COVID-19 Vaccine Explainer

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

WHO EUL holder: BioNTech Manufacturing GmbH, Germany

03 JUNE 2022 UPDATE INCLUDES NEW INFORMATION ON:

- recommended age indication and schedule (primary and primary extended vaccination series, booster doses, and heterologous schedule);
- insights with regard to use of COMIRNATY® in special populations (i.e. moderately and severely immunocompromised persons, pregnant and lactating women);
- safety information;
- ready-to-use/fully liquid formulation; and
- vaccine performance reflecting circulation of variants of concern.

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.

In clinical trials, high vaccine efficacy of generally 90 to 100% was observed against symptomatic SARS-CoV-2 infection with the ancestral strain in persons 16 years and older. Post-introduction effectiveness studies showed very high protection against hospitalization and death and moderate vaccine impact against transmission. However, with the emergence of variants of concern since the ancestral strain, lower vaccine effectiveness (VE) has been observed, in particular for mild breakthrough infections and impact on transmission. Booster doses restore vaccine effectiveness against Delta and Omicron variants, though waning of VE is observed for Omicron even after the booster dose.

Date of WHO Emergency Use Listing (EUL) recommendation: **31 December 2020**
Updated EUL recommendation: **17 December 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	**Multi-dose vials with purple cap** 'PBS/Sucrose': Frozen, sterile, preservative-free, multi-dose concentrate for dilution before administration	**Multi-dose vials with grey cap** 'Tris/Sucrose' formulation: Frozen, sterile, preservative-free, multi-dose solution, ready-to-use/fully liquid (no dilution required)
Number of doses	One vial (0.45 mL) contains 6 doses of vaccine after dilution	One vial (2.25 mL) contains 6 doses of vaccine

[1]Contents are updated as new information becomes available.

Product characteristics contd.

Vaccine syringe type and needle size	Auto-disable (AD) syringe: 0.3 mL[†] for both PBS/Sucrose (purple cap) and Tris/Sucrose (grey cap) formulation (12 years and older) Needle for intramuscular injection 23G x 1" (0.60 × 25 mm) [†]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: • dead-space of syringe and needle combination: lowest possible (e.g. equivalent to ISO7886-3) • graduation: 0.05–0.1 ml • co-packaged needle and syringe as preferred packaging configuration • needle type: fixed

Schedule and administration

Recommended for age	12 years of age and older, without an upper age limit WHO SAGE recommends prioritization of different population groups according to the WHO Prioritization Roadmap.	
Recommended schedule – primary vaccination series	2 doses at a recommended interval of 21–28 days: Dose 1: at the start date Dose 2: 21–28 days after first dose. If the second dose is inadvertently administered earlier than 21 days, the dose does not need to be repeated. WHO SAGE recommends that the second dose should be provided 4 to 8 weeks after the first dose, preferentially 8 weeks as a longer interval between doses is associated with higher vaccine effectiveness and potentially lower risk of myocarditis/pericarditis.	
Recommended schedule – booster doses	At least six months after completion of primary vaccination series in individuals 18 years of age and older, in accordance with the WHO Prioritization Roadmap. Using the same product to complete primary and booster schedule is considered standard practice. However, WHO supports programmatic flexibility and supports use of vectored vaccines and recombinant protein subunit vaccine to complete primary series and/or booster vaccination (**'heterologous schedule'**).	
Route and site of administration	Intramuscular (i.m.) administration The preferred site is deltoid muscle.	
Dosage	0.3 mL/dose	
Diluent	**For multi-dose vials with purple cap** 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	**For multi-dose vials with grey cap** Not applicable since already diluted
Mixing syringe	Reuse prevention (RUP) syringe: 3 mL (5 mL RUP syringe acceptable) Needle: 21G or narrower	Not applicable

Schedule and administration contd.

