temperatures between 8 °C and 30 °C.

Thawed vials can be handled in room light conditions.

Once thawed, the vaccine should not be re-frozen.

Handling of temperature excursions during refrigerated storage
- Stability data indicate that the unopened vial is stable for up to 10 weeks when stored at temperatures from -2 °C to 2 °C, and within the 10 weeks storage period between 2 °C and 8 °C.
- Stability data indicate the vial can be stored for up to 24 hours at temperatures of 8 °C to 30 °C, including up to 12 hours following first puncture.

This information is intended to guide healthcare professionals only in case of temporary temperature excursion.

Diluted medicinal product

Chemical and physical in-use stability has been demonstrated for 12 hours at 2 ºC to 30 ºC, after dilution with sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a freezer at -90 °C to -60 °C.
Store in the original package in order to protect from light.
During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

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

6.5 Nature and contents of container

1.3 mL concentrate for dispersion in a 2 mL clear multidose vial (type I glass) with a stopper (synthetic bromobutyl rubber) and an orange flip-off plastic cap with aluminium seal. Each vial contains 10 doses, see section 6.6.

Pack sizes: 10 vials or 195 vials

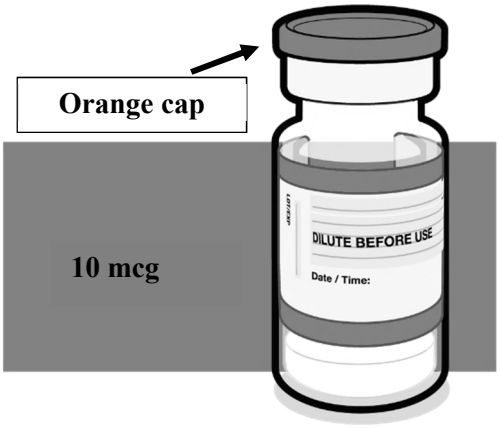
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions

Comirnaty 10 micrograms/dose should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

DOSE VERIFICATION OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)

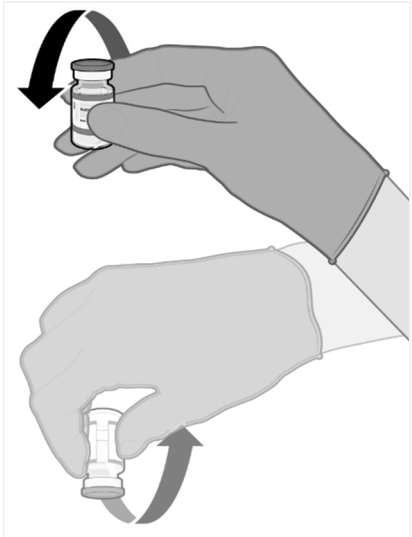


- Verify that the vial has an orange plastic cap.
- If the vial has a purple plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose concentrate for dispersion for injection.
- If the vial has a grey plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose dispersion for injection.

HANDLING PRIOR TO USE OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)

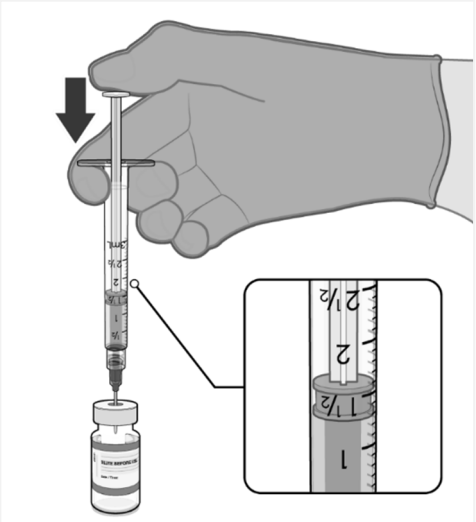
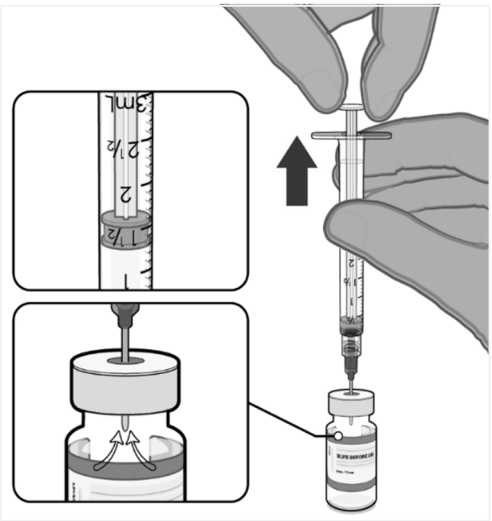
- If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 10 vial pack may take 4 hours to thaw. Ensure vials are completely thawed prior to use.
- Upon moving vials to 2 °C to 8 °C storage, update the expiry date on the carton.
- Unopened vials can be stored for up to 10 weeks at 2 °C to 8 °C within the 6-month shelf life.
- Alternatively, individual frozen vials may be thawed for 30 minutes at temperatures up to 30 °C.
- Prior to use, the unopened vial can be stored for up to 12 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions.

MIXING PRIOR TO DILUTION OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)

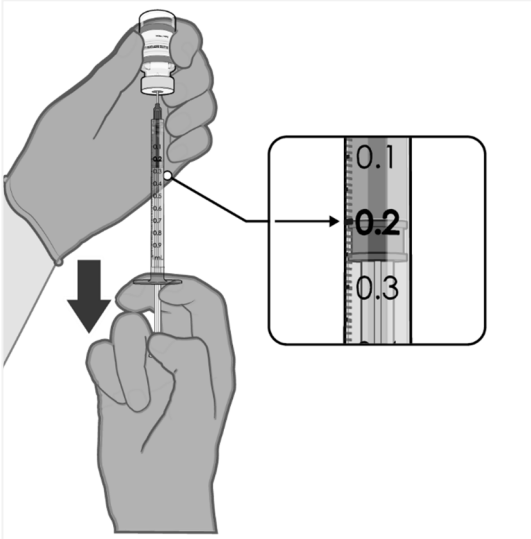


Gently × 10

- Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. Do not shake.
- Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.

DILUTION OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)	
 **1.3 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.3 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.
 **Pull back plunger to 1.3 mL to remove air from vial.**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.3 mL air into the empty diluent syringe.

 **Gently × 10**	• Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as a white to off-white dispersion with no particulates visible. Do not use the diluted vaccine if particulates or discolouration are present.
 **Record appropriate date and time.** **Use within 12 hours after dilution.**	• The diluted vials should be marked with the appropriate date and time. • After dilution, store at 2 ºC to 30 ºC and use within 12 hours. • Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.2 mL DOSES OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)	
 **0.2 mL diluted vaccine**	• After dilution, the vial contains 2.6 mL from which 10 doses of 0.2 mL can be extracted. • Using aseptic technique, cleanse the vial stopper with a single use antiseptic swab. • Withdraw 0.2 mL of Comirnaty for children age 5 to 11 years. Low dead-volume syringes and/or needles should be used in order to extract 10 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract ten doses from a single vial. • 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. • Discard any unused vaccine within 12 hours after dilution.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1528/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 December 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance(s)

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany

BioNTech Manufacturing Marburg GmbH
Emil-von-Behring-Strasse 76
35401 Marburg
Germany

Rentschler Biopharma SE
Erwin-Rentschler-Strasse 21
88471 Laupheim
Germany

Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC
1 Burtt Road
Andover, MA 01810
USA

Name and address of the manufacturers responsible for batch release

BioNTech Manufacturing GmbH
Kupferbergterrasse 17 - 19
55116 Mainz
Germany

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs
Belgium

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

In view of the declared Public Health Emergency of International Concern and in order to ensure early supply this medicinal product is subject to a time-limited exemption allowing reliance on batch control testing conducted in the registered site(s) that are located in a third country. This exemption ceases to be valid on 31 August 2021. Implementation of EU based batch control arrangements, including the necessary variations to the terms of the marketing authorisation, has to be completed by 31 August 2021 at the latest, in line with the agreed plan for this transfer of testing. Progress reports have to be submitted on 31 March 2021 and included in the annual renewal application.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to complete the characterisation of the active substance and finished product, the MAH should provide additional data.	July 2021. Interim reports: 31 March 2021
In order to ensure consistent product quality, the MAH should provide additional information to enhance the control strategy, including the active substance and finished product specifications.	July 2021. Interim reports: March 2021
In order to confirm the purity profile and ensure comprehensive quality control and batch-to-batch consistency throughout the lifecycle of the finished product, the MAH should provide additional information about the synthetic process and control strategy for the excipient ALC-0315.	July 2021. Interim reports: January 2021, April 2021
In order to confirm the purity profile and ensure comprehensive quality control and batch-to-batch consistency throughout the lifecycle of the finished product, the MAH should provide additional information about the synthetic process and control strategy for the excipient ALC-0159.	July 2021. Interim reports: January 2021, April 2021

Description	Due date
In order to confirm the efficacy and safety of Comirnaty, the MAH should submit the final Clinical Study Report for the randomized, placebo-controlled, observer-blind study C4591001.	December 2023

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON BOX LABEL

1. NAME OF THE MEDICINAL PRODUCT

COMIRNATY 30 micrograms/dose concentrate for dispersion for injection
Adults and adolescents from 12 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After dilution, each vial contains 6 doses of 0.3 mL.

3. LIST OF EXCIPIENTS

Excipients: ALC-0315, ALC-0159, DSPC, cholesterol, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium phosphate dihydrate, sucrose, water for injections, sodium hydroxide, hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for dispersion for injection
195 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use after dilution.
Read the package leaflet before use.

Scan QR code for more information.

Dilute before use: Dilute each vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (at -90 °C to -60 °C)
Expiry date at 2 °C to 8 °C: …….

(Maximum 1 month. Cross out former expiry date.)

