COVID-19 Vaccine Explainer

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COVID-19 Vaccine Moderna (nucleoside modified), (mRNA-1273)

EUL holder: Moderna Biotech

24 AUGUST 2021 UPDATE INCLUDES:

- information on WHO EUL listing;
- information on thawing vaccine before use and shelf life at different temperatures for thawed unopened and punctured vaccine vials;
- information on labelling and packaging;
- information on precautions to vaccination;
- insights with regard to use of COVID-19 Vaccine Moderna in special populations (i.e. pregnant and lactating women, HIV-positive persons, and persons in special settings);
- addition on the effect of COVID-19 Vaccine Moderna with regard to SARS-CoV-2 variants and on currently available SARS-CoV-2 tests.

Sections that have been updated are indicated with **.

The COVID-19 Vaccine Moderna is a messenger RNA (mRNA) based vaccine against coronavirus disease 2019 (COVID-19). The host cells receive the instruction from the mRNA to produce protein of the S-antigen unique to SARS-CoV-2, allowing the body to generate an immune response and to retain that information in memory immune cells. Efficacy shown in clinical trials in participants who received the full series of vaccine (2 doses) and had negative baseline SARS-CoV-2 status, was approximately 94% based on a median follow-up of two months. The data reviewed at this time support the conclusion that the known and potential benefits of Covid-19 Vaccine Moderna outweigh the known and potential risks.

Date of WHO Emergency Use Listing (EUL) recommendation: 30 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 suspension
Number of doses	One vial contains 10 doses of vaccine after thawing
Vaccine syringe type and needle size	Auto-disable (AD) syringe: 0.5 mL Needle for intramuscular injection 23G × 1” (0.60 × 25 mm)

[1]Contents will be updated as new information becomes available.

Schedule and administration

Recommended for age	18 years of age and above Based on the data reviewed, WHO SAGE recommends use in older persons without an upper age limit.
Recommended schedule**	2 doses (100 µg, 0.5 mL each) at a recommended interval of 28 days: Dose 1: at the start date Dose 2: 28 days after first dose. If the second dose is inadvertently administered earlier than 28 days after the first, the dose does not need to be repeated. If the second dose is inadvertently delayed, it should be given as soon as possible thereafter, at the earliest possible opportunity. If a delay is judged necessary, WHO currently recommends that the interval between doses may be extended up to 42 days. Both doses are necessary for protection. According to current recommendation, the same product should be used for both doses. 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 mRNA COVID-19 vaccine 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.
Route and site of administration	Intramuscular (i.m.) administration The preferred site is deltoid muscle.
Dosage	0.5 mL (single dose)
Diluent	None needed
Mixing syringe	None needed
Preparation/ reconstitution/ dilution requirement**	**No dilution is required.** **Thaw each vial before use:** • Thaw vaccine in refrigerator at +2 to +8 °C for 2 hours and 30 minutes. **Vaccine administration:** 1. Once thawed, vaccine is ready to use, do not dilute. 2. Swirl the vial gently, do not shake. 3. Inspect the vial to make sure that the liquid is white to off-white in colour. The vaccine may contain white or translucent product-related particles. Do not use if any other particles or discoloration are present, discard the vial. 4. Record date and time of the first use (first puncture and withdrawal of the dose) on the vial label. 5. Before each vaccine withdrawal, swirl the vial gently again and do not shake. 6. Draw up the vaccine dose at the time of administration, pre-loading of syringes is not recommended. 7. Use all vaccine within 6 hours after first puncture. Discard vial when there is not enough vaccine to obtain a complete dose of 0.5 mL. Do not combine residual vaccine from multiple vials. Discard any remaining vaccine in the vial after 10 doses have been withdrawn.
Multi-dose vial policy**	After the first dose has been withdrawn, keep between 2 °C and 8 °C and discard any unused vaccine after 6 hours, or at the end of the immunization session, whichever comes first.

Schedule and administration contd.

Contraindications	• Known history of anaphylaxis to any component of the vaccine. In particular, COVID-19 Vaccine Moderna should not be administered to individuals with a known history of anaphylaxis to polyethylene glycol (PEG). • Persons who developed anaphylaxis after the first dose should not receive a second dose of COVID-19 Vaccine Moderna.
Precautions**	• For persons with known history of anaphylaxis to any other vaccine or injectable therapy, a risk assessment should be conducted by the relevant specialist. Such persons may still receive vaccination but they should be counselled about the potential risks of anaphylaxis; risks should be weighed against benefits of vaccination. • Persons with an immediate non-anaphylactic allergic reaction to the first dose that occur within 4 hours of administration (i.e. any signs and symptoms such as urticaria, angioedema or respiratory symptoms without cough, wheezing or stridor), should not receive additional doses, unless recommended after review by a specialist with relevant expertise. However, subject to individual risk-benefit assessment, COVID-19 Vaccine Moderna could be provided under close medical supervision if it is the only available option for persons at high risk of severe COVID-19. • Food, contact or seasonal allergies, including to eggs, gelatin and latex, and allergic rhinitis, eczema and asthma are not considered precautions or contraindications to vaccination. • Vaccination of people suffering from acute severe febrile illness (body temperature over 38.5 °C) should be postponed until they are afebrile. • Vaccination of persons with acute COVID-19 should be postponed until they have recovered from acute illness and criteria for discontinuation of isolation have been met.
Special population groups (based on available data as of June 2021)**	For persons with **comorbidities** such as chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease and human immunodeficiency virus (HIV) infection, that have been identified as increasing the risk of severe COVID-19, vaccination is recommended. Clinical trial data on safety and immunogenicity in **pregnancy** are not currently available. To date, post-introduction vaccine pharmacovigilance data have not identified any acute safety problems, and reactogenicity and adverse event profile is similar to that reported in the absence of pregnancy. 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 and breast milk, suggesting possible neonatal as well as maternal protection. Until more data are available, pregnant women should receive the COVID-19 Vaccine Moderna when the benefits of vaccination to the pregnant woman 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. COVID-19 Vaccine Moderna effectiveness in **lactating women** is expected to be similar as in other adults. Data are not available on the potential benefits or risks of the COVID-19 Vaccine Moderna to breastfed children. 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 children. WHO recommends the use of COVID-19 Vaccine Moderna in lactating women as in other adults. WHO does not recommend discontinuing breastfeeding because of vaccination.