	Multi-dose vials with purple cap (requires use of diluent)	Multi-dose vials with grey cap (ready-to-use/fully liquid)
Preparation/ reconstitution/ dilution requirement	**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 the diluted vaccine immediately returned to +2 to +8 °C. **Dilute before use.** **Preparation:** 1. Verify that the vaccine vial has a purple plastic cap. 2. Before dilution, invert vaccine vial gently 10 times, **do not shake**. 3. Visually inspect the diluent and draw 1.8 mL into the mixing syringe. 4. 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. 5. Discard diluent syringe in safety box (do not reuse) and discard diluent vial. 6. Gently invert the vial with diluted vaccine 10 times to mix; **do not shake**. 7. Inspect to make sure that the vaccine is an off-white uniform suspension; if discoloured or if containing visible particulate matter, do not use and discard the vial. 8. Record date and time of dilution on the vaccine vial label. 9. 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. If any liquid remains in the vial after withdrawing the final dose, discard the vial and do not combine residual vaccine from multiple vials.	**Thaw each vial before opening:** Thaw vaccine in refrigerator at +2 to +8 °C; a carton of 10 vials may take up to 6 hours to thaw. During vaccination session, keep the vials between +2 to +8 °C and protected from light. **No dilution is required, DO NOT DILUTE!** **Preparation:** 1. Verify that the vaccine vial has a grey plastic cap. 2. Before opening, invert vaccine vial gently 10 times, **do not shake**. The thawed vaccine may contain white to off-white opaque particles. 3. Visually inspect the contents of the vial after inverting to ensure that the liquid is white to off-white uniform suspension and that no visible particulate matter or other coloration is present in the vial. If visible particles or discoloration are present, do not use and discard the vial. 4. Record the date and time of the first use (first puncture and withdrawal of the first dose) on the vial label. 5. Draw up the vaccine dose (0.3 mL) from the vial at the time of administration, preloading of syringes is not recommended. 6. Before withdrawing each following vaccine dose, invert the vial gently, do not shake. 7. Preferably, use the vaccine from the vial immediately after first puncture or within 6 hours afterwards. Discard if vaccine is not used within this time or at the end of the vaccination session, whichever comes first. If any liquid remains in the vial after withdrawing the final dose, discard the vial and do not combine residual vaccine from multiple vials.
Multi-dose vial policy	Discard any unused vaccine 6 hours after dilution, or at the end of the immunization session, whichever comes first.	

Schedule and administration contd.

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. • Anxiety related reactions in association with the vaccination process may occur; precautions should be in place to avoid injury from fainting.
Special population groups (based on available data as of 19 January 2022)	• 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 (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 5-17 years of age with comorbidities that put them at significantly higher risk of serious COVID-19 disease, should 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. The obstetric outcomes including spontaneous abortion and neonatal outcomes are similar to reported background rates. WHO recommends the use of COMIRNATY® in pregnant women. Pregnant women should be informed that they can receive the vaccine and be provided with information about the increased risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiological context, and the current limitations of safety data. 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.

Schedule and administration contd.

Special population groups (contd.)	• Based on the emerging evidence and higher risk of severe COVID-19 for **moderately and severely immunocompromised persons (ICP)** (i.e. transplant recipients, persons with active cancer, immunodeficiency, on active treatment with immunosupressives and persons living with HIV with CD4 count of <200 cells/µL) if infected and regardless of age, WHO recommends an extended primary series including an additional dose (dose 3) to be given 1 to 3 months after the dose 2 of the primary series. If more than 3 months have elapsed since dose 2 in the primary vaccination series, the additional dose should be given at the earliest opportunity. Information and, where possible, counselling about the limitations around the data on administration of an additional dose to ICP should be provided to inform individual benefit-risk assessment. Given the emergence of Omicron, a booster may be considered, to be administered 4 to 6 months after dose 3. • **HIV-positive persons** who are well controlled on highly active antiretroviral therapy should be vaccinated. Information and, where possible counselling about vaccine safety and efficacy in ICP 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. • 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	For vials with purple and with grey cap Ultra-low temperatures: • at -90 to -60 °C in ULT freezer or 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	**For multi-dose vials with purple cap (requires diluent)** **Unopened/undiluted vaccine at ultra-low storage temperature (ULT)** -90 to -60 °C: until expiry date (12 months after the time of manufacturing) **Unopened/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 12-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').	**For multi-dose vials with grey cap (ready-to-use/fully liquid)** **Unopened vaccine vials at storage temperature** -90 to -60 °C: until expiry date (12 months after the time of manufacturing) **Do not store in freezer at -25 to -15 °C!**

Stability and storage contd.