9. SPECIAL STORAGE CONDITIONS

Storage:
Prior to dilution, store at -90 °C to -60 °C in the original package in order to protect from light.
After dilution, store the vaccine at 2 °C to 30 °C and use within 6 hours.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1528/001

13. BATCH NUMBER

LOT

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

COMIRNATY 30 mcg sterile concentrate
COVID-19 mRNA Vaccine
tozinameran
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

LOT

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6 doses of 30 mcg after dilution

6. OTHER

Discard time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

COMIRNATY 30 micrograms/dose dispersion for injection
Adults and adolescents from 12 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 6 doses of 0.3 mL.

3. LIST OF EXCIPIENTS

Excipients: ALC-0315, ALC-0159, DSPC, cholesterol, trometamol, trometamol hydrochloride, sucrose, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
195 multidose vials
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Do not dilute prior to use

Scan QR code for more information.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (at -90 °C to -60 °C)
Expiry date at 2 °C to 8 °C: …….
(Maximum 10 weeks. Cross out the former expiry date.)

9. SPECIAL STORAGE CONDITIONS

Storage:
Store at 2 °C to 8 °C after receipt. Do not refreeze once thawed.
Store in the original package in order to protect from light.
Read the package leaflet before use and for additional storage information.
After first puncture, store at 2 °C to 30 °C and use within 12 hours.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1528/003 195 multidose vials
EU/1/20/1528/002 10 multidose vials

13. BATCH NUMBER

LOT

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

COMIRNATY 30 mcg injection
COVID-19 mRNA Vaccine
tozinameran
IM

2. METHOD OF ADMINISTRATION

Do not dilute

3. EXPIRY DATE

EXP

4. BATCH NUMBER

LOT

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6 doses of 30 mcg

6. OTHER

Discard time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

COMIRNATY 10 micrograms/dose concentrate for dispersion for injection
Children 5 to 11 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After dilution, each vial contains 10 doses of 0.2 mL.

3. LIST OF EXCIPIENTS

Excipients: ALC-0315, ALC-0159, DSPC, cholesterol, trometamol, trometamol hydrochloride sucrose, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for dispersion for injection
10 multidose vials
195 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use after dilution.
Read the package leaflet before use and additional storage information.

Scan QR code for more information.

Dilute before use: Dilute each vial with 1.3 mL sodium chloride 9 mg/mL (0.9%) solution for injection.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (at -90 °C to -60 °C)
Expiry date at 2 °C to 8 °C: …….
(Maximum 10 weeks. Cross out former expiry date.)

9. SPECIAL STORAGE CONDITIONS

Storage:
Store at 2 °C to 8 °C after receipt. Do not refreeze once thawed.
Keep in the original package in order to protect from light.
After dilution, store the vaccine at 2 °C to 30 °C and use within 12 hours.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

12. MARKETING AUTHORISATION NUMBER(S)

13. BATCH NUMBER

LOT

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

COMIRNATY 10 mcg sterile concentrate
COVID-19 mRNA Vaccine
tozinameran
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

LOT

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses of 10 mcg after dilution

6. OTHER

Discard date/time:

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Comirnaty 30 micrograms/dose concentrate for dispersion for injection
Adults and adolescents from 12 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

▼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 the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Comirnaty is and what it is used for

Comirnaty is a vaccine used for preventing COVID-19 caused by SARS-CoV-2 virus.

Comirnaty 30 micrograms/dose concentrate for dispersion for injection is given to adults and adolescents from 12 years of age and older.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and blood cells that work against the virus, so giving protection against COVID-19.

As Comirnaty does not contain the virus to produce immunity, it cannot give you COVID-19.

2. What you need to know before you receive Comirnaty

Comirnaty should not be given
- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given the vaccine if:
- you have ever had a severe allergic reaction or breathing problems after any other vaccine injection or after you were given Comirnaty in the past.
- you are feeling nervous about the vaccination process or have ever fainted following any needle injection.
- you have a severe illness or infection with high fever. However, you can have your vaccination if you have a mild fever or upper airway infection like a cold.
- you have a bleeding problem, you bruise easily or you use a medicine to prevent blood-clots.

- you have a weakened immune system, because of a disease such as HIV infection or a medicine such as corticosteroid that affects your immune system.

Very rare cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported after vaccination with Comirnaty. The cases have primarily occurred within two weeks following vaccination, more often after the second vaccination, and more often occurred in younger men. Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

As with any vaccine, Comirnaty may not fully protect all those who receive it and it is not known how long you will be protected.

You may receive a third dose of Comirnaty. The efficacy of Comirnaty, even after a third dose, may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Children
Comirnaty is not recommended for children aged under 12 years.

Other medicines and Comirnaty
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines or have recently received any other vaccine.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you receive this vaccine.

Driving and using machines
Some of the effects of vaccination mentioned in section 4 (Possible side effects) may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

Comirnaty contains potassium and sodium
This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially ‘potassium-free’.

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

3. How Comirnaty is given

Comirnaty is given after dilution as an injection of 0.3 mL into a muscle of your upper arm.

You will receive 2 injections.

It is recommended to receive the second dose of the same vaccine 3 weeks after the first dose to complete the vaccination course.

A booster dose (third dose) of Comirnaty may be given at least 6 months after the second dose in individuals 18 years of age and older.

If you are immunocompromised, you may receive a third dose of Comirnaty at least 28 days after the second dose.

If you have any further questions on the use of Comirnaty, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Very common side effects: may affect more than 1 in 10 people
- injection site: pain, swelling
- tiredness
- headache
- muscle pain
- chills
- joint pain
- diarrhoea
- fever

Some of these side effects were slightly more frequent in adolescents 12 to 15 years than in adults.

Common side effects: may affect up to 1 in 10 people
- injection site redness
- nausea
- vomiting

Uncommon side effects: may affect up to 1 in 100 people
- enlarged lymph nodes (more frequently observed after the booster dose)
- feeling unwell
- arm pain
- insomnia
- injection site itching
- allergic reactions such as rash or itching
- feeling weak or lack of energy/sleepy
- decreased appetite
- excessive sweating
- night sweats

Rare side effects: may affect up to 1 in 1,000 people
- temporary one sided facial drooping
- allergic reactions such as hives or swelling of the face

Not known (cannot be estimated from the available data)
- severe allergic reaction
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain
- extensive swelling of the vaccinated limb
- swelling of the face (swelling of the face may occur in patients who have had facial dermatological fillers)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V and include batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Comirnaty

Keep this medicine out of the sight and reach of children.

The following information about storage, expiry and use and handling is intended for healthcare professionals.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in freezer at -90 °C to -60 °C. Within the 9-month shelf life unopened vials may be stored and transported at -25 °C to -15 °C for a single period of up to 2 weeks and can be returned to -90 °C to -60 °C.

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

When stored frozen at -90 °C to -60 °C, 195-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 3 hours or individual vials can be thawed at room temperature (up to 30 °C) for 30 minutes.

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

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

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

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

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

After thawing, the vaccine should be diluted and used immediately. However, in-use stability data have demonstrated that once removed from freezer, the undiluted vaccine can be stored for up to 1 month at 2 °C to 8 °C within the 9-month shelf life. Within the 1-month shelf life at 2 °C to 8 °C, up to 12 hours may be used for transportation. Prior to use, the unopened vaccine can be stored for up to 2 hours at temperatures up to 30 °C.

Thawed vials can be handled in room light conditions.

After dilution, store and transport the vaccine at 2 °C to 30 °C and use within 6 hours. Discard any unused vaccine.

Once removed from the freezer and diluted, the vials should be marked with the new discard date and time. Once thawed, the vaccine cannot be re-frozen.

Do not use this vaccine if you notice particulates in the dilution or discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Comirnaty contains

- The active substance is COVID-19 mRNA Vaccine called tozinameran. After dilution, the vial contains 6 doses of 0.3 mL with 30 micrograms tozinameran each.
- The other ingredients are:
  - ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
  - 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
  - 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
  - cholesterol
  - potassium chloride
  - potassium dihydrogen phosphate
  - sodium chloride
  - disodium phosphate dihydrate
  - sucrose
  - water for injections
  - sodium hydroxide (for pH adjustment)
  - hydrochloric acid (for pH adjustment)

What Comirnaty looks like and contents of the pack

The vaccine is a white to off-white dispersion (pH: 6.9 - 7.9) provided in a multidose vial of 6 doses in a 2 mL clear vial (type I glass), with a rubber stopper and a purple flip-off plastic cap with aluminium seal.

Pack size: 195 vials

Marketing Authorisation Holder

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

Manufacturers

BioNTech Manufacturing GmbH
Kupferbergterrasse 17 - 19
55116 Mainz
Germany

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Luxembourg/Luxemburg
Pfizer S.A./N.V.
Tél/Tel: +32 (0)2 554 62 11

Lietuva
Pfizer Luxembourg SARL filialas Lietuvoje
Tel. +370 52 51 4000

България
Пфайзер Люксембург САРЛ, Клон България
Тел: +359 2 970 4333

Česká republika
Pfizer, spol. s r.o.
Tel: +420 283 004 111

Danmark
Pfizer ApS
Tlf: +45 44 201 100

Deutschland
BioNTech Manufacturing GmbH
Tel: +49 6131 90840

Eesti
Pfizer Luxembourg SARL Eesti filiaal
Tel: +372 666 7500

Ελλάδα
Pfizer Ελλάς A.E.
Τηλ.: +30 210 6785 800

España
Pfizer, S.L.
Tel:+34914909900

France
Pfizer
Tél +33 1 58 07 34 40

Hrvatska
Pfizer Croatia d.o.o.
Tel: +385 1 3908 777

Ireland
Pfizer Healthcare Ireland
Tel: 1800 633 363 (toll free)
+44 (0)1304 616161

Ísland
Icepharma hf
Simi: +354 540 8000

Italia
Pfizer S.r.l.
Tel: +39 06 33 18 21

Κύπρος
Pfizer Ελλάς A.E. (Cyprus Branch)
Τηλ: +357 22 817690

Magyarország
Pfizer Kft
Tel: +36 1 488 3700

Malta
Vivian Corporation Ltd.
Tel: +35621 344610

Norge
Pfizer AS
Tlf: +47 67 526 100

Nederland
Pfizer BV
Tel: +31 (0)10 406 43 01

Österreich
Pfizer Corporation Austria Ges.m.b.H
Tel: +43 (0)1 521 15-0

Polska
Pfizer Polska Sp. z o.o.
Tel.: +48 22 335 61 00

Portugal
Laboratórios Pfizer, Lda.
Tel: +351 21 423 5500

România
Pfizer Romania S.R.L
Tel: +40 (0) 21 207 28 00

Slovenija
Pfizer Luxembourg SARL
Pfizer, podružnica za svetovanje s področja farmacevtske dejavnosti, Ljubljana
Tel.: +386 (0) 1 52 11 400

Slovenská republika
Pfizer Luxembourg SARL,
organizačná zložka
Tel: +421 2 3355 5500

Suomi/Finland
Pfizer Oy
Puh/Tel: +358 (0)9 430 040

Sverige
Pfizer AB
Tel: +46 (0)8 550 520 00

United Kingdom (Northern Ireland)
Pfizer Limited
Tel: +44 (0) 1304 616161

Latvija
Pfizer Luxembourg SARL filiāle Latvijā
Tel.: +371 670 35 775

This leaflet was last revised in {MM/YYYY}

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine. The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Scan the code with a mobile device to get the package leaflet in different languages.

