COVID-19 Vaccine Explainer

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World Health Organization

COMIRNATY® (Tozinameran), COVID-19 mRNA vaccine (nucleoside modified, 10 micrograms/dose) – **paediatric** Pfizer-BioNTech COVID-19 vaccine

WHO EUL holder: **BioNTech Manufacturing GmbH, Germany**

COMIRNATY® (10 micrograms/dose), also known as paediatric Pfizer-BioNTech COVID-19 vaccine, is a messenger RNA (mRNA) based vaccine against coronavirus disease 2019 (COVID-19) for children from 5 years to 11 years of age. 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. As COMIRNATY® does not contain the virus to produce immunity the vaccine cannot give the child COVID-19.

Date of WHO Emergency Use Listing (EUL) recommendation: 31 December 2020 (adult formulation)
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 orange cap** Frozen, sterile, preservative-free, multi-dose concentrate for dilution before administration
Number of doses	One vial (1.30 mL) contains 10 paediatric doses of vaccine after dilution
Vaccine syringe type and needle size	Auto-disable (AD) syringe: 0.2 mL[†] Needle for intramuscular injection 23G × 1” (0.60 × 25 mm) [†]In the absence of 0.2 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

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

Schedule and administration

Recommended for age	5 years to 11 years of age 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. **Extended primary vaccination series:** A third dose may be given at least 28 days after the second dose to severely immunocompromised children aged 5 years and older. Using the same product to complete primary schedule is considered standard practice. The interchangeability of COMIRNATY® (10 micrograms/dose) with other COVID-19 vaccines has not been established. The same vaccine product, i.e. COMIRNATY® (10 micrograms/dose) should be used to complete the vaccination course in children.
Route and site of administration	Intramuscular (i.m.) administration The preferred site is deltoid muscle
Dosage	0.2 mL/dose
Diluent	0.9% sodium chloride solution for injection, unpreserved, in a 10 mL vial for single use or in a 2 mL vial 1.3 mL diluent required per 10 dose vaccine vial
Mixing syringe	Reuse prevention (RUP) syringe: 3 mL (5 mL RUP syringe acceptable) Needle: 21G or narrower
Preparation/ reconstitution/ dilution requirement	**Thaw each vial before dilution:** • Thaw vaccine in refrigerator at +2 to +8 °C; a carton of 10 vials may take up to 4 hours to thaw. After removal from +2 to +8 °C, the vials should be diluted and immediately returned back to +2 to +8 °C. **Dilute before use.** **Preparation:** 1. Verify that the vaccine vial has an orange plastic cap. 2. Before dilution, invert vaccine vial gently 10 times, **do not shake**. 3. Visually inspect the diluent and draw 1.3 mL into the mixing syringe. 4. Add 1.3 mL of diluent into the vaccine vial; level/equalize the pressure in the vial before removing the needle by withdrawing 1.3 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 (0.2 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.

Schedule and administration contd.

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 children 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/guardians should be counselled about the potential risk of anaphylaxis and the risk 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.

Stability and storage

Vaccine storage temperature	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	**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!** **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 the vaccine was removed 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. Diluted vaccine at +2 to +8 °C: 6 hours after dilution.

Stability and storage contd.

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. Do not freeze diluted/opened 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.

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 (orange 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	• Trayboxes holding 195 vials/1950 doses, 231 × 231 × 42 mm Volume per dose: 1.2 cm^3 • Cartons holding 10 vials/100 doses, 89 × 37 × 47 mm Volume per dose: 1.6 cm^3
Tertiary packaging dimension	**Vaccine:** • Insulated box containing 5 secondary cartons with a total of 975 vials (9750 doses); external dimensions 400 × 400 × 560 mm • Insulated box containing 60 secondary cartons with a total of 600 vials (6000 doses); external dimensions 400 × 400 × 560 mm **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; volume per vial: 12.6 cm^3

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

Safety information

Possible events* (by frequency)	The overall safety profile of COMIRNATY® in clinical trials in individuals 5 years to 15 years of age was similar to events seen in individuals 16 years of age and older. **Very common (≥1/10):** Injection site pain, swelling and redness, headache, arthralgia, myalgia, fatigue, chills, pyrexia (higher frequency after 2nd dose), diarrhoea **Common (≥1/100 to <1/10):** Nausea, vomiting **Uncommon (≥1/1 000 to <1/100):** Lymphadenopathy, insomnia, pain in extremity, malaise, injection site itching, decreased appetite, excessive sweating, night sweats, feeling weak or lack of energy/sleepy **Rare (≥1/10 000 to < 1/1 000):** Bell's palsy (acute peripheral facial paralysis) **Very rare (<1/10 000):** Myocarditis/pericarditis[†] (resulting in breathlessness, palpitations, or chest pain) **Not known (cannot be estimated from available data):** Anaphylaxis[‡], hypersensitivity, erythema multiforme, paraesthesia, hypoaesthesia [†]Very rare cases of myocarditis and pericarditis have been reported after mRNA COVID-19 vaccines. These conditions can develop within just a few days of vaccination and have primarily occurred within 14 days, and more often in younger males. Available data suggest that the clinical course is not different from myocarditis or pericarditis in general. [‡]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	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 settings 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.

Special storage and handling precaution:

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.

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