Shelf life at different temperatures (contd.)	• If a 2-week period is longer than the original expiry date printed on the traybox, respect the original expiry date. • The transfer from ULT 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.	
	Unopened/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 a maximum temperature of 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.	**Unopened thawed** vaccine in the refrigerator at +2 to +8 °C for storage and/or transportation: up to 10 weeks after removal from the ULT. • Upon moving the vaccine from the ULT, before it is stored at +2 to +8 °C, the expiry date on the traybox/carton must be updated ('dynamic labelling'). • If a 10-week period is within the expiry date on the traybox/carton, cross out the original expiry date to mark as not valid. Write down the new expiry date which would be 10 weeks from the date you removed the vaccine from the ULT to thaw. • If a 10-week period is longer than the expiry date on the tray and/or vaccine label, respect the original expiry date. If the vaccine is received thawed at +2 to +8 °C, check that the expiry date has been updated on the traybox/carton to reflect the 10-week period.
Shelf life extensions	Shelf-life extensions from 9 months to the current 12 months have been granted to this vaccine by the national regulatory authority of the manufacturing country. This may exceptionally result in shelf-life extensions being granted retro-actively to previously produced and packaged vials. Please note that per regulatory principles WHO does not recommend use of vaccines beyond their labelled expiry date.	
Freeze sensitivity	Do not refreeze thawed vials, discard if re-frozen. Do not freeze diluted/opened vaccine, discard if re-frozen.	

Stability and storage contd.

Light sensitivity	Minimize exposure to room light. Avoid exposure to direct sunlight and ultraviolet light.	
Conditions before use	**For multi-dose vials with purple cap (requires dilution)** At +2 to +8 °C before dilution and use	**For multi-dose vials with grey cap (ready-to use/fully liquid)** At +2 to +8 °C before opening 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.

Vaccine Vial Monitor (VVM)	Not included	
Information on vial label	Name and type of vaccine, method of administration, dosage, batch number, expiry date, colour coding (purple or grey label border)	
Information on secondary packaging	Name of vaccine, pharmaceutical form, method of administration, dosage, batch number, expiry date, QR code	
Information on tertiary packaging	Type of vaccine, name of manufacturer, quantity, batch number, expiry date, QR code	
Secondary packaging dimension and volume per dose	**Multi-dose vials with purple cap** • Trayboxes holding 195 vials/ 1170 doses, 229 × 229 × 40 mm Volume per dose: 1.8 cm^3 **Diluent:** • 10 mL vials for single use: cartons containing 50 vials, 8.8×18.7×10.5 cm; volume per vial: 34.6 cm^3 • 2 mL vials: cartons containing 25 vials, 8.7 × 8.6 × 4.2 cm Volume per vial: 12.6 cm^3	**Multi-dose vials with grey cap** • Trayboxes holding 195 vials/ 1170 doses, 231 × 231×x 42 mm Volume per dose: 1.9 cm^3 • Cartons holding 10 vials/60 doses, 89 × 37 × 47 mm Volume per dose: 2.6 cm^3
Tertiary packaging dimension	• Insulated box containing 5 secondary cartons with a total of 975 vials (5850 doses); external dimensions 400 × 400 × 560 mm **Diluent:** • 10 mL vials for single use: boxes containing 12 secondary cartons (600 ampoules), external dimensions 19.5 × 43.5 × 27 cm • 2 mL vials: boxes containing 40 secondary cartons (1 000 ampoules), external dimensions 45.7 × 17.78 × 19.78 cm	• Insulated box containing 5 secondary cartons with a total of 975 vials (5850 doses); external dimensions 400 × 400 × 560 mm • Insulated box containing 60 secondary cartons with a total of 600 vials (3600 doses); external dimensions 400 × 400 × 560 mm

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

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 (≥1/1 000 to <1/100):** Lymphadenopathy, insomnia, pain in extremity, malaise, injection site itching **Rare (≥1/10 000 to < 1/1 000):** Bell's palsy (acute peripheral facial paralysis) **Very rare (<1/10 000):** Myocarditis/pericarditis[†] **Not known (cannot be estimated from available data):** Anaphylaxis[‡], hypersensitivity [†]Very rare cases of myocarditis and pericarditis have been reported after mRNA COVID-19 vaccines, with the observed risk highest in males aged 12–29 years, higher after the second dose, and of mild clinical course. [‡]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.
Co-administration of vaccines/medicines	Limited safety and immunogenicity data suggest that co-administration of the second dose of COMIRNATY® with inactivated influenza vaccines is acceptable. When administering both vaccines during the same visit, use different arm for each vaccine injection. 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, but an interval of 3 to 6 months could be considered.

Vaccination should be offered regardless of a person's history of 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 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**. 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 primary vaccination series and receive a booster dose.

Special storage and handling precaution (relevant for both presentations):

Transfer 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.

Transfer 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 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 for 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. A positive nucleocapsid protein-based assay indicates prior infection. Antibody testing is not currently recommended to assess immunity to COVID-19 following COMIRNATY®.

Resources and more information at:

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

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