

FIRST PUBLICATION DATE: 18 JANUARY 2021¹

FIRST UPDATE: 10 MAY 2021

UPDATED: 21 SEPTEMBER 2021

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

EUL holder: BioNTech Manufacturing GmbH, Germany

21 SEPTEMBER 2021 UPDATE INCLUDES:

- information on approved age indication and schedule;
- insights with regard to use of COMIRNATY® in special populations (i.e. persons with comorbidities, pregnant and lactating women, HIV-positive persons, and persons in special settings);
- update of safety information;
- information on extended shelf life for frozen unopened vials, approved shelf life at different temperatures for unopened vials, and application of dynamic labelling;
- specification of alternative syringe choices in the absence of 0.3 mL RUP syringes;
- information on diluent options and packaging; and
- addition on the effects of COMIRNATY® with regard to SARS-CoV-2 variants and on currently available SARS-CoV-2 tests.

Sections that have been updated are indicated with**.



COMIRNATY®, also known as Pfizer-BioNTech COVID-19 vaccine, is a messenger RNA (mRNA) based vaccine against coronavirus disease 2019 (COVID-19). The mRNA instructs the cell to produce proteins of the S antigen (a piece of the spike protein unique to SARS-CoV-2) to stimulate an immune response. Efficacy shown in clinical trials in participants with or without evidence of prior infection with SARS-CoV-2 and who received the full series of vaccine (2 doses) was approximately 95% based on a median follow-up of two months.

Date of WHO Emergency Use Listing (EUL) recommendation: 31 December 2020

Updated EUL recommendation: 27 April 2021

Date of prequalification (PQ): not applicable

National regulatory authorities (NRAs) can use reliance approaches for in-country authorization of vaccines based on WHO PQ/EUL or emergency use authorizations by stringent regulatory authorities (SRAs).

Product characteristics

Presentation	Frozen, sterile, preservative-free, multi-dose concentrate for dilution before administration
Number of doses	One vial (0.45 mL) contains 6 doses of vaccine after dilution.

¹Contents are updated as new information becomes available.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Product characteristics contd.

Vaccine syringe type and needle size**	<p>Auto-disable (AD) syringe: 0.3 mL[†] Needle for intramuscular injection 23G × 1" (0.60 × 25 mm)</p> <p>[†]In the absence of 0.3 mL AD syringes, 1 mL or 2 mL RUP syringes with intramuscular injection needle (23G × 1", 0.60 × 25 mm) that meet the following requirements can be used:</p> <ul style="list-style-type: none"> • dead-space of syringe and needle combination: ≤0.035ml • graduation: ≤0.1 ml increments • co-packaged needle and syringe as preferred packaging configuration • needle prioritization: 1) fixed, 2) safety luer, 3) standard luer.
---	--

Schedule and administration

Recommended for age**	<p>12 years of age and older Vaccination is recommended for older persons without an upper age limit.</p>
Recommended schedule**	<p>2 doses at a recommended interval of 21–28 days: Dose 1: at the start date Dose 2: 21–28 days after first dose.</p> <p>If the second dose is inadvertently administered earlier than 21 days, the dose does not need to be repeated. If administration of the second dose is inadvertently delayed, it should be given as soon as possible thereafter, according to the manufacturer's instructions.</p> <p>For countries that have not yet achieved high vaccination coverage rates in the high-priority groups who are experiencing a high incidence of COVID-19 cases combined with vaccine supply constraints, WHO recommends that such countries should focus on achieving a high first dose coverage in the high priority groups by extending the interval between doses up to 12 weeks.</p> <p>Both doses are necessary for protection. It is currently recommended that the same product should be used for both doses.</p> <p>Heterologous ('mix and match') studies are ongoing with regard to the interchangeability of this vaccine with other COVID-19 vaccines. Preliminary results from a schedule where AstraZeneca COVID-19 vaccine was given as a first and COMIRNATY® as a second dose showed superior or similar immunogenicity results and slightly increased but acceptable reactogenicity, supporting the use of such a schedule where the second dose for the AstraZeneca COVID-19 vaccine (ChAdOx1-S [recombinant]) is not available due to supply constraints or other concerns.</p>
Route and site of administration	<p>Intramuscular (i.m.) administration The preferred site is deltoid muscle.</p>
Dosage	<p>0.3 mL (single dose after dilution)</p>
Diluent	<p>0.9% sodium chloride solution for injection, unpreserved, in a 10 mL vial for single use or in a 2 mL vial 1.8 mL diluent required per 6 dose vaccine vial</p>
Mixing syringe	<p>Reuse prevention (RUP) syringe: 3 mL (5 mL RUP syringe acceptable) Needle: 21G or narrower</p>