URL: www.comirnatyglobal.com

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This package leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Administer Comirnaty intramuscularly after dilution as a primary course of 2 doses (0.3 mL each) 3 weeks apart.

A booster dose (third dose) of Comirnaty may be given at least 6 months after the second dose in individuals 18 years of age and older.

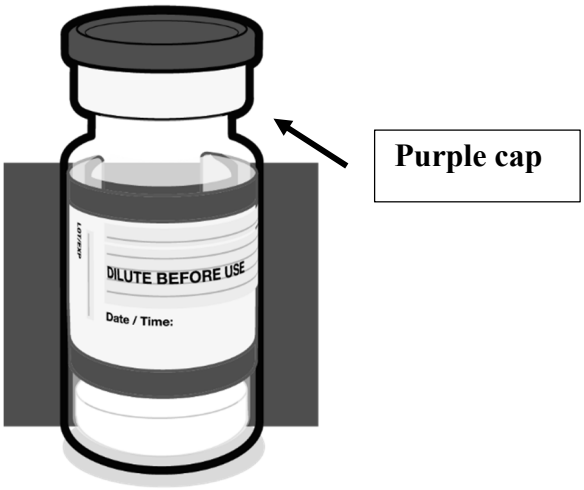
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised.

Traceability

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

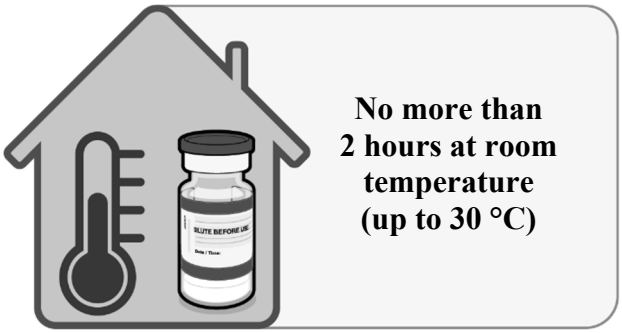
Handling instructions
Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

DOSE VERIFICATION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)

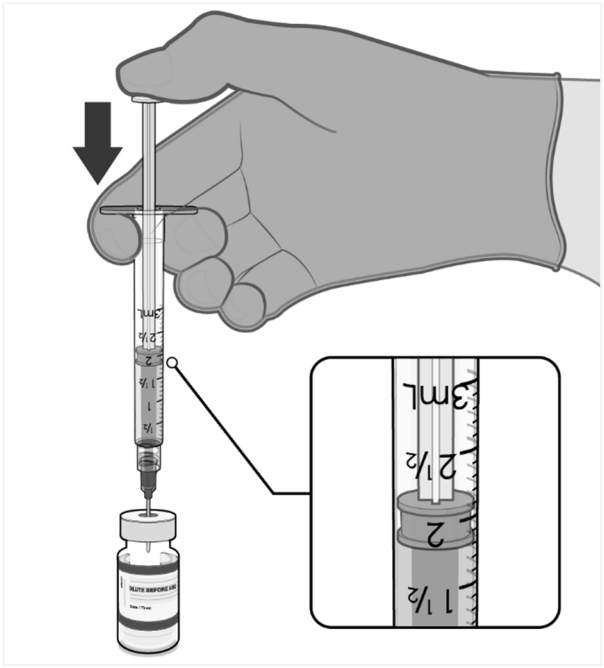
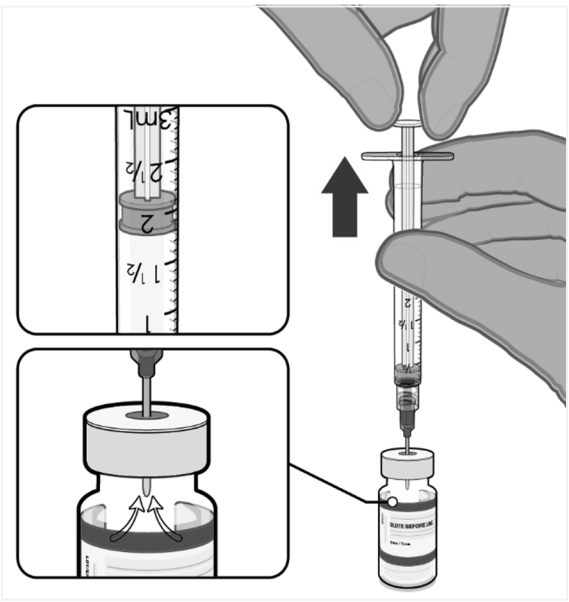


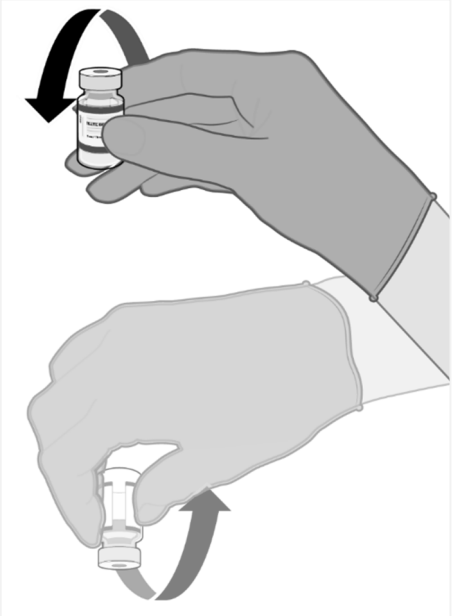
- Verify that the vial has a purple plastic cap.
- If the vial has a grey plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose dispersion for injection.
- If the vial has an orange plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.

THAWING PRIOR TO DILUTION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)

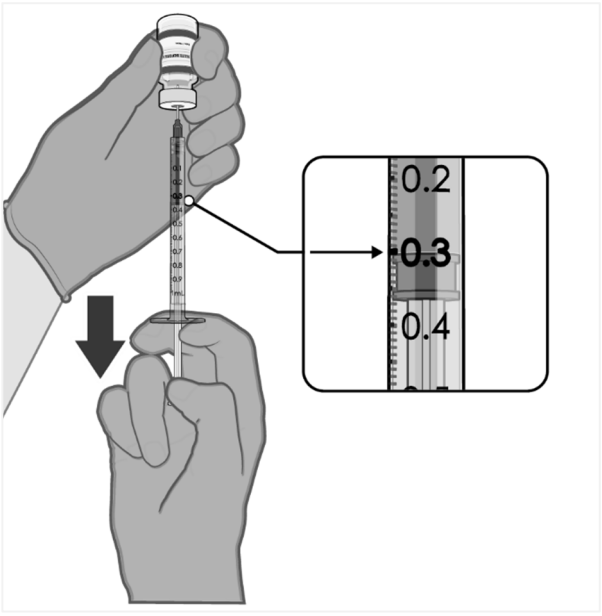


- The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use.
- The unopened vial can be stored for up to 1 month at 2 °C to 8 °C within the 9-month shelf life. Within the 1-month shelf life at 2 °C to 8 °C, up to 12 hours may be used for transportation.
- Allow the thawed vial to come to room temperature. Prior to use, the unopened vial can be stored for up to 2 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions.
- Gently invert the vial 10 times prior to dilution. Do not shake.
- Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.

DILUTION OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)	
 **1.8 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.
 **Pull back plunger to 1.8 mL to remove air from vial.**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

 **Gently × 10**	• Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as an off-white dispersion with no particulates visible. Do not use the diluted vaccine if particulates or discolouration are present.
 **Record appropriate date and time.** **Use within 6 hours after dilution.**	• The diluted vials should be marked with the appropriate date and time. • After dilution, store at 2 ºC to 30 ºC and use within 6 hours, including any transportation time. • Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY 30 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (12 YEARS AND OLDER)



0.3 mL diluted vaccine

- After dilution, the vial contains 2.25 mL from which 6 doses of 0.3 mL can be extracted.
- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab.
- Withdraw 0.3 mL of Comirnaty.

  Low dead-volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres.

  If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Discard any unused vaccine within 6 hours after dilution.

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

Package leaflet: Information for the user

Comirnaty 30 micrograms/dose dispersion for injection
Adults and adolescents from 12 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

▼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 the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Comirnaty is and what it is used for

Comirnaty is a vaccine used for preventing COVID-19 caused by SARS-CoV-2 virus.

Comirnaty 30 micrograms/dose dispersion for injection is given to adults and adolescents from 12 years of age and older.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and blood cells that work against the virus, so giving protection against COVID-19.

As Comirnaty does not contain the virus to produce immunity, it cannot give you COVID-19.

2. What you need to know before you receive Comirnaty

Comirnaty should not be given
- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given the vaccine if:
- you have ever had a severe allergic reaction or breathing problems after any other vaccine injection or after you were given Comirnaty in the past.
- you are feeling nervous about the vaccination process or have ever fainted following any needle injection.
- you have a severe illness or infection with high fever. However, you can have your vaccination if you have a mild fever or upper airway infection like a cold.
- you have a bleeding problem, you bruise easily or you use a medicine to prevent blood-clots.