Schedule and administration contd.

Special population groups (based on available data as of June 2021)** contd.	Available data are currently insufficient to access 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. 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	Store in the original carton in a freezer at -25 to -15 °C. **Do not store on dry ice or below -40 °C.**
Shelf life at different temperatures**	**Frozen unopened** vaccine vial in freezer at -25 and -15 °C: from receipt until expiration date **Thawed unopened** vaccine vial in refrigerator at +2 to +8 °C: up to 30 days, protected from light **Thawed punctured vial** at +2 to +8 °C: 6 hours after the first dose has been withdrawn. Do not refreeze after thawing.
Freeze sensitivity	**Never** refreeze thawed vials. Do not store in insulated passive container with dry ice or ultra-low temperature phase-change material (PCM), or in freezer below -40 °C.
Light sensitivity	Store in the original carton to protect from light. Avoid exposure to direct sunlight and ultraviolet light.
Conditions before use**	After thawing, visual inspection, and gentle swirling of the vial, vaccine is ready for use.
Wastage rates	Will be dependent on country context.
Buffer stock needed	Will be dependent on country context.

Labelling and packaging **

Vaccine Vial Monitor (VVM) (if yes, location and type)	Initial pandemic supply will not include a VVM.
Information on vial label	Lot number, expiry date, QR code*
Information on secondary packaging	Lot number, expiry date QR code*
Information on tertiary packaging	Lot number, expiry date QR code*
Secondary packaging dimension and volume	Carton box holding 10 vials/100 doses: 12.7 × 5.5 × 6.1 cm Volume per dose: 4.3 cm^3/dose
Tertiary packaging dimension	Carton containing 12 secondary carton boxes with a total of 120 vials (1200 doses) External dimensions 27.6 × 18.5 × 15.1 cm† †Tertiary packaging and pallet configuration may vary according to the mode of transport.

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

Safety information*

Possible events (by frequency)**	• Observed events frequent, mostly mild to moderate and short lived • Less frequent and severe in older (≥65 years) than in younger adults (18–64 years) • Generally more frequent after the second dose compared to the first across all age groups **Very common (≥1/10)** Headache, nausea, vomiting, myalgia, arthralgia and stiffness, pain and swelling at the injection site, fatigue, chills, fever, lymphadenopathy **Common (≥1/100 to <1/10):** Rash, injection site redness, urticaria and rash or swelling **Uncommon (≥1/1 000 to <1/100):** Itchiness at the injection site **Rare (≥1/10 000 to < 1/1 000):** Facial swelling, Bell's palsy (acute peripheral facial paralysis) **Not known (cannot be estimated from available data):** Anaphylaxis, hypersensitivity Outside of clinical trials, very rare cases of myocarditis and pericarditis have been observed following vaccination with the mRNA COVID-19 vaccines. These cases occurred more often in younger men and after the second dose of the vaccine, typically within few days after vaccination. A possible causal association with very rare cases of myocarditis in young men 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 presenting with COVID-19 symptoms should not be vaccinated. Vaccination may be offered to people who have recovered from symptomatic or asymptomatic COVID-19. 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, that is, settings with (i) the necessary resources and trained health workers, and (ii) 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 and other conditions listed in the warnings and/or precautions in the package insert should be observed **30 minutes** post vaccination.

To alleviate post-vaccination symptoms, antipyretic or analgesics may be taken (routine prophylaxis to prevent the symptoms is not recommended due to lack of information on impact on immune response).

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. When scheduling vaccination for occupational groups (e.g. health workers) consideration should be given to the reactogenicity profile of mRNA-1273 vaccine observed in clinical trials, occasionally 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.

When scheduling vaccination for occupational groups (e.g. health workers) consideration should be given to the reactogenicity profile of COVID-19 Vaccine Moderna observed in clinical trials, occasionally leading to time off work in the 24-48 hours following vaccination.

For countries that have not yet achieved high vaccine coverage rates in the high-priority groups in settings with high incidence of COVID-19 cases and limited vaccine supply, WHO recommends that such countries focus on achieving a high first dose coverage in the high priority groups by extending the inter-dose interval up to 12 weeks.

Important reminders contd.

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. The impact of variants of concern on vaccine effectiveness remains unknown to date, especially for the Delta variant (B.1.617.2). Preliminary data show some reduction in neutralization activity of COVID-19 Vaccine Moderna against the Beta variant (B.1.351), and less marked reduction against the other variants of concern such as Gamma (P1), Alpha (B.1.1.7) and Epsilon (B.1.429). Emerging vaccine effectiveness data however show a maintained protection against severe disease, hospitalization 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.

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 COVID-19 Vaccine Moderna, 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 COVID-19 Vaccine Moderna.

Prior receipt of the vaccine will not affect the results of SARS-CoV-2 nucleid acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection.

Resources and more information at:

https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19

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

https://www.modernatx.com/covid19vaccine-eua/providers/about-vaccine

https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax-previously-covid-19-vaccine-moderna