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Schedule and administration contd.**Reconstitution/
dilution required******Thaw each vial before dilution:**

- Thaw vaccine in refrigerator for up to 3 hours at +2 to +8 °C. After removal from +2 to +8 °C, the vials should be diluted and immediately returned back to +2 to +8 °C.

Dilute before use:

1. Before dilution, invert vaccine vial gently 10 times, **do not shake**.
2. Visually inspect the diluent and draw 1.8 mL into the mixing syringe.
3. Add 1.8 mL of diluent into the vaccine vial; level/equalize the pressure in the vial before removing the needle by withdrawing 1.8 mL of air into the empty diluent syringe.
4. Discard diluent syringe in safety box (do not reuse) and discard diluent vial.
5. Gently invert the vial with diluted vaccine 10 times to mix; **do not shake**.
6. Inspect to make sure that the vaccine is an off-white uniform suspension; do not use if discoloured or if containing particles.
7. Record date and time of dilution on the vaccine vial label.
8. Draw up the vaccine dose (0.3 mL) at the time of administration, pre-loading vaccine into syringes is not recommended. Use all vaccine within 6 hours after dilution.

Multi-dose vial policy

Discard any unused vaccine 6 hours after dilution, or at the end of the immunization session, whichever comes first.

Contraindications**

- Known history of anaphylaxis to any component of COMIRNATY® vaccine.
- Persons with anaphylaxis occurring after the first dose of COMIRNATY® should not receive additional doses.
- Persons with an immediate non-anaphylactic reaction to the first dose (e.g. urticaria, angioedema or respiratory symptoms) without any other symptoms (e.g. cough, wheezing, stridor) that occur within 4 hours of administration should not receive additional doses, unless recommended after review by a health specialist. If it is the only available vaccine for persons at high risk of severe COVID-19, and subject to individual risk-benefit assessment, COMIRNATY® could be provided under close medical supervision.

Precautions**

- For persons with known history of any immediate allergic reaction to any other vaccine or injectable therapy, a risk assessment should be conducted by a health professional. It remains uncertain if there is an increased risk of anaphylaxis, but these persons should be counselled about the potential risks of anaphylaxis and the risks should be weighed against the benefits of vaccination. Such persons should be observed for **30 minutes** after vaccination in health care settings where anaphylaxis can be immediately treated.
- Food, contact or seasonal allergies, including to eggs, gelatine and latex, eczema and asthma are not considered precautions or contraindications.
- Vaccination of people suffering from acute severe febrile illness (body temperature over 38.5 °C) or acute infection, including symptomatic SARS-CoV-2 infection, should be deferred until they have recovered from acute illness.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Schedule and administration contd.**Special population groups** (based on available data as of 15 June 2021)**

Post introduction vaccine effectiveness studies have shown high effectiveness and good safety profile in older people, including very old persons and vaccination is recommended without an upper age limit.

For persons with **comorbidities** that have been identified as increasing the risk of severe COVID-19 and studied in Phase 2/3 clinical trials (i.e. hypertension, diabetes, asthma, and pulmonary, liver and kidney disease, as well as stable and controlled HIV infection, hepatitis C and hepatitis B virus) vaccination is recommended.

Children 12–15 years of age with comorbidities that put them at significantly higher risk of serious COVID-19 disease, may be offered vaccination.