- you have a weakened immune system, because of a disease such as HIV infection or a medicine such as corticosteroid that affects your immune system.

Very rare cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported after vaccination with Comirnaty. The cases have primarily occurred within two weeks following vaccination, more often after the second vaccination, and more often occurred in younger men. Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

As with any vaccine, Comirnaty may not fully protect all those who receive it and it is not known how long you will be protected.

You may receive a third dose of Comirnaty. The efficacy of Comirnaty, even after a third dose, may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Children
Comirnaty is not recommended for children aged under 12 years.

Other medicines and Comirnaty
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines or have recently received any other vaccine.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you receive this vaccine.

Driving and using machines
Some of the effects of vaccination mentioned in section 4 (Possible side effects) may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

3. How Comirnaty is given

Comirnaty is given as an injection of 0.3 mL into a muscle of your upper arm.

You will receive 2 injections.

It is recommended to receive the second dose of the same vaccine 3 weeks after the first dose to complete the vaccination course.

A booster dose (third dose) of Comirnaty may be given at least 6 months after the second dose in individuals 18 years of age and older.

If you are immunocompromised, you may receive a third dose of Comirnaty at least 28 days after the second dose.

If you have any further questions on the use of Comirnaty, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Very common side effects: may affect more than 1 in 10 people
- injection site: pain, swelling
- tiredness
- headache
- muscle pain
- chills
- joint pain
- diarrhoea
- fever

Some of these side effects were slightly more frequent in adolescents 12 to 15 years than in adults.

Common side effects: may affect up to 1 in 10 people
- injection site redness
- nausea
- vomiting

Uncommon side effects: may affect up to 1 in 100 people
- enlarged lymph nodes (more frequently observed after the booster dose)
- feeling unwell
- arm pain
- insomnia
- injection site itching
- allergic reactions such as rash or itching
- feeling weak or lack of energy/sleepy
- decreased appetite
- excessive sweating
- night sweats

Rare side effects: may affect up to 1 in 1,000 people
- temporary one sided facial drooping
- allergic reactions such as hives or swelling of the face

Not known (cannot be estimated from the available data)
- severe allergic reaction
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain
- extensive swelling of the vaccinated limb
- swelling of the face (swelling of the face may occur in patients who have had facial dermatological fillers)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V and include batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Comirnaty

Keep this medicine out of the sight and reach of children.

The following information about storage, expiry and use and handling is intended for healthcare professionals.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in freezer at -90 °C to -60 °C for 6 months.

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

The vaccine may be received frozen at -90 °C to -60 °C or at -25 °C to -15 °C. Frozen vaccine can be stored either at -90 °C to -60 °C or 2 °C to 8 °C upon receipt.

When stored frozen at -90 °C to -60 °C, 10-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 6 hours or individual vials can be stored at room temperature (up to 30 °C) for 30 minutes.

Once removed from the freezer, the unopened vial may be stored refrigerated at 2 °C to 8 °C for a single period of up to 10 weeks within the 6-month shelf life. The outer carton should be marked with the new discard date at 2 °C to 8 °C. Once thawed, the vaccine cannot be re-frozen.

Prior to use, the unopened vials can be stored for up to 12 hours at temperatures between 8 °C and 30 °C.

Thawed vials can be handled in room light conditions.

After first puncture, store and transport the vaccine at 2 °C to 30 °C and use within 12 hours. Discard any unused vaccine.

Do not use this vaccine if you notice particulates or discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Comirnaty contains

- The active substance is COVID-19 mRNA Vaccine called tozinameran. The vial contains 6 doses of 0.3 mL with 30 micrograms tozinameran each.
- The other ingredients are:
  - ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
  - 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
  - 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
  - cholesterol
  - trometamol
  - trometamol hydrochloride
  - sucrose
  - water for injections

What Comirnaty looks like and contents of the pack
The vaccine is a white to off-white dispersion (pH: 6.9 - 7.9) provided in a multidose vial of 6 doses in a 2 mL clear vial (type I glass), with a rubber stopper and a grey flip-off plastic cap with aluminium seal.

Pack sizes: 195 vials or 10 vials

Not all pack sizes may be marketed.

Marketing Authorisation Holder
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

Manufacturers
BioNTech Manufacturing GmbH
Kupferbergterrasse 17 - 19
55116 Mainz
Germany

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Luxembourg/Luxemburg
Pfizer S.A./N.V.
Tél/Tel: +32 (0)2 554 62 11

България
Пфайзер Люксембург САРЛ, Клон България
Тел: +359 2 970 4333

Česká republika
Pfizer, spol. s r.o.
Tel: +420 283 004 111

Danmark
Pfizer ApS
Tlf: +45 44 201 100

Deutschland
BioNTech Manufacturing GmbH
Tel: +49 6131 90840

Lietuva
Pfizer Luxembourg SARL filialas Lietuvoje
Tel. +370 52 51 4000

Magyarország
Pfizer Kft
Tel: +36 1 488 3700

Malta
Vivian Corporation Ltd.
Tel: +35621 344610

Norge
Pfizer AS
Tlf: +47 67 526 100

Nederland
Pfizer BV
Tel: +31 (0)10 406 43 01

Eesti
Pfizer Luxembourg SARL Eesti filiaal
Tel: +372 666 7500

Ελλάδα
Pfizer Ελλάς A.E.
Τηλ.: +30 210 6785 800

España
Pfizer, S.L.
Tel:+34914909900

France
Pfizer
Tél +33 1 58 07 34 40

Hrvatska
Pfizer Croatia d.o.o.
Tel: +385 1 3908 777

Ireland
Pfizer Healthcare Ireland
Tel: 1800 633 363 (toll free)
+44 (0)1304 616161

Ísland
Icepharma hf
Simi: +354 540 8000

Italia
Pfizer S.r.l.
Tel: +39 06 33 18 21

Κύπρος
Pfizer Ελλάς A.E. (Cyprus Branch)
Τηλ: +357 22 817690

Latvija
Pfizer Luxembourg SARL filiāle Latvijā
Tel.: +371 670 35 775

Österreich
Pfizer Corporation Austria Ges.m.b.H
Tel: +43 (0)1 521 15-0

Polska
Pfizer Polska Sp. z o.o.
Tel.: +48 22 335 61 00

Portugal
Laboratórios Pfizer, Lda.
Tel: +351 21 423 5500

România
Pfizer Romania S.R.L
Tel: +40 (0) 21 207 28 00

Slovenija
Pfizer Luxembourg SARL
Pfizer, podružnica za svetovanje s področja farmacevtske dejavnosti, Ljubljana
Tel.: +386 (0) 1 52 11 400

Slovenská republika
Pfizer Luxembourg SARL,
organizačná zložka
Tel: +421 2 3355 5500

Suomi/Finland
Pfizer Oy
Puh/Tel: +358 (0)9 430 040

Sverige
Pfizer AB
Tel: +46 (0)8 550 520 00

United Kingdom (Northern Ireland)
Pfizer Limited
Tel: +44 (0) 1304 616161

This leaflet was last revised in {MM/YYYY}

This medicine has been given ‘conditional approval’. This means that there is more evidence to come about this medicine. The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Scan the code with a mobile device to get the package leaflet in different languages.

URL: www.comirnatyglobal.com

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This package leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Administer Comirnaty intramuscularly as a primary course of 2 doses (0.3 mL each) 3 weeks apart.

A booster dose (third dose) of Comirnaty may be given at least 6 months after the second dose in individuals 18 years of age and older.

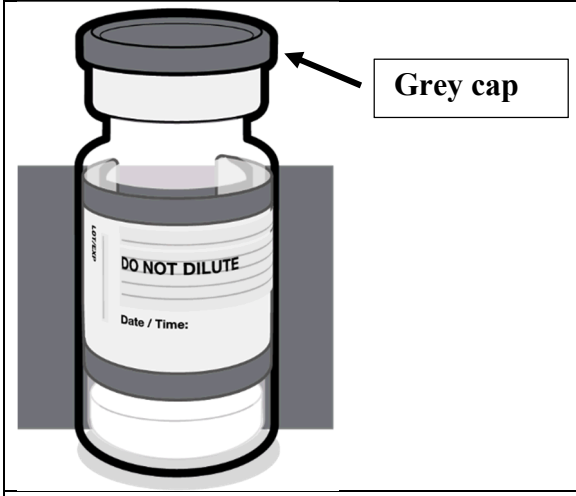
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised.

Traceability

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

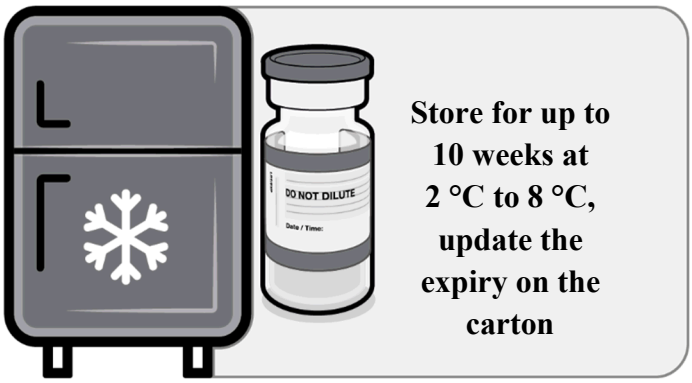
Handling instructions
Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

DOSE VERIFICATION OF COMIRNATY 30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER)

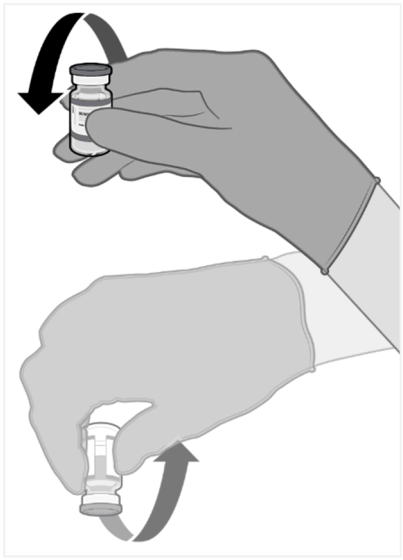


- Verify that the vial has a grey plastic cap.
- If the vial has a purple plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose concentrate for dispersion for injection.
- If the vial has an orange plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 10 micrograms/dose concentrate for dispersion for injection.

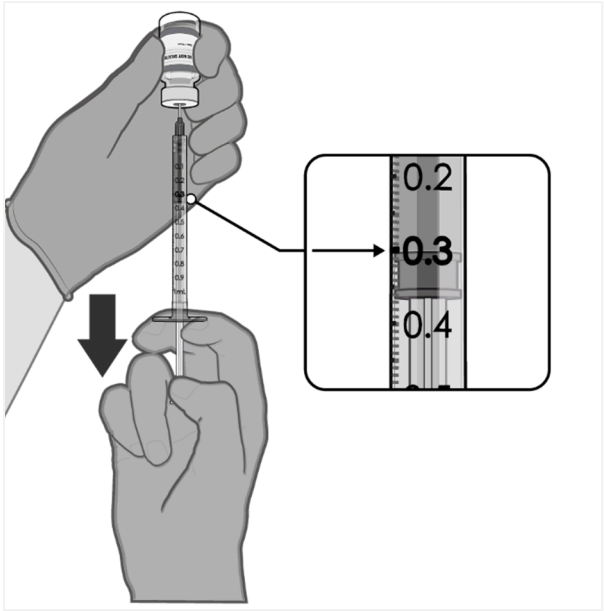
HANDLING PRIOR TO USE OF COMIRNATY 30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER)



- If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 10 vial pack may take 6 hours to thaw. Ensure vials are completely thawed prior to use.
- Upon moving vials to 2 °C to 8 °C storage, update the expiry date on the carton.
- Unopened vials can be stored for up to 10 weeks at 2 °C to 8 °C within in the 6-month shelf life.
- Alternatively, individual frozen vials may be thawed for 30 minutes at temperatures up to 30 °C. Prior to use, the unopened vial can be stored for up to 12 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions.

<table>
<tr>
<td> 
Gently x 10</td>
<td>

Gently mix by inverting vials 10 times prior to use. Do not shake.
Prior to mixing, the thawed dispersion may contain white to off-white opaque amorphous particles.
After mixing, the vaccine should present as an off-white dispersion with no particulates visible. Do not use the vaccine if particulates or discolouration are present.

</td>
</tr>
<tr>
<td colspan="2">PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY
30 MICROGRAMS/DOSE DISPERSION FOR INJECTION (12 YEARS AND OLDER)</td>
</tr>
<tr>
<td> 

0.3 mL vaccine</td>
<td>

Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab.
Withdraw 0.3 mL of Comirnaty.

Low dead-volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres.

If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial.
Each dose must contain 0.3 mL of vaccine.
If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
Discard any unused vaccine 12 hours after first puncture. Record the appropriate date/time on the vial.

</td>
</tr>
</table>

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

Package leaflet: Information for the user

Comirnaty 10 micrograms/dose concentrate for dispersion for injection
Children 5 to 11 years
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects your child may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Comirnaty is and what it is used for

Comirnaty is a vaccine used for preventing COVID-19 caused by SARS-CoV-2 virus.

Comirnaty 10 micrograms/dose concentrate for dispersion for injection is given to children from 5 to 11 years of age.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and blood cells that work against the virus, so giving protection against COVID-19.

As Comirnaty does not contain the virus to produce immunity, it cannot give your child COVID-19.

2. What you need to know before your child receives Comirnaty

Comirnaty should not be given
- if your child is allergic to the active substance or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions
Talk to your doctor, pharmacist or nurse before your child is given the vaccine if your child:
- has ever had a severe allergic reaction or breathing problems after any other vaccine injection or after having been given Comirnaty in the past.
- is feeling nervous about the vaccination process or has ever fainted following any needle injection.
- has a severe illness or infection with high fever. However, your child can have the vaccination if he/she have a mild fever or upper airway infection like a cold.
- has a bleeding problem, bruises easily or uses a medicine to prevent blood-clots.

- has a weakened immune system, because of a disease such as HIV infection or a medicine such as corticosteroid that affects the immune system.

Very rare cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported after vaccination with Comirnaty. The cases have primarily occurred within two weeks following vaccination, more often after the second vaccination, and more often occurred in younger men. Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

As with any vaccine, Comirnaty may not fully protect all those who receive it and it is not known how long you will be protected.

Your child may receive a third dose of Comirnaty. The third dose may still not provide full immunity to COVID-19 in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Children
Comirnaty is not recommended for children aged under 5 years.

Other medicines and Comirnaty
Tell your doctor or pharmacist if your child is using, has recently used or might use any other medicines or has recently received any other vaccine.

Pregnancy and breast-feeding
If your child is pregnant or breast-feeding, ask your doctor or pharmacist for advice before your child receives this vaccine.

Driving and using machines
Some of the effects of vaccination mentioned in section 4 (Possible side effects) may temporarily affect your ability to use machines or undertake activities such as cycling. Wait until these effects have worn off before resuming activities that require your full attention.

3. How Comirnaty is given

Comirnaty is given after dilution as an injection of 0.2 mL into a muscle of the upper arm.

Your child will receive 2 injections.

It is recommended to receive the second dose of the same vaccine 3 weeks after the first dose to complete the vaccination course.

If your child is immunocompromised, he or she may receive a third dose of Comirnaty at least 28 days after the second dose.

If you have any further questions on the use of Comirnaty, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Very common side effects: may affect more than 1 in 10 people
- injection site: pain, swelling, redness
- tiredness

- headache
- muscle pain
- chills
- joint pain
- diarrhoea
- fever

Some of these side effects were slightly more frequent in adolescents 12 to 15 years than in adults.

Common side effects: may affect up to 1 in 10 people
- nausea
- vomiting

Uncommon side effects: may affect up to 1 in 100 people
- enlarged lymph nodes (more frequently observed after the booster dose)
- feeling unwell
- arm pain
- insomnia
- injection site itching
- allergic reactions such as rash or itching

Rare side effects: may affect up to 1 in 1,000 people
- temporary one sided facial drooping
- allergic reactions such as hives or swelling of the face

Not known (cannot be estimated from the available data)
- severe allergic reaction
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain
- extensive swelling of the vaccinated limb
- swelling of the face (swelling of the face may occur in patients who have had facial dermatological fillers)

Reporting of side effects
If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V and include batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Comirnaty

Keep this medicine out of the sight and reach of children.

The following information about storage, expiry and use and handling is intended for healthcare professionals.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in freezer at -90 °C to -60 °C for 6 months.

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

The vaccine may be received frozen at -90 °C to -60 °C or at -25 °C to -15 °C. Frozen vaccine can be stored either at -90 °C to -60 °C or 2 °C to 8 °C upon receipt.

When stored frozen at -90 °C to -60 °C, 10-vial packs of the vaccine can be thawed at 2 °C to 8 °C for 4 hours or individual vials can be thawed at room temperature (up to 30 °C) for 30 minutes.

Once removed from the freezer, the unopened vial may be stored refrigerated at 2 °C to 8 °C for a single period of up to 10 weeks within the 6-month shelf life. The outer carton should be marked with the new discard date at 2 °C to 8 °C. Once thawed, the vaccine cannot be re-frozen.

Thawed vials can be handled in room light conditions.

After dilution, store and transport the vaccine at 2 °C to 30 °C and use within 12 hours. Discard any unused vaccine.

Do not use this vaccine if you notice particulates in the dilution or discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Comirnaty contains

- The active substance is COVID-19 mRNA Vaccine called tozinameran. After dilution, the vial contains 10 doses of 0.2 mL with 10 micrograms tozinameran each.
- The other ingredients are:
  - ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
  - 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
  - 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
  - cholesterol
  - trometamol
  - trometamol hydrochloride
  - sucrose
  - water for injections

What Comirnaty looks like and contents of the pack

The vaccine is a white to off-white dispersion (pH: 6.9 - 7.9) provided in a multidose vial of 10 doses in a 2 mL clear vial (type I glass), with a rubber stopper and an orange flip-off plastic cap with aluminium seal.

Pack sizes: 195 vials or 10 vials

Not all pack sizes may be marketed.

Marketing Authorisation Holder

BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz
Germany
Phone: +49 6131 9084-0
Fax: +49 6131 9084-2121
service@biontech.de

Manufacturers

BioNTech Manufacturing GmbH
Kupferbergterrasse 17 - 19
55116 Mainz

Germany

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Luxembourg/Luxemburg
Pfizer S.A./N.V.
Tél/Tel: +32 (0)2 554 62 11

България
Пфайзер Люксембург САРЛ, Клон България
Тел: +359 2 970 4333

Česká republika
Pfizer, spol. s r.o.
Tel: +420 283 004 111

Danmark
Pfizer ApS
Tlf: +45 44 201 100

Deutschland
BioNTech Manufacturing GmbH
Tel: +49 6131 90840

Eesti
Pfizer Luxembourg SARL Eesti filiaal
Tel: +372 666 7500

Ελλάδα
Pfizer Ελλάς A.E.
Τηλ.: +30 210 6785 800

España
Pfizer, S.L.
Tel:+34914909900

France
Pfizer
Tél +33 1 58 07 34 40

Hrvatska
Pfizer Croatia d.o.o.
Tel: +385 1 3908 777

Lietuva
Pfizer Luxembourg SARL filialas Lietuvoje
Tel. +370 52 51 4000

Magyarország
Pfizer Kft
Tel: +36 1 488 3700

Malta
Vivian Corporation Ltd.
Tel: +35621 344610

Norge
Pfizer AS
Tlf: +47 67 526 100

Nederland
Pfizer BV
Tel: +31 (0)10 406 43 01

Österreich
Pfizer Corporation Austria Ges.m.b.H
Tel: +43 (0)1 521 15-0

Polska
Pfizer Polska Sp. z o.o.
Tel.: +48 22 335 61 00

Portugal
Laboratórios Pfizer, Lda.
Tel: +351 21 423 5500

România
Pfizer Romania S.R.L
Tel: +40 (0) 21 207 28 00

Slovenija
Pfizer Luxembourg SARL
Pfizer, podružnica za svetovanje s področja farmacevtske dejavnosti, Ljubljana
Tel.: +386 (0) 1 52 11 400

Ireland
Pfizer Healthcare Ireland
Tel: 1800 633 363 (toll free)
+44 (0)1304 616161

Ísland
Icepharma hf
Simi: +354 540 8000

Italia
Pfizer S.r.l.
Tel: +39 06 33 18 21

Κύπρος
Pfizer Ελλάς A.E. (Cyprus Branch)
Τηλ: +357 22 817690

Latvija
Pfizer Luxembourg SARL filiāle Latvijā
Tel.: +371 670 35 775

Slovenská republika
Pfizer Luxembourg SARL,
organizačná zložka
Tel: +421 2 3355 5500

Suomi/Finland
Pfizer Oy
Puh/Tel: +358 (0)9 430 040

Sverige
Pfizer AB
Tel: +46 (0)8 550 520 00

United Kingdom (Northern Ireland)
Pfizer Limited
Tel: +44 (0) 1304 616161

This leaflet was last revised in {MM/YYYY}

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine. The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Scan the code with a mobile device to get the package leaflet in different languages.