Data from small studies have demonstrated that COVID-19 mRNA vaccines are immunogenic in **pregnant women** and that vaccine-elicited antibodies are transported to infant cord blood and breast milk, suggesting possible neonatal as well as maternal protection. Post-introduction pharmacovigilance data thus far have not identified any acute safety problems, while reactogenicity and adverse events profile is similar to that reported in the absence of pregnancy. Clinical trial data on safety and immunogenicity in pregnancy are being collected. In the interim, WHO recommends the use of COMIRNATY® in pregnant women when the benefits of vaccination outweigh the potential risks. To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiological context, and the current limitations of the safety data in pregnant women. WHO does not recommend pregnancy testing prior to vaccination or delaying or terminating pregnancy because of vaccination.

Data are not available on the potential benefits or risks of COMIRNATY® on breastfed children. Vaccine effectiveness is expected to be similar in **lactating women** as in other adults. As this is not a live virus vaccine and the mRNA does not enter the nucleus of the cell and is degraded quickly, it is therefore biologically and clinically unlikely to pose a risk to the breastfeeding child. WHO recommends the use of COMIRNATY® in lactating women as in other adults. WHO does not recommend discontinuing breastfeeding because of vaccination.

Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in **severely immunocompromised persons**, who may have diminished immune response to vaccine. Nevertheless, if part of a recommended group for vaccination, they may be vaccinated, given that the vaccine is not live virus. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit-risk assessment.

HIV-positive persons who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination can be vaccinated. Available data for HIV-positive persons who are not well controlled on therapy are currently insufficient to allow assessment of vaccine efficacy and safety in this group. Information and, where possible counselling should be provided to inform individual benefit-risk assessment. Testing for HIV infection prior to vaccine administration is not necessary.

For persons who have received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment, as a precautionary measure, vaccination should be deferred for at least 90 days to avoid interference of treatment with vaccine-induced immune response.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Schedule and administration contd.

Special population groups (based on available data as of 15 June 2021)**

Persons in special settings such as refugee and detention camps, prisons, slums and other settings with high population densities where physical distancing is not implementable, should be prioritized for vaccination, taking into account national epidemiological data, vaccine supply and other relevant considerations.

Stability and storage

Vaccine storage temperature

Ultra-low temperatures:

- at -80 to -60 °C in freezer, or
- at -90 to -60 °C in thermal shipper as temporary storage for up to 30 days from delivery (should be re-iced every 5 days if opened up to 2 times a day, less than 3 minutes at a time)

Diluent storage temperature

Store supply at room temperature (not exceeding 25 °C); during session store at +2 to +8 °C. Do not freeze.

Shelf life at different temperatures**

Undiluted vaccine at storage temperature of -90 to -60 °C: until expiry date (9 months after the time of manufacturing)

Undiluted vaccine at alternative temperature of -25 to -15 °C for storage and/or transportation, before thawing for use: single period of up to 2 weeks within 9-month shelf life

- The expiry date must be manually updated when the vaccine is removed from -90 to -60 °C and before it is stored at -25 to -15 °C ('dynamic labelling').
- If a 2-week period is within the original expiry date printed on the traybox, cross out the original expiry date on the traybox to mark as not valid. Write down the new expiry date which would be 2 weeks from the date you removed the vaccine from the -90 to -60 °C.
- If a 2-week period is longer than the original expiry date printed on the traybox, respect the original expiry date.
- The transfer from ultra-low temperature to alternative storage temperature and dynamic labelling should be done within 5 minutes for closed-lid vial trayboxes and within 3 minutes for a number of vials or open-lid vial trayboxes in the ambient temperatures of up to 25 °C.

Undiluted thawed vaccine at +2 to +8 °C for storage and/or transportation: up to 31 days prior to dilution

- Upon moving the vaccine from freezer, before it is stored at +2 to +8 °C, the expiry date on the vial label must be updated ('dynamic labelling').
- If a 31-day period is within the expiry date on the traybox and/or vaccine label, cross out the original expiry date to mark as not valid. Write down the new expiry date which would be 31 days from the date you removed the vaccine from the freezer to thaw.
- If a 31-day period is longer than the expiry date on the tray and/or vaccine label, respect the original expiry date.
- The transfer from freezing temperatures of -25 to -15 °C to +2 to +8 °C and dynamic labelling should be done within 3 minutes when closed-lid vial trayboxes are transferred and within 1 minute when open-lid vial trayboxes or a number of vials are transferred in the ambient temperatures of up to 25 °C.
- To avoid excess transportation stress, do not transport the thawed vaccine longer than 12 hours.