URL: www.comirnatyglobal.com

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This package leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

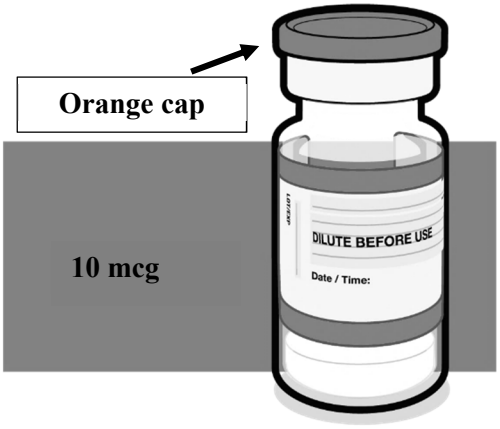
Administer Comirnaty intramuscularly after dilution as a course of 2 doses (0.3 mL each) 3 weeks apart.

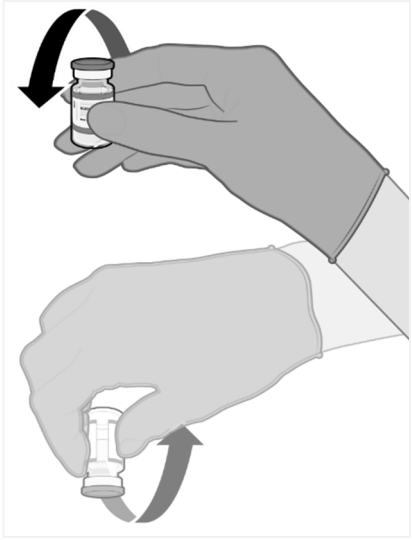
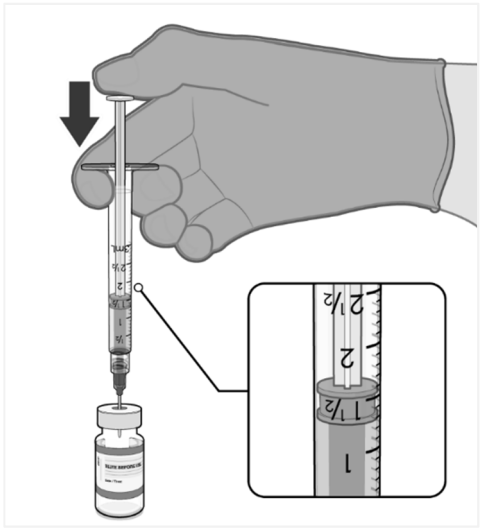
A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised.

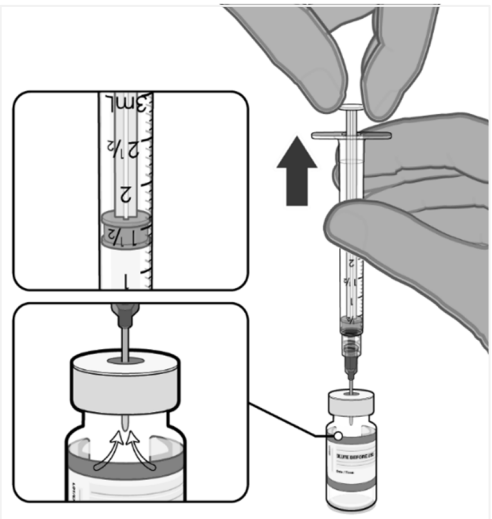
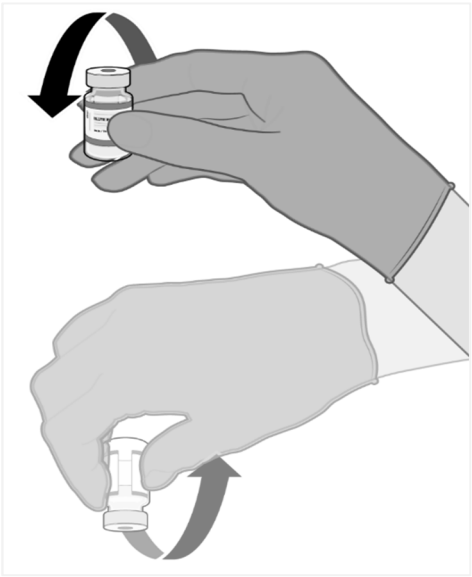
Traceability

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

Handling instructions
Comirnaty 10 micrograms/dose should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

<table>
<tr><th colspan="2">DOSE VERIFICATION OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)</th></tr>
<tr><td> 
</td><td>• Verify that the vial has an orange plastic cap.
• If the vial has a purple plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose concentrate for dispersion for injection.
• If the vial has a grey plastic cap, please make reference to the Summary of Product Characteristics for Comirnaty 30 micrograms/dose dispersion for injection.</td></tr>
<tr><th colspan="2">HANDLING PRIOR TO USE OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)</th></tr>
<tr><td> 
</td><td>• If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 10 vial pack may take 4 hours to thaw. Ensure vials are completely thawed prior to use.
• Upon moving vials to 2 °C to 8 °C storage, update the expiry date on the carton.
• Unopened vials can be stored for up to 10 weeks at 2 °C to 8 °C within the 6-month shelf life.
• Alternatively, individual frozen vials may be thawed for 30 minutes at temperatures up to 30 °C.
• Prior to use, the unopened vial can be stored for up to 12 hours at temperatures up to 30 °C. Thawed vials can be handled in room light conditions.</td></tr>
</table>

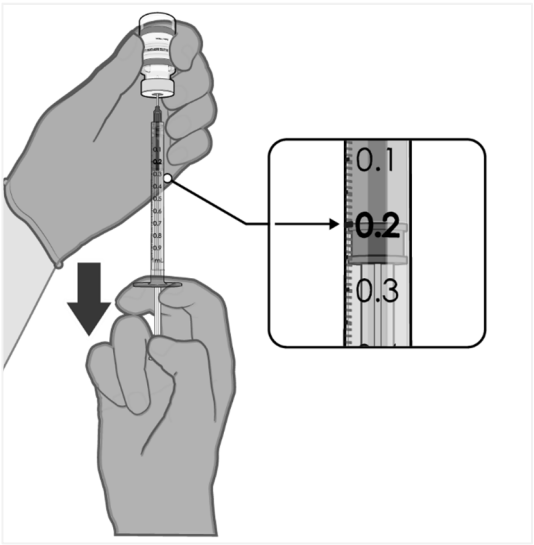
MIXING PRIOR TO DILUTION OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)	
 **Gently × 10**	• Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. Do not shake. • Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.
DILUTION OF COMIRNATY10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)	
 **1.3 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.3 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.

 **Pull back plunger to 1.3 mL to remove air from vial.**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.3 mL air into the empty diluent syringe.
 **Gently × 10**	• Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as a white to off-white dispersion with no particulates visible. Do not use the diluted vaccine if particulates or discolouration are present.

Record appropriate date and time.
Use within 12 hours after dilution.

- The diluted vials should be marked with the appropriate date and time.
- After dilution, store at 2 ºC to 30 ºC and use within 12 hours.
- Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.2 mL DOSES OF COMIRNATY 10 MICROGRAMS/DOSE CONCENTRATE FOR DISPERSION FOR INJECTION (CHILDREN 5 TO 11 YEARS)



0.2 mL diluted vaccine

- After dilution, the vial contains 2.6 mL from which 10 doses of 0.2 mL can be extracted.
- Using aseptic technique, cleanse the vial stopper with a single use antiseptic swab.
- Withdraw 0.2 mL of Comirnaty for children age 5 to 11 years.

  Low dead-volume syringes and/or needles should be used in order to extract 10 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres.

  If standard syringes and needles are used, there may not be sufficient volume to extract ten doses from a single vial.
- 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.
- Discard any unused vaccine within 12 hours after dilution.

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

PREPARED BY PFIZER INC

CDS EFFECTIVE DATE: [redacted]

Date of Superseded CDS: [redacted]

COVID-19 mRNA Vaccine

CORE DATA SHEET

VERSION [redacted]

[redacted]

*以下，非開示のため，CDS 3～68頁を削除

ワクチン接種に関する医療従事者（ワクチン接種従事者）向けファクトシートの翻訳
（COVID-19 ワクチン接種従事者に対する説明の要約～他のワクチンとの併用の項まで）

ワクチン接種に関する医療従事者（ワクチン接種従事者）向けファクトシート

コロナウイルス感染症 2019（COVID-19）予防のための
PFIZER-BIONTECH COVID-19 ワクチンの緊急使用許可（EUA）

5～11歳の小児用
使用前に希釈すること

米国食品医薬品局（FDA）は未承認の Pfizer-BioNTech COVID-19 ワクチンの緊急使用を許可した。このワクチンは 5～11 歳を対象者とし，COVID-19 の予防を目的とした能動免疫を賦与する。

本ファクトシートでは，オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンについてのみ記載しており，本ワクチンは 5～11 歳の小児に 2 回接種（初回シリーズ）の目的で使用することが認められている（バイアル表示：5～12 歳未満，カートン表示：5～12 歳未満）。

オレンジ色のキャップ／ラベル枠の枠線表示の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは，12 歳以上には使用できない[1]。

COVID-19 ワクチン接種従事者に対する説明の要約

米国連邦政府の COVID-19 ワクチン接種プログラムに登録されたワクチン接種従事者は，すべてのワクチン接種過誤，すべての重篤な有害事象，成人および小児における多臓器炎症症候群（MIS）の症例および Pfizer-BioNTech COVID-19 ワクチン接種後に入院または死亡に至った COVID-19 発症例を報告しなければならない。報告要件については「緊急使用許可に基づく PFIZER-BIONTECH COVID-19 ワクチン接種の必須要件」を参照のこと。

Pfizer-BioNTech COVID-19 ワクチンは，筋肉内注射用懸濁液である。

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは，初回シリーズとして 5～11 歳の小児に対して 3 週間間隔で 2 回（各 0.2mL），希釈したものを接種する。

[1] 初回シリーズの 1 回目接種から 2 回目接種までの期間に 12 歳となる者には，上記の年齢制限にかかわらず，次のいずれかの接種が可能である。

（1）5～11 歳で使用が許可されている Pfizer-BioNTech COVID-19 ワクチン（10 µg modRNA を含有する 1 回 0.2 mL 用量）（オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供）

（2）COMIRNATY（COVID-19 ワクチン，mRNA）または 12 歳以上で使用が許可されている Pfizer-BioNTech COVID-19 ワクチン（30 µg modRNA を含有する 1 回 0.3 mL 用量）（灰色または紫色のキャップの反復投与バイアルで提供）

調製および接種に関する説明については，本ファクトシートを参照のこと。本ファクトシートは今後更新されることもあるため，最新のファクトシートを www.cvdvaccine.com で参照すること。

Pfizer-BioNTech COVID-19 ワクチンの COVID-19 に対する能動免疫を検討している臨床試験情報については，www.clinicaltrials.gov を参照のこと。

COVID-19 の概要

COVID-19 は，2019 年後半に出現した新型コロナウイルス SARS-CoV-2 に起因する感染症であり，主に，他の臓器に影響を及ぼす可能性のある呼吸器系疾患である。COVID-19 に罹患した患者は，軽度の症状から重度の疾患まで，幅広い症状が報告されている。ウイルスに曝露してから 2～14 日後に症状が現れると考えられており，それらの症状には以下が含まれる：発熱または悪寒，咳嗽，息切れ，疲労，筋肉痛または身体の疼痛，頭痛，新たな味覚消失または嗅覚消失，咽喉痛，鼻閉または鼻汁，悪心または嘔吐，下痢。

用法・用量

本ファクトシートに記載されている保管，準備，接種に関する情報は，オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンに適用される。本ワクチンは使用前に希釈しなければならない。

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンについて

年齢層	希釈の情報	1バイアルでの接種回数（希釈後）	接種量
5～11歳（バイアル表示：5～12歳未満）	使用前に無菌の米国薬局方（USP）0.9%塩化ナトリウム注射液1.3 mLを用いてバイアル内の液を希釈する	10	0.2 mL

保管および取り扱い

保管中は，室内光への曝露を最小限にし，直射日光や紫外線を避けること。

解凍したバイアルを再凍結しないこと。

使用前のバイアル保管

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンのカートンは，ドライアイスを入れた保温容器に入れて超低温で冷凍された状態で届く。

ワクチン受領後は凍結されたバイアルを直ちに冷蔵庫［2°C～8°C（35ºF～46ºF）］に移す。解凍後は最長 10 週間保管できる。移し替えの際に 10 週間の冷蔵保管の有効期限をカートンに記入すること。1 カートン（10 バイアル）の解凍には 4 時間かかる。

また，凍結したバイアルを-90℃～-60℃（-130ºF～76ºF）の超低温フリーザーで保管することもできる。-25℃～-15℃（-13ºF～5ºF）での保管や一度解凍したバイアルの再凍結はしないこと。

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンのカートンは，2℃～8℃で届く場合がある。2℃～8℃で受領した場合は，2℃～8℃で保管し，カートンに 10 週間の冷蔵保管の有効期限が記入されていることを確認すること。

保管状態にかかわらず，ワクチンはバイアルやカートンに印刷されている製造日から 9 ヵ月以降は使用しないこと。

使用中のバイアルの保管

2℃～8℃（35ºF～46ºF）で解凍していない場合は，室温［最高 25℃（77ºF）］で 30 分間解凍する。

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは，希釈前は室温［8ºC～25ºC（46ºF～77ºF）］で 12 時間まで保管可能である。

希釈後のバイアルは，2℃～25℃（35ºF～77ºF）で保管する。バイアルは希釈から 12 時間後には廃棄すること。

バイアルのラベルやカートンには，最初の接種から 6 時間後に廃棄するよう記載されている場合がある。本ファクトシートの情報は，バイアルのラベルやカートンに印刷されているものよりも優先される。

バイアルの輸送

現地での再配送が必要な場合，希釈前のバイアルは-90℃～-60℃（-130ºF～-76ºF），または 2℃～8℃（35ºF～46ºF）で輸送する。

接種およびスケジュール

オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは，初回シリーズとして 5～11 歳の小児に対して 3 週間間隔で 2 回（各 0.2mL）接種する。

灰色または紫色のキャップの反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは，投与量の過誤を含め，接種に誤りが生じる可能性があるため，5～11 歳の小児に使用してはならない。

用量調製

ワクチン接種前にバイアルを希釈すること。

希釈前

- オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供される Pfizer-BioNTech COVID-19 ワクチンは 1.3 mL の容量で，防腐剤を含まない凍結懸濁液が含まれている。
- 希釈前に各バイアルを解凍すること。
  - バイアルは，冷蔵庫［2ºC～8ºC（35ºF～46ºF）］または室温［25ºC（77ºF）以下］で解凍すること。
  - 下表の解凍手順を参照のこと。

希釈

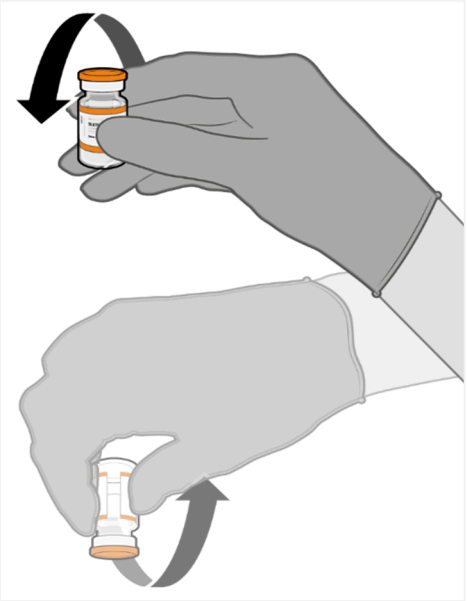
無菌の米国薬局方（USP）0.9%塩化ナトリウム注射液 1.3 mL を用いてバイアル内の液を希釈し，Pfizer-BioNTech COVID-19 ワクチンを調製する。

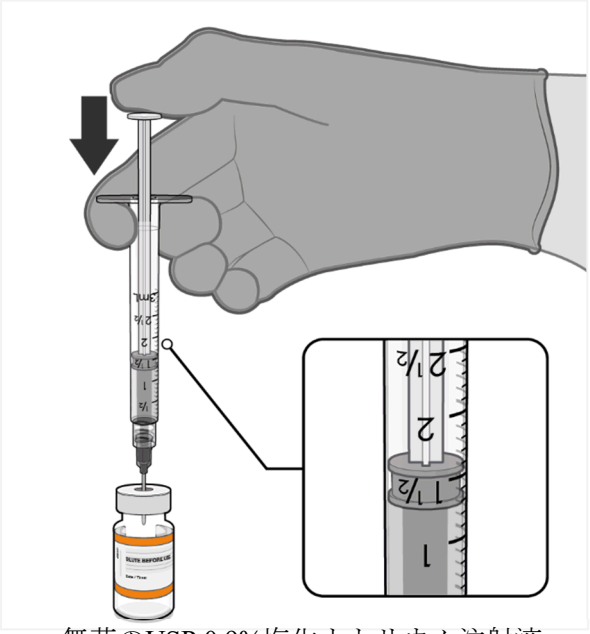
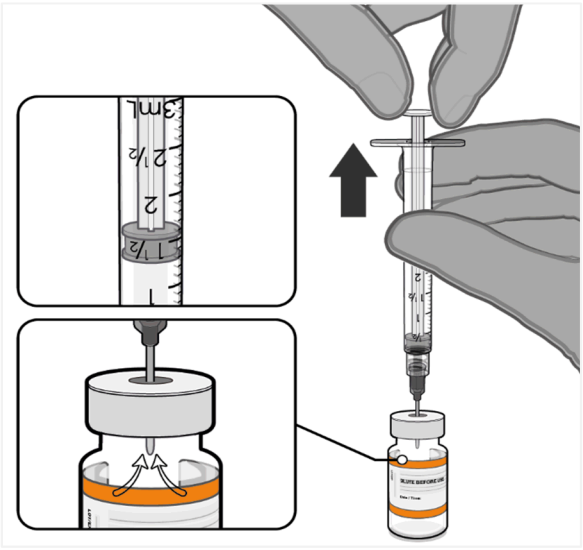
希釈剤として無菌の USP 0.9%塩化ナトリウム注射液のみを使用すること。この希釈剤はワクチンと同梱されていないため，別途調達しなければならない。静菌性の 0.9%塩化ナトリウム注射液やその他の希釈剤を使用しないこと。また，希釈剤は 1.3 mL を超えないこと。