Diluted vaccine at +2 to +8 °C: 6 hours after dilution

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Stability and storage contd.

Freeze sensitivity	Do not refreeze thawed vials. Do not freeze diluted vaccine.
Light sensitivity	Minimize exposure to room light. Avoid exposure to direct sunlight and ultraviolet light.
Conditions before use**	At +2 to +8 °C before dilution and use.
Wastage rates	Will be dependent on country context.
Buffer stock needed	Will be dependent on country context.

Labelling and packaging*

For AMC92 countries, UNICEF will supply vaccines and diluents (10 mL vials for single use).	
Vaccine Vial Monitor (VVM) (if yes, location and type)	Initial pandemic supply will not include a VVM.
Information on vial label**	Batch number, expiry date
Information on secondary packaging**	Batch number, expiry date, QR code
Information on tertiary packaging**	Batch number, expiry date, QR code
Secondary packaging dimension and volume**	<p>Vaccine: Trayboxes holding 195 vials/1170 doses, 229 x 229 x 40 mm Volume per dose: = 1.8 cm³/dose</p> <p>Diluent: • 10 mL vials for single use: cartons containing 50 vials, 8.8 x 18.7 x 10.5 cm; volume: 34.6 cm³/vial • 2 mL vials: cartons containing 25 vials, 8.7 x 8.6 x 4.2; volume 12.6 cm³/vial</p>
Tertiary packaging dimension**	<p>Vaccine: Insulated box containing 5 secondary cartons with a total of 975 vials (5850 doses) External dimensions 400 x 400 x 560 mm</p> <p>Diluent: • 10 mL vials for single use: boxes containing 12 secondary cartons (600 ampoules), external dimensions 19.5 x 43.5 x 27 cm. • 2 mL vials: boxes containing 40 secondary cartons (1000 ampoules), external dimensions 45.7 x 17.78 x 19.78 cm.</p>

*Labelling and packaging may be subject to change, depending on supply source.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Safety information****Possible events***
(by frequency)**Very common (≥1/10):**Headache, arthralgia, myalgia, injection site pain, fatigue, chills, pyrexia (higher frequency after 2nd dose), injection site swelling**Common (≥1/100 to <1/10):**

Nausea, injection site redness

Uncommon (≥1/1000 to <1/100):

Lymphadenopathy, insomnia, pain in extremity, malaise, injection site itching

Rare (≥1/10 000 to < 1/1000):

Bell's palsy (acute peripheral facial paralysis)

Not known (cannot be estimated from available data):Anaphylaxis[†], hypersensitivity

[†]A small number of anaphylactic reactions have been reported (outside of clinical trials) in persons without a history of anaphylaxis. Until more data are available, **WHO recommends that all persons should be observed for at least 15 minutes after vaccination and that COMIRNATY® is administered only in settings where anaphylaxis can be treated.**

A possible causal association with very rare cases of myocarditis in young men (16–24 years) observed outside of clinical trials, is currently being investigated.

Co-administration of vaccines/medicines

There should be a minimum interval of 14 days between administration of this and any other vaccine against other diseases, until data on co-administration become available.

*From clinical studies

Important reminders**Vaccination session and vaccine administration:**

Before, during, and after vaccination, all people should continue to follow current guidance for protection from COVID-19 in their area (e.g. wearing a mask, keeping physical distance, hand hygiene).

A person with acute PCR-confirmed COVID-19, including occurrence in-between doses, should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met. The optimal minimum interval between a natural infection and vaccination is not yet known.

Vaccination may be offered to people who have recovered from symptomatic or asymptomatic SARS-CoV-2 infection. Testing is not recommended for the purpose of decision-making about vaccination. Based on current data, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may choose to delay vaccination until near the end of this period, as available data show that within this period, symptomatic reinfection is uncommon. However, emerging data indicate that symptomatic reinfection may occur in settings where variants of concern with evidence of markedly reduced vaccine effectiveness are circulating. In these settings, earlier vaccination after infection (e.g. within 90 days) is advisable.