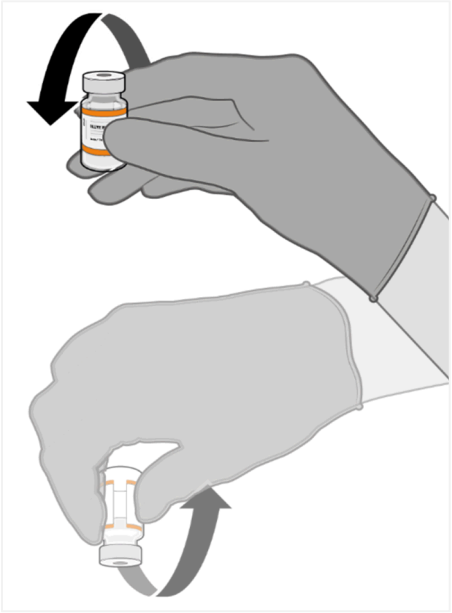
希釈後，1 バイアルに 10 回分（1 回 0.2 mL）のワクチンが含まれる。

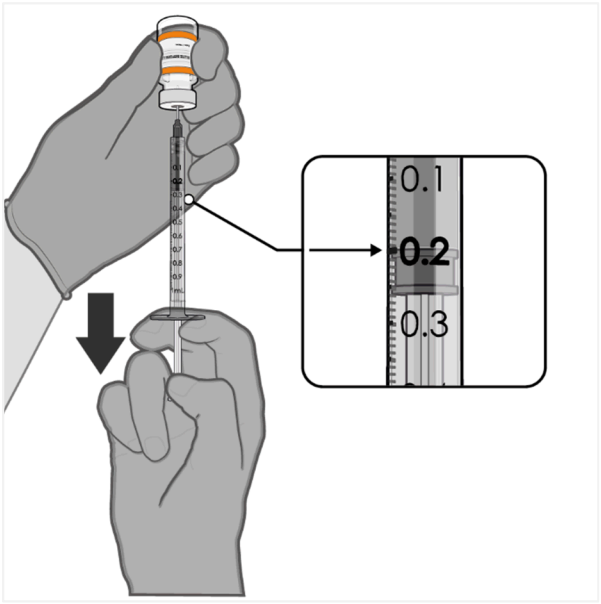
<table>
<tr><td colspan="2">希釈および調製の方法</td></tr>
<tr><td colspan="2">オレンジ色のキャップ／ラベル枠の反復投与バイアルで提供されるPfizer-BioNTech COVID-19ワクチンのバイアル確認</td></tr>
<tr><td> 

✓　オレンジ色のキャップ／ラベル枠</td><td>• Pfizer-BioNTech COVID-19 ワクチンのバイアルにオレンジ色のキャップ／ラベル枠が付いていて，「5～12 歳未満」の記載があることを確認してください。</td></tr>
<tr><td colspan="2">希釈前の解凍</td></tr>
<tr><td> 
</td><td>• 使用前に以下のいずれかの方法で Pfizer-BioNTech COVID-19 ワクチンのバイアルを解凍する。
○ 冷蔵庫内［2ºC～8ºC（35ºF～46ºF）］でバイアルを解凍する。カートンによっては解凍に最長 4 時間を要する場合があり，解凍したバイアルは 10 週間冷蔵保存することができる。
○ バイアルを室温［25°C（77°F）以下］で 30 分間解凍する。
○ 希釈前は室温［最高 25°C（77°F）］で 12 時間まで保管可能である。</td></tr>
</table>

 **ゆっくり10回**	• 希釈前に，ワクチンバイアルをゆっくり 10 回転倒混和する。 • 振とうしないこと。 • 希釈前にバイアル内の液を点検する。性状は白色～オフホワイトの懸濁液であり，不透明な粒子を含むことがある。 • 液が変色している場合や他の粒子が認められる場合は使用しないこと。

希釈	
 無菌のUSP 0.9%塩化ナトリウム注射液 1.3 mLを加える	• 無菌の USP 0.9%塩化ナトリウム注射液を入手する。希釈剤としてこれ以外は使用しないこと。 • 無菌的に 1.3 mL の希釈剤をトランスファーシリンジ（21 ゲージ，またはより細い注射針）に吸引する。 • 単回使用消毒綿でワクチンバイアルの栓を清拭する。 • 無菌の USP 0.9%塩化ナトリウム注射液 1.3 mL をワクチンバイアルに加える。
 プランジャーを1.3 mL目盛りまで引き戻し，バイアルから空気を抜く	• バイアルから針を抜く前に，空になった希釈剤シリンジに 1.3 mL の空気を吸引してバイアル圧を均一にする。

 **ゆっくり10回**	• Pfizer-BioNTech COVID-19 ワクチンのバイアルをゆっくり 10 回転倒混和する。 • 振とうしないこと。 • バイアル内のワクチンを点検する。 • ワクチンは白色からオフホワイトの懸濁液になる。ワクチンが変色している場合や粒子状物質が含まれている場合は使用しないこと。
 **希釈後12時間以内に使用する。**	• 初回の希釈日時をバイアルラベルに記録する。 • 2°C～25°C（35°F～77°F）で保管すること。 • 未使用のワクチンは希釈後 12 時間経過したら廃棄すること。

個別用量0.2 mLの準備	
 **0.2 mLのワクチンを吸引する**	• 無菌的に，単回使用消毒綿でバイアルの栓を清拭し，デッドボリュームの少ないシリンジおよび注射針を優先的に使用して，0.2 mL の Pfizer-BioNTech COVID-19 ワクチンをバイアルからシリンジに吸引する。 • 1 回の接種量は必ず 0.2 mL とすること。 • バイアルに残っている量から 0.2 mL の接種量を採取できない場合は，そのバイアルと残った内容物は廃棄すること。 • 直ちに接種すること。

接種

接種前にシリンジ内のワクチンを目視で確認する。ワクチンは白色からオフホワイトの懸濁液になる。目視での確認中，

- 最終的な接種量が 0.2 mL であることを確認する。
- 微粒子がないこと，変色がないことを確認する。
- ワクチンが変色している場合や粒子状物質が含まれている場合は接種しないこと。

Pfizer-BioNTech COVID-19 ワクチンを筋肉内接種する。

希釈後，1 バイアルに 10 回分（1 回 0.2 mL）の Pfizer-BioNTech COVID-19 ワクチン接種量が含まれる。デッドボリュームの少ないシリンジおよび注射針を使用することで，1 バイアルから 10 回分の接種量を採取することができるが，標準的なシリンジおよび注射針を使用した場合は，10 回分を採取できないことがある。シリンジおよび注射針の種類を問わず，以下の事項に留意すること。

- 1 回の接種量は必ず 0.2 mL とすること。
- バイアルに残っている量から 0.2 mL の接種量を採取できない場合は，そのバイアルと残った内容物は廃棄すること。
- 複数のバイアルから余ったワクチンを足し合わせないこと。

禁忌

Pfizer-BioNTech COVID-19 ワクチンの成分に対する重度のアレルギー反応（アナフィラキシーなど）の既往がある者には，Pfizer-BioNTech COVID-19 ワクチンを接種しないこと（詳細な EUA の処方情報を参照）。

警告

急性アレルギー反応の管理

Pfizer-BioNTech COVID-19 ワクチン接種後に急性アナフィラキシー反応が発現した場合，即時型アレルギー反応に対処するための適切な治療を直ちに実施できるようにしておかなければならない。

米国疾病管理・予防センター（CDC）のガイドライン（https://www.cdc.gov/vaccines/covid-19/）に従って，Pfizer-BioNTech COVID-19 ワクチン接種者の即時型副反応の発現を観察すること。

心筋炎および心膜炎

市販後データでは，心筋炎および心膜炎のリスク増加が認められており，特に 2 回目接種後 7 日以内に増加している。40 歳未満の男性では，女性や 40 歳以上の男性よりリスクが高く，12～17 歳までの男性で最も高いリスクが認められる。集中治療室での治療が必要な場合もあるが，短期間での追跡調査データでは，ほとんどが通常の治療により回復した。長期にわたる潜在的な後遺症に関する情報は，まだ得られていない。米国疾病管理・予防センター（CDC）から，ワクチン接種後の心筋炎と心膜炎に関する見解が公開されており，本公開情報には心筋炎および心膜炎の既往者へのワクチン接種に関する情報も含まれる。

（https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html）

失神

注射用ワクチンの接種に関連して，特に青年において失神が起こることがある。失神による傷害を避けるために予防措置を講じることが重要である。

免疫機能の変化

免疫抑制療法を受けている者を含む免疫不全者は，Pfizer-BioNTech COVID-19 ワクチンに対する免疫反応が低下している可能性がある。

有効性の限界

Pfizer-BioNTech COVID-19 ワクチンは，すべてのワクチン接種者に対して予防効果を保証するものではない。

副反応

臨床試験で報告された副反応

5～11 歳の小児での初回シリーズ接種後の副反応は，注射部位疼痛，疲労，頭痛，注射部位発赤，注射部位腫脹，筋肉痛，悪寒，発熱，関節痛，リンパ節症，悪心，倦怠感，食欲減退および発疹である（詳細な EUA の処方情報を参照）。

市販後に 12 歳以上で報告された副反応

臨床試験以外では，Pfizer-BioNTech COVID-19 ワクチン接種後にアナフィラキシーを含む重度のアレルギー反応，その他の過敏症反応（発疹，そう痒，蕁麻疹，血管浮腫など），下痢，嘔吐、四肢痛（腕），失神などが報告されている。

心筋炎および心膜炎は，臨床試験以外での Pfizer-BioNTech COVID-19 ワクチン接種後に報告されている。

Pfizer-BioNTech COVID-19 ワクチンが広く使用されるようになると，さらなる副反応が明らかになる可能性があり，その中には重篤なものもあると考えられる。

他のワクチンとの併用

Pfizer-BioNTech COVID-19 ワクチンと他のワクチンとの同時接種に関する情報は得られていない。