This vaccine should only be administered in settings where appropriate medical treatment to manage anaphylaxis is immediately available, hence, in settings with the necessary resources and trained health workers, and in setting that allow for at least 15 minutes of post-vaccination observation. For more information on AEFI kits and treatment, please refer to the training materials – COVID-19 vaccination training for health workers, Module 4: AEFI monitoring at <https://openwho.org/courses/covid-19-vaccination-healthworkers-en>.

Before vaccination, advise vaccine recipient about possible post-vaccination symptoms and observe post-vaccination for at least **15 minutes**.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

Persons with history of allergic reactions should be observed **30 minutes** post vaccination.

To alleviate post-vaccination symptoms, antipyretic or analgesics may be used. When scheduling vaccination for occupational groups (e.g. health workers), consideration should be given to the reactogenicity profile of this vaccine observed in clinical trials, leading to time off work in the 24–48 hours following vaccination.

Encourage a vaccine recipient to complete the vaccination series to optimize protection and schedule the time for the second dose. The same vaccine product should be used for both doses.

There is currently no evidence on the need for a booster dose(s) after two-dose vaccine series is complete. The need and timing of booster doses will be evaluated as further data accumulate.

Special storage and handling precaution:**

Transfers of frozen vaccine vials at ultra-low temperatures:

Closed-lid vial trayboxes removed from frozen storage (<-60 °C) may be at room temperature (< 25 °C) for a maximum of **5 minutes when transferring from one ultra-low temperature environment to another**. After vial trayboxes are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.

Open-lid vial trayboxes, or trayboxes with less than 195 vials removed from frozen storage (< -60 °C) may be at room temperature (< 25 °C) for a maximum of **3 minutes when removing a number of vials needed for the vaccination session or when transferring from one ultra-low temperature environment to another**. Once a vial is removed from the vial traybox, it should be thawed for use. After vial trayboxes are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.

Transfers of frozen vaccine vials at freezing storage:

Closed-lid vial trayboxes removed from frozen storage (-20 °C) may be at room temperature (< 25 °C) for a maximum of 3 minutes when transferring from one freezing temperature environment to another.

Open-lid vial trayboxes, or trayboxes with less than 195 vials removed from frozen storage (-20 °C) may be at room temperature (< 25 °C) for a maximum of **1 minute when removing a number of vials needed for the vaccination session or when transferring from one freezing temperature environment to another**.

SARS-CoV-2 variants**

As SARS-CoV-2 viruses undergo evolution, new variants may be associated with higher transmissibility, disease severity, risk of reinfection, or a change in antigenic composition, resulting in lower vaccine effectiveness. Preliminary data show some reduction in neutralization activity of COMIRNATY® against the Beta (B.1.351) variant, as well as against Gamma (P.1) and Delta (B.1.617.2), and less marked reduction against Alpha (B.1.1.7). Vaccine effectiveness after 2 doses against symptomatic SARS-CoV-2 infection with the Beta (B.1.351) variant has been estimated as 75.0%, 88% against symptomatic disease from the Delta (B.1.617.2) variant, and 93% against the Alpha (B.1.1.7) variant. Emerging vaccine effectiveness evidence however shows a maintained protection against severe disease outcomes and death against the variants of concern. These preliminary findings highlight the urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness. WHO will continue to monitor the situation; as new data become available, recommendations will be updated accordingly.

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified) – Pfizer-BioNTech COVID-19 vaccine

SARS-CoV-2 tests**

Currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein and as the vaccine contains mRNA that encodes the spike protein, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate evidence of prior infection in an individual who has received COMIRNATY®, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. Antibody testing is not currently recommended to assess immunity to COVID-19 following COMIRNATY®. Prior receipt of the vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection.

Resources and more information at**:

<https://extranet.who.int/pqweb/vaccines/who-recommendation-covid-19-mrna-vaccine-nucleoside-modified-comirnaty>

<https://extranet.who.int/pqweb/sites/default/files/documents/Comirnaty-Pfizer-BioNTech-COVID-19-vaccine-injectionPlt.pdf>

https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1

https://www.who.int/docs/default-source/coronaviruse/act-accelerator/covax/pfizer-specific-training_full-deck_19aug.pdf?sfvrsn=22d66